# The Impact of the COVID-19 Pandemic on Antimicrobial Stewardship in Acute-Care Settings and the Pharmacist Role


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## Dedication

To my dearest family, To my beloved parents, Abdelsalam Elshenawy and Lotfia Elmandooh,

Your unconditional love, support, and prayers have been my guiding light. Dad, your unwavering presence and support made my dreams attainable. I deeply regret that you couldn't witness the completion of my thesis; your interest and encouragement in my academic pursuits have been a cornerstone of my journey. Losing you during my PhD was heartbreaking. I cherish the memories of your curiosity about my studies and hope to honour your legacy through my scholarly work. May my achievements make you proud and keep your memory alive. You are always in my heart. Mom, it means the world to me that you always surround me with unconditional love, support, and prayers. They say, “Women become their mothers,” and I hope I can be like you, Mom. You have always made difficult moments easier and possible.

To my beloved husband, Waleed Marzok,

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## Abstract

**Introduction**: Antimicrobial resistance (AMR) is a major global health issue, causing 1.2 million deaths yearly and increasing by 15% during the COVID-19 pandemic. In the UK, bloodstream infection (BSIs) cases rose by 11.7% from 2018 to 2022. The overall AMR infections and priority pathogen AMR BSIs decreased by 1.6% and 4.6%, respectively. Antimicrobial stewardship (AMS) promotes judicious antibiotic use, but the COVID-19 pandemic increased AMR by 15%. Although there are paramount data on the impact of COVID-19 on AMS, empirical data on AMS implementation during the pandemic are lacking. The UK aims to reduce antimicrobial-resistant infections by 10% by 2025. As of 2021, efforts to monitor and regulate antibiotic use in secondary care settings are ongoing. Despite extensive data on COVID-19's impact on AMS, detailed information on AMS practices during the pandemic is scarce.

**Aim:** To investigate antibiotic prescribing and AMS implementation in 2019, prior to the pandemic, and in 2020, during the pandemic, at an NHS Foundation Trust in England. Additionally, the study aimed to explore healthcare professionals' perspectives on antibiotic prescribing and AMS practices during the COVID-19 pandemic.

**Methods and data analysis**: This study employed both retrospective and prospective postpositivist research methods. Study 1 involved conducting a systematic literature review to investigate the implementation of AMS in acute care settings, both Prior-to-pandemic (PP) and During-the-pandemic (DP). Study 2, a retrospective cross-sectional study, focused on assessing the prevalence of inappropriate antibiotic prescribing among hospitalised adults during the PP and DP periods. Data from this study were analysed using descriptive statistics and regression analysis in SPSS. Study 3 was a cross-sectional, prospective survey involving healthcare professionals. It aimed to understand their knowledge, attitudes, and perceptions towards antibiotic prescribing and AMS practices during the pandemic, with the findings similarly analysed using descriptive statistics and regression analysis.

**Results**: Study 1 identified AMS implementation strategies and quality improvement projects used in acute care settings before and during the COVID-19 pandemic. Study 2, conducted at Bedfordshire Hospitals NHS Foundation Trust, revealed that the prevalence of inappropriate empirical antibiotic prescribing was 50% PP and 49% DP among hospitalised adults. Significant differences were observed in the AMS interventions 'Continue Antibiotics' and 'De-escalation' during the pandemic, with odds ratios of 3.36 and 2.77, respectively, indicating notable changes in prescribing practices. Study 3 showed that healthcare professionals had good knowledge in only two areas related to AMR, recognising its impact on public health. Over 80% reported negative effects of the pandemic on AMS activities, especially in antibiotic review and education. Furthermore, (42% n=240) strongly agreed that antimicrobial misuse during COVID-19 could worsen resistance. The study also highlighted the importance of age, gender, professional background, and experience in influencing AMS-related knowledge, attitudes, and practices.

These findings underline the pandemic's profound impact on AMS and the necessity for evolved strategies in future health crises.

**Conclusion**: The COVID-19 pandemic has had a detrimental impact on AMS activities, highlighting the urgent need to enhance antibiotic prescribing practices and ensure the sustainability of AMS implementation in the UK. Continuously developing the skills of healthcare professionals through education and innovative tools, such as an AMS dynamic dashboard and an AMS card, is vital for improving patient care and combating AMR effectively. These tools will help adapt to changing antibiotic resistance patterns and enhance broad-spectrum antibiotic use. Data sharing on AMS practices and multidisciplinary communication is essential for effective AMS. Further research is necessary, as this study, confined to a secondary care setting, focused only on respiratory tract infections and did not include children.

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**Rasha Abdelsalam Elshenawy**, Nkiruka Umaru, Amal Bandar Alharbi and Aslanpour, Z. (2023). Antimicrobial stewardship implementation before and during the COVID-19 pandemic in the acute care settings: a systematic review. BMC Public Health, 23(1). https://doi.org/10.1186/s12889-023-15072-5.

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## Abbreviations

| | |
|---|---|
| A&E | Accident and Emergency |
| ACCP | American College of Clinical Pharmacists |
| AHRQ | Agency for Healthcare Research and Quality |
| AKI | Acute Kidney Injury |
| AMR | Antimicrobial Resistance |
| AMS | Antimicrobial Stewardship |
| ARIs | Acute respiratory tract infections |
| ARK | Antibiotic review kit |
| ASP | Antimicrobial stewardship program |
| BNF | British National Formulary |
| BSIs | Bloodstream infections |
| C&C | Capacity and capability |
| CAG | Confidentiality advisory group |
| CAP | Community-acquired pneumonia |
| CARES | Cease, amend, refer, extend or switch |
| CBA | Controlled before-after |
| CCG | Clinical commissioning group |
| CDC | Centers for disease control and prevention |
| CDIs | Clostridioides difficile Infections |
| CDSS | Computerised decision support systems |
| CIA | Critically important antimicrobials |
| COPD | Chronic obstructive pulmonary disease |

Abbreviations

| | |
|---|---|
| CQC | Care Quality Commission's |
| CRP | C-reactive protein levels |
| CwPAMS | Commonwealth partnerships for antimicrobial stewardship |
| DDD | Defined daily doses |
| DOT | Day of therapy |
| DP | During-the-pandemic |
| ECDC | European Centre for Disease Prevention and Control |
| HER | Electronic health record |
| EML | Essential Medicines List |
| ESPAUR | English surveillance programme for antimicrobial utilisation and Resistance |
| FIP | International Pharmaceutical Federation |
| GCP | Good Clinical Practice |
| GDPR | General data protection regulations |
| GLASS | Global antimicrobial resistance and use surveillance system |
| GMC | General Medical Council |
| GPhC | General Pharmaceutical Council |
| HAIs | Hospital-acquired infections. |
| HCPs | Healthcare professionals |
| HRA | Health Research Authority |
| IDSA | Infectious Disease Society of America |
| IHI | Institute for healthcare improvement |
| IRAS | Integrated Research Application System |
| IVOS | Intravenous-to-oral switch |
| KAP | Knowledge, attitude, and practice |

Abbreviations

| | |
|---|---|
| KPIs | Key performance indicators |
| LOS | Length of stay |
| LOT | Length of therapy |
| LRTIs | lower respiratory tract infections |
| MDR | Multi-drug resistance |
| MDT | Multidisciplinary team |
| MMAT | Mixed Method Appraisal Tool |
| MRC | Medical Research Council |
| MRSA | Methicillin resistant staphylococcus aureus |
| NAHQ | National Association for Healthcare Quality |
| NHS | National Health Service |
| NICE | The National Institute for Health and Care Excellence |
| NMC | Nursing and Midwifery Council |
| OPAT | Outpatient parenteral antibiotic therapy. |
| PAT | Postoperative antibiotic therapy |
| PCT | Procalcitonin |
| PHE | Public Health England |
| PI | Principal Investigator |
| PIS | Participant Information Sheet |
| PP | Prior-to-pandemic |
| PPE | Personal protective equipment. |
| PPS | Point prevalence surveys |
| R&D | Research and development |
| RCTs | Randomised controlled trials |

Abbreviations

| | |
|---|---|
| REC | Research Ethics Committee |
| RPS | Royal Pharmaceutical Society |
| SIDP | Society of Infectious Disease Pharmacists |
| SSCP | Saudi Society for the Clinical Pharmacy |
| SSI | Surgical site infection |
| SSTF | Start Smart, Then Focus |
| STHNFT | Sheffield Teaching Hospitals NHS Foundation Trust |
| TARF | Team antibiotic review form |
| UKHSA | UK Health Security Agency |
| VAP | Ventilator-associated pneumonia |
| VRE | Vancomycin resistant enterococcus |
| WAAW | World Antibiotic Awareness Week |
| WBCs | White blood cell counts |
| WHO | World Health Organisation |

## Glossary of terms

**Antibiotic**: An agent or substance that is produced by or derived from a microorganism that kills or inhibits the growth of another living microorganism. Antibiotic substances that are synthetic, semi-synthetic, or derived from plants or animals are, strictly speaking, not antibiotics. However, they are included in the toolkit. In this document, “antibiotic” refers to an antimicrobial agent with the ability to kill or inhibit bacterial growth.

**Antimicrobial**: An agent or substance derived from any source (microorganisms, plants, animals, synthetic or semi-synthetic) that acts against any type of microorganism, such as bacteria (antibacterial), mycobacteria (anti-mycobacterial), fungi (antifungal), parasite (anti-parasitic) and viruses (antiviral). All antibiotics are antimicrobials, but not all antimicrobials are antibiotics.

**Antimicrobial resistance (AMR):** Microorganisms such as bacteria, fungi, viruses, and parasites change when exposed to antimicrobial drugs such as antibiotics (= antibacterial), antifungals, antivirals, antimalarials and anthelmintics. As a result, the medicines become ineffective.

**Antimicrobial stewardship (AMS):** A coherent set of actions which promote the responsible use of antimicrobials. This definition can be applied to actions at the individual level as well as the national and global level and across human health, animal health and the environment.

**Antimicrobial stewardship program (AMP)**: An organisational or system-wide healthcare strategy to promote the appropriate use of antimicrobials through the implementation of evidence-based interventions.

**Days of therapy (DOTs)**: The number of days a patient receives an antibiotic independent of dose.

**Defined daily dose (DDD):** Assumed average maintenance dose per day for a medicine used for its main indication in adults as established by the WHO Collaborating Centre for Drug Statistics and Methodology.

**Empirical antibiotic treatment:** Initial antibiotic treatment targeted at the most probable causative microorganism. The recommendations should be based on local susceptibility data, available scientific evidence, or expert opinion when evidence is lacking.

**Health-care-associated infection** (also referred to as “nosocomial” or “hospital infection”): An infection occurring in a patient during care in a hospital or other healthcare facility, which was not present or incubating at the time of admission. Healthcare-associated infections can also appear after discharge. They represent the most frequent adverse event associated with patient care.

**The knowledge, Attitudes and Practice (KAP)** survey is meant to be a representative survey of a target population; it aims to elicit what is known (knowledge), believed (attitude), and done (practice) in the context of the topic of interest.

**Multidrug-resistant bacteria:** Bacteria that are resistant to at least one agent in three or more antibiotic categories. Extensively drug-resistant (XDR) is non-susceptibility to at least one agent in all but two or fewer antibiotic categories (i.e., bacterial isolates remain susceptible to only one or two categories) and pan drug-resistant (PDR) is non-susceptibility to all agents in all antibiotic categories.

**Outcome measures/indicators for AMS programmes:** Outcome measures/indicators are used in AMS activities to capture quantitative change in, e.g., patient or economic outcomes, but most of all in antibiotic use. Antibiotic consumption is expressed with a numerator indicating the quantity used (i.e., DDDs or DOTs) per defined denominator (i.e., patient days, admissions, consultations), to enable comparisons over time in the same setting or with other settings.

**Process measures/indicators for AMS programmes:** Process measures/indicators aim to capture information about the fundamental processes that contribute to achieving the desired outcome(s). An example in AMS would be the proportion of patients prescribed antibiotic treatment in compliance with standard treatment guidelines.

**Structural measures/indicators for AMS programmes:** Structure refers to the characteristics (capacity, systems, and processes) of the setting in which AMS programmes are conducted. Structures may be material or human resources, such as availability of financial resources, number of personnel, availability of guidelines, availability of information technology tools, etc.

# Chapter 1

# Introduction

# Chapter 1: Background & Introduction

This thesis focuses on the implementation of antimicrobial stewardship (AMS) in acute care settings in the United Kingdom, both prior to and during the COVID-19 pandemic. It also delves into the knowledge, attitudes, and perceptions of healthcare professionals, including doctors, nurses, and pharmacists, regarding antibiotic prescribing and AMS prior to and during the pandemic. Furthermore, this thesis proposes an educational intervention to enhance knowledge, attitudes, and awareness related to antibiotic misuse. It also provides a roadmap and toolkit for implementing AMS in acute care settings. This opening chapter presents an introduction to antimicrobial resistance (AMR), AMS, and the worldwide influence of COVID-19 on AMR. The study's motivation, aims, and research questions will be addressed. The chapter concludes by defining the terms used and laying out the structure and content of all subsequent chapters in this thesis.

## 1.1. Background

### 1.1.1. Antimicrobial resistance

Antimicrobials are essential for treating infections in humans and animals, supporting surgeries, and cancer therapies. However, their effectiveness is threatened by antimicrobial resistance (AMR), a significant global public health issue recognised by the UK government and the World Health Organization (WHO) (UK.GOV, 2024; WHO, 2018). AMR leads to increased healthcare costs, treatment failures, and higher mortality rates, posing severe economic and health challenges worldwide (WHO, 2018). Resistant organisms spread through people, animals, food, and the environment, exacerbating the problem (UK.GOV, 2024).

In response, the UK launched a 20-year vision in 2019 to control and contain AMR by 2040. This vision is supported by a series of 5-year national action plans. The first plan, 'Tackling Antimicrobial Resistance 2019 to 2024', achieved significant progress, including reducing antibiotic use in food-producing animals, enhancing surveillance systems, and piloting new antibiotic payment schemes in the NHS. Building on these achievements, the latest plan, 'Confronting Antimicrobial Resistance 2024 to 2029', outlines nine strategic outcomes across human health, animal health, agriculture, and the environment to further address AMR (UK.GOV, 2024).

The historical roots of AMR date back to Alexander Fleming's discovery of penicillin in 1928 and his subsequent warning about antibiotic resistance in 1945 (Aminov, 2010). Today, AMR is exacerbated by inappropriate antibiotic prescriptions, which occur in 30-50% of acute care settings, significantly contributing to the problem (Shrestha et al., 2018). Hospitals are major contributors, with approximately 65% of broad-spectrum antibiotic usage occurring in these settings (Department of Health and Social Care, 2019). High antibiotic consumption rates in various countries correlate with elevated rates of resistant infections (Browne et al., 2021). If unaddressed, the rise of multi-drug-resistant infections could result in 10 million annual deaths by 2050, highlighting the urgent need for continued action and innovation (O'Neill, 2016). Figure 1.1. elucidates the looming threat posed by AMR. As projected, by 2050, the mortality rate could escalate to one individual every three seconds if proactive measures are not implemented immediately. The pronounced countdown timer, complemented by the distinct purple hue, emphasises the magnitude and imminence of this public health concern. Figure 1.1. serves not merely as an alarm but as an urgent call to action for strategic AMS intervention. In 2019 alone, over 1.2 million people died from AMR-related infections (Murray et al., 2022). Reducing antibiotic use and implementing effective antimicrobial stewardship strategies are crucial to preventing the spread of resistant bacteria and ensuring the continued efficacy of these vital medications.

**Figure 1.1.** Antimicrobial resistance: a global threat with potentially devastating consequences if not tackled (Adopted from O'Neill, 2016)

### 1.1.2. Antimicrobial stewardship

Antimicrobial stewardship involves system-wide strategies to ensure appropriate use of antimicrobials, preserving their efficacy. The NICE and PHE define antimicrobials as all anti-infective therapies—antiviral, antifungal, antibacterial, and antiparasitic, in all forms. AMR is the reduced effectiveness of these medicines. Antimicrobial stewardship programs (ASPs), as outlined by WHO, promote the judicious use of antimicrobials through evidence-based interventions. Antimicrobial stewardship represents an organisational approach aimed at promoting judicious antibiotic usage, forming a vital component of the UK's five-year antimicrobial resistance strategy (NHS England, 2018). AMS initiatives strive to enhance patient care quality and safety while significantly reducing the emergence and spread of AMR. An organised antimicrobial management programme meets these objectives by optimising antimicrobial prescribing. In reaction to the escalating issue of AMR, multiple regulatory entities worldwide have mandated the execution of AMS, a comprehensive series of actions designed to endorse the appropriate use of antibiotics (NICE, 2015). For more definitions of antimicrobial stewardship, see Table 1.1.

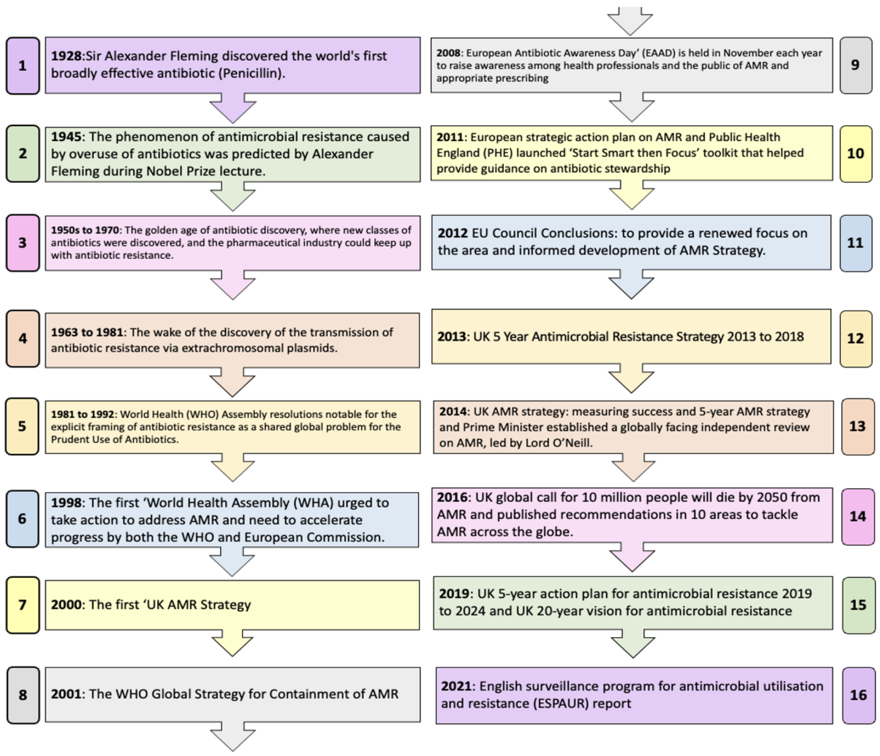
**Table 1.1.** Descriptive definitions of antimicrobial stewardship (Rasha Abdelsalam Elshenawy *et al*., 2022).

| Antimicrobial Stewardship Definitions | |
|---|---|
| **Antimicrobials and antimicrobial medicines** | The NICE and PHE defined the term 'antimicrobials' and 'antimicrobial medicines' as all anti-infective therapies (antiviral, antifungal, antibacterial and antiparasitic medicines) and all formulations (oral, parenteral, and topical agents) (NICE, 2015; ESPAUR, 2021). |
| **Antimicrobial resistance (AMR)** | The NICE and PHE defined the term 'antimicrobial resistance' as the 'loss of effectiveness of any anti-infective medicine, including antiviral, antifungal, antibacterial and antiparasitic medicines' (NICE, 2015; Gov.UK, 2019). |
| **Antimicrobial stewardship (AMS)** | The NICE and PHE defined 'antimicrobial stewardship' as 'an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness' (NICE, 2015; ESPAUR, 2021). |
| **Antimicrobial stewardship program (ASP)** | The WHO defined ASP as an organisational or system-wide healthcare strategy to promote the appropriate use of antimicrobials through the implementation of evidence-based interventions (WHO, 2019). |

NICE, National Institute for Health and Care Excellence; PHE, Public Health England; ESPAUR, English Surveillance Programme for Antimicrobial Utilisation and Resistance; AMS, antimicrobial stewardship; AMR, antimicrobial resistance; ASP, antimicrobial stewardship program; and WHO, World Health Organisation.

The golden era of antibiotics kicked off in 1963, paralleled by the rise of AMR, escalating into a global issue (Hutchings *et al*., 2019). AMS initiatives aim to guarantee access to potent antimicrobials for all who require them, both now and in the future (Majumder *et al*., 2020). Figure 1.2 illustrates the pivotal moments in the history of antimicrobial resistance and antimicrobial stewardship in the UK from 1928 to 2021. It highlights critical milestones such as the discovery of penicillin in 1928, the onset of the golden era of antibiotics in the 1960s, and the escalating global concern over AMR. This figure references the English Surveillance Programme for Antimicrobial Utilisation (ESPAUR), which underlines the urgency and response to the AMR crisis (ESPAUR, 2021).

**Figure 1.2.** Chronology of antimicrobial resistance and stewardship in the UK (1928 - 2021) (Rasha Abdelsalam Elshenawy *et al*., 2022).




AMR, antimicrobial resistance; BAA, European Antibiotic Awareness Day; ECDC, European Centre for Disease Prevention and Control; ESPAUR, English Surveillance Programme for Antimicrobial Utilisation and Resistance; HPA, Health Protection Agency, NICE, National Institute for Health and Care Excellence; UK, United Kingdom; WHO, World Health Organisation; and WHA, World Health Assembly.

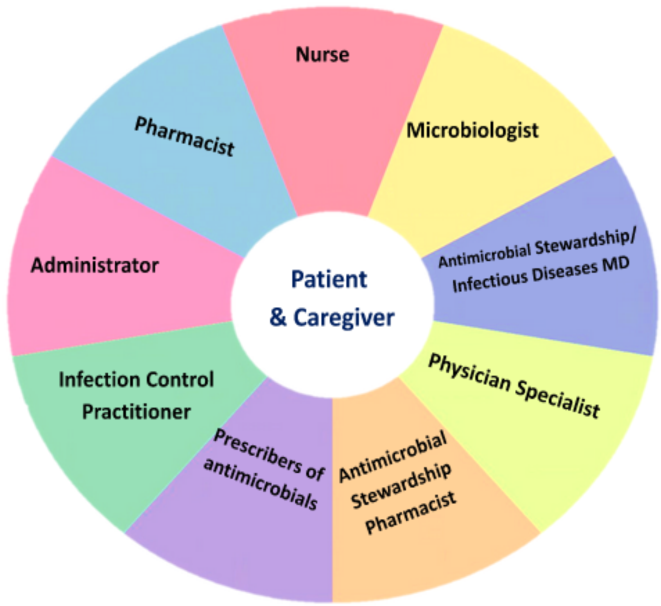
AMS necessitates a multidisciplinary approach involving healthcare professionals such as doctors, pharmacists, nurses, microbiologists, and administrators (Mendelson et al., 2019). This team-based strategy, leveraging diverse expertise, is crucial for the success and sustainability of AMS programmes.

Effective antimicrobial stewardship demands a strong, collaborative effort from a variety of healthcare professionals. Each member plays a vital role in stewardship initiatives. Their combined expertise allows for the implementation of targeted interventions that optimise antimicrobial use. Microbiologists, in particular, contribute significantly through susceptibility reports, rapid diagnostics, and educating healthcare professionals on the best practices for antimicrobial utilisation (Morency-Potvin et al., 2017).

Additionally, pharmacists, as frontline medicine experts, play a crucial co-leadership role in AMS, particularly highlighted during emergencies through AMS education, antibiotic review, and developing treatment guidelines (RPS, 2022; Kusuma *et al*., 2022). The Royal Pharmaceutical Society (RPS) has introduced an AMS pharmacy guide, enabling pharmacists to co-lead in combating AMR and advocating for safer antimicrobial practices. The guide's recommendations encompass judicious antibiotic prescribing, verifying prescriptions, patient education, and staff training, which are effective utilisation of AMS resources and performing AMS audits. Pharmacists' collaborative efforts are further emphasised in developing guidelines, monitoring drug use, and advocating for best prescribing practices. These combined efforts are essential for reinforcing stewardship and elevating antimicrobial safety (RPS, 2022).

Central to this collaboration is the patient and caregiver, whose engagement is vital in ensuring adherence and understanding of antimicrobial treatments. Engaging in open communication, education, and shared decision-making is essential. Such a coordinated effort not only streamlines the use of antimicrobials but is also a crucial strategy in mitigating the pressing global challenge of AMR, ensuring long-term, sustainable healthcare outcomes. In this concerted fight against resistance, each discipline contributes to a holistic strategy that empowers better patient care and combats the risk of superbugs, aligning with the global health community's goals (BSAC, 2018) (Figure 1.3).

**Figure 1.3.** A multidisciplinary approach to implementing AMS (Rasha Abdelsalam Elshenawy *et al*., 2022).




MD, medical doctor; ID, infectious diseases; and AMS, antimicrobial stewardship.

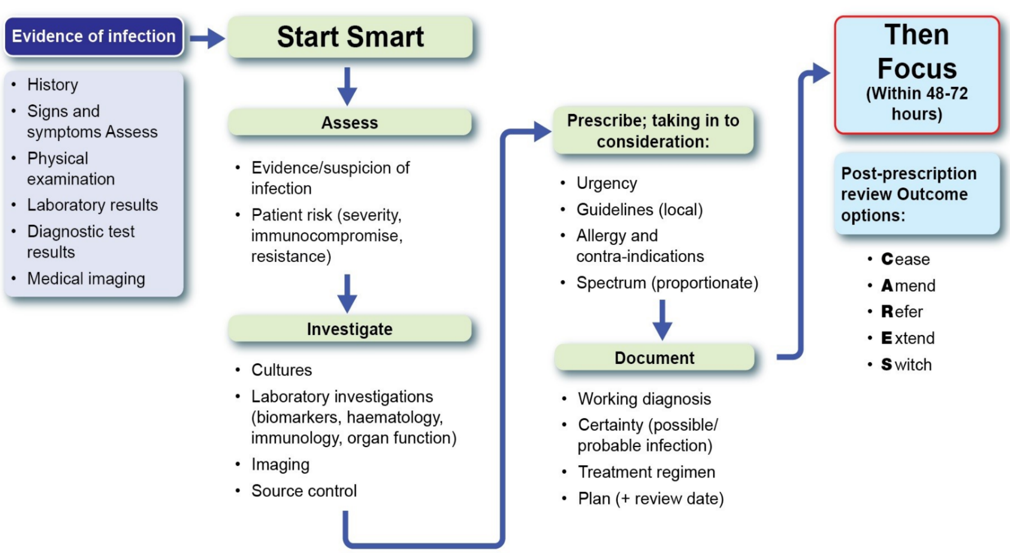
### 1.1.3. Antimicrobial stewardship implementation.

Public Health England recognised the crucial role of antimicrobial stewardship in tackling antimicrobial resistance and provided the SSTF toolkit to implement AMS in acute care settings (GOV.UK, 2023). This approach involves timely and responsible antibiotic use, using effective antibiotics to treat infections followed by an active ‘antibiotic review’ 24-72 hours later. The Start Smart-Then Focus (SSTF) approach encourages careful antibiotic usage through timely AMS initiation, review, and implementation (Figure 1.4). The recommended SSTF approach is applied to all antibiotic prescriptions. The Health and Social Care Act 2008's Code of Practice concerning infection prevention and control, alongside related guidance, sets forth compliance standards for registered organisations, emphasising prudent prescribing and antimicrobial stewardship. Additionally, the UK Care Quality Commission's (CQC) essential standards for quality and safety in relation to cleanliness and infection control refer to the code of practice (Gov.UK, 2023).

The "Start Smart" SSTF approach provides a structured approach to antimicrobial treatment. Firstly, patients should be thoroughly evaluated to confirm signs of infection, ensuring antimicrobials are administered only when necessary. Investigations, such as cultures and imaging, assist in identifying the origin of the infection and its antimicrobial susceptibility. When prescribing, adherence to guidelines is vital, with particular attention to drug allergies and cautious use of broad-spectrum antimicrobials (GOV.UK, 2023). Documentation is crucial, capturing every detail from diagnosis to medication specifics. In essence, the SSTF principles stress methodical assessment, investigation, prescription, and documentation to optimise patient outcomes, preserve antimicrobial efficiency, and avoid potential risks (Figure 1.4.).

The 'Then Focus' approach is a vital aspect of antimicrobial stewardship, focusing on the period after the initial administration of antimicrobials. It advises healthcare professionals to "review and revise" the treatment within 48 to 72 hours, considering new diagnostic information and changes in the patient's condition. This approach follows the "CARES" framework for antimicrobial review outcomes, which includes ceasing treatment if no infection evidence is present, amending the prescription based on new findings leaning towards a narrower antimicrobial spectrum when feasible, referring patients to specialised antimicrobial services, such as outpatient antibiotics or virtual wards for efficient treatment outside traditional hospital settings, extending the antimicrobial treatment in certain instances but setting clear review or end dates, and switching from IVOS when clinically appropriate, offering benefits like reduced hospital stays and lowered infection risks. Significantly, all decisions, from the choice of antimicrobial to the length of treatment, must be meticulously documented to ensure clarity and informed continuation of care (Gov.UK, 2023).

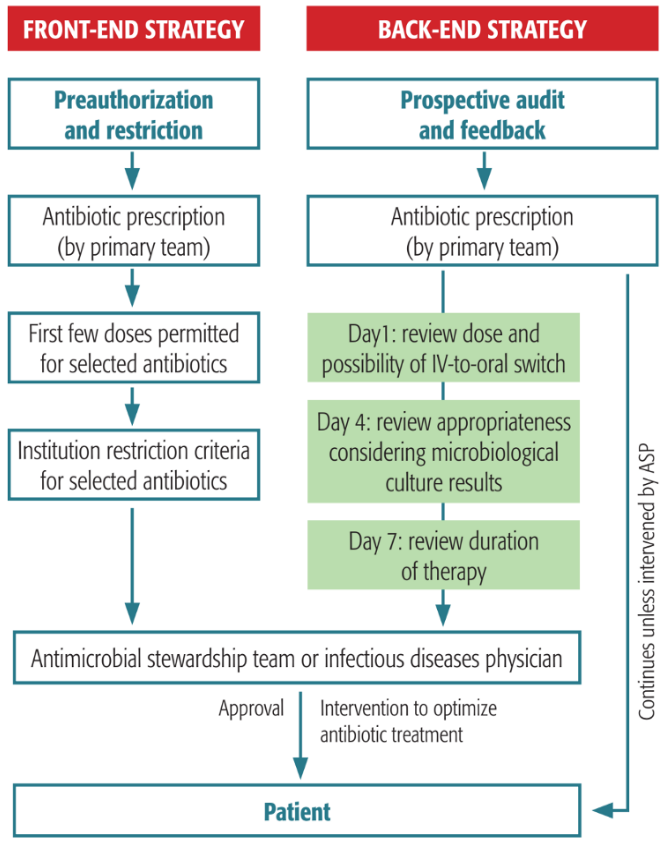
**Figure 1.4.** Antimicrobial stewardship clinical management algorithm (Adopted from Gov.UK, 2023).




The main objectives of AMS encompass enhancing patient results, curtailing adverse incidents, such as Clostridioides difficile infection (CDI) and side effects, and mitigating the development of AMR (Al-Omari *et al.*, 2020). In acute-care environments, oral and Intravenous (IV) antibiotics are routinely dispensed for diverse indications, encompassing upper respiratory tract infections (URTIs) and pneumonia. The commencement of IV antibiotics is typically the first response when patients arrive at the hospital with presumed infections (NICE, 2015).

Antimicrobial stewardship involves strategies and interventions aimed at improving appropriate antibiotic prescriptions in all healthcare settings. The literature provides tools, interventions, and activities collectively termed "strategies" to streamline and improve antimicrobial use and educate prescribers (ESPAUR, 2015). These strategies include "front-end" and "back-end" approaches. Front-end strategies require an approval process for antimicrobials, while back-end strategies involve reviewing therapy after initiation, often using prospective audit with intervention and feedback (Appendix 9). Research indicates that back-end strategies are widely practised, easily accepted by clinicians, and offer greater educational opportunities. Although more labour-intensive, back-end strategies are likely to provide a more sustained impact in improving antimicrobial prescribing quality (Chung *et al.,* 2013). Employed to encourage judicious antibiotic use and prescriber education (BSAC, 2018) (Figure 1.5).

**Figure 1.5.** Front and back-end antimicrobial stewardship strategies (Adopted from BSAC, 2018)




ASP, antimicrobial stewardship program; IV, Intravenous; and IV-to-oral, intravenous to oral.

The principle underlying AMS is enhancing antibiotic therapy to improve patient health outcomes, reduce antibiotic resistance, and cut unnecessary costs (Gov.UK, 2015). Such stewardship initiatives are aimed at significantly contributing to the reduction and spread of AMR. PHE has highlighted the necessity for the implementation of AMS. There is also an immediate requirement to examine the AMS strategies that could be effectively deployed in any emergency or crisis (UK Government, 2019).

Table 1.2 from Chung *et al.*, 2013, outlined common antimicrobial stewardship strategies aimed at optimising antibiotic use and combating AMR. Strategies include formulary restrictions, drug preauthorisation, and prospective audits with feedback to ensure antibiotics are prescribed appropriately. Education for prescribers and patients is considered effective, especially when combined with other methods. Institution-specific clinical guidelines and decision support systems are crucial, as is the selective reporting by microbiology labs to influence prescribing patterns. Additionally, point-of-care diagnostic tests, although still under research, could potentially reduce unnecessary antibiotic use by distinguishing non-bacterial infections. Hospitals must select suitable strategies to develop, expand, and improve their antimicrobial stewardship programs (ASPs). The selection of strategies by a hospital will be influenced by various factors, including its size, patient population, culture, priorities, and available resources. Detailed descriptions of each strategy, including its benefits, drawbacks, effectiveness metrics, and supporting references, resources, and tools, are provided (Appendix 10). Each strategy significantly impacts hospital outcome measures (Appendix 11).

Table 1.2. List of common antimicrobial stewardship strategies (Adapted from Chung *et al.*, 2013).

| **Intervention/ Strategies** | **Description** |
|---|---|
| **Formulary restriction** | Antibiotic prescriptions should be restricted to specific approved clinical indications and may only be authorised by designated doctors, such as those specialising in infectious diseases. |
| **Drug preauthorisation** | Permission (from an ASP team member or infectious diseases specialist) is required for the release of certain antibiotics. Often implemented together with formulary restrictions. |
| **Prospective audit and feedback** | Case review by trained ASP team members and feedback of recommendations if reviewed antibiotics are deemed to be inappropriately prescribed. |
| **Prescriber AMS education** | More effective as a supplementary strategy to other interventions |
| **Patient AMS education** | Usually, focus groups or mass media campaigns |
| **Clinical guidelines** | Treatment protocols for various infections – should be institution-specific |
| **Clinical decision support systems** | Information technology systems for improving antibiotic prescription. Requires existing electronic records and electronic prescribing system to be effective |
| **Point-of-care diagnostic tests** | Mainly undergoing research evaluation. Diagnosis of non-bacterial etiologies may help reduce antibiotic prescriptions. |
| **Microbiology laboratory susceptibility reporting** | Selective reporting of susceptibility profiles for positive cultures may dramatically alter the prescribing patterns of physicians |

ASP, antimicrobial stewardship program; and AMS, antimicrobial stewardship.

The main aim of the AMS implementation strategies is to maintain the judicious use of antibiotics and educate prescribers. Furthermore, the AMS should be measured in order to evaluate the outcomes of AMS implementation (Dellit *et al.*, 2007; BSAC, 2019). To enhance antimicrobial use, it is essential to implement measurable metrics that evaluate the effectiveness of ASPs. These measures serve various purposes, including quality assurance, improvement, and facilitating comparisons for benchmarking both within and between hospitals. The measurement of stewardship activities can be categorised into four distinct groups: antimicrobial consumption, process measures, outcome measures, and financial impacts. Before 2019, there was a lack of reliable methods to measure antimicrobial use and link it with resistance patterns. However, the WHO introduced measurable tools in 2019 that enable a consistent and accurate reflection of antimicrobial usage globally (WHO, 2019). Hospitals should carefully select measures to support the effective implementation of their AMS programs. Understanding the advantages and disadvantages of each measure is crucial to making an informed choice that aligns with the hospital's goals and resources (Table 1.3.) (WHO, 2019).

**Table 1.3.** Suggested measures for antimicrobial stewardship (Adopted from Matuluko *et al.*, 2020).

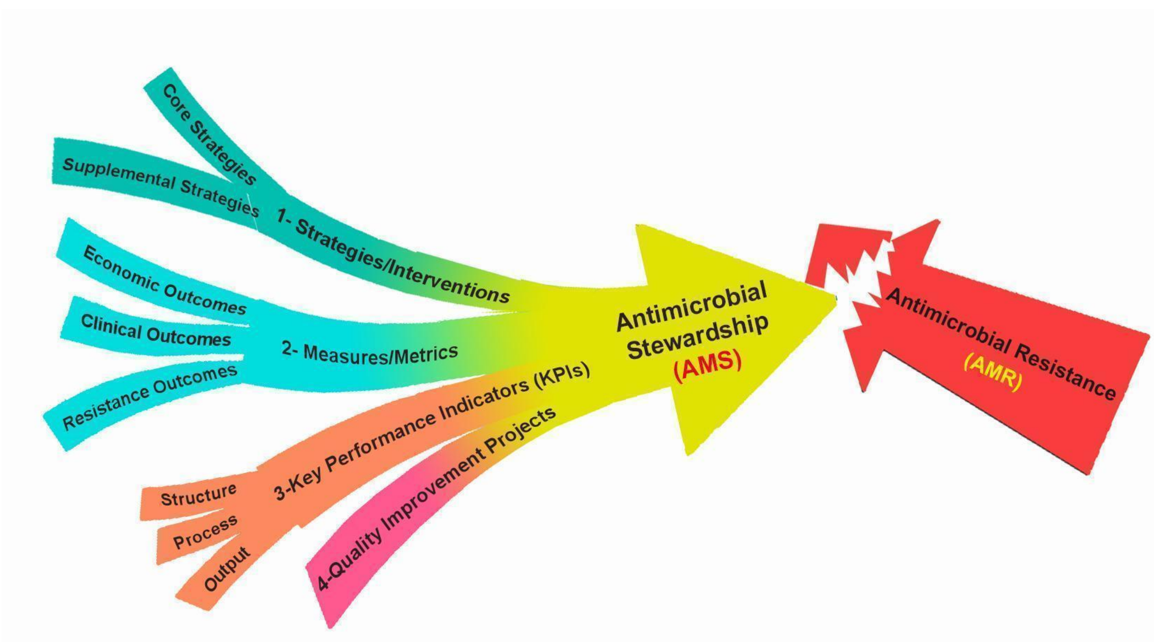
| **Antimicrobial stewardship measures for quality improvement** |
| --- |
| **Structural indicators** |
| • Availability of multi-disciplinary antimicrobial stewardship team<br>• Availability of guidelines for empiric treatment and surgical prophylaxis<br>• Provision of education in the last two years |
| **Process measures** |
| • Amount of antibiotic in Defined Daily Dose (DDD)/100 bed days, either promoted antibiotics or restricted antibiotics<br>• Compliance with acute empiric guidance (policy compliance)<br>• % Appropriate de-escalation; % appropriate switch from IV to oral<br>• Compliance with surgical prophylaxis (<60 min from incision, <24 hours and compliance with local policy)<br>• Compliance with care “bundles” – (3-day antibiotic review bundle, ventilator-associated pneumonia, community-acquired pneumonia, sepsis) |
| **Outcome measures** |
| • Clostridioides difficile infection (CDI) rates<br>• Surgical Site Infection (SSI) rates<br>• Surveillance of resistance<br>• Mortality Rates |

- Treatment-related toxicity (e.g., aminoglycoside-related toxicity)
- Rate of complications
- Readmission within 30 days of discharge

AMS, antimicrobial stewardship; DDD, Defined Daily Dose; IV, Intravenous; and CDI, Clostridioides difficile infection.

The AMS implementation bundle, as per the literature, includes AMS intervention strategies, measures/metrics, key performance indicators (KPIs) and quality improvement projects (Public Health Ontario, 2019). They complement each other to provide an effective way to measure and improve the implementation of AMS (CDC, 2019). NICE has also established AMS guidelines, advocating for its adoption in acute care (NICE, 2015). Effective AMS application is critical for addressing AMR and improving antibiotic prescribing through core and supplemental strategies. The sustainability of AMS relies on continuous quality improvement to identify and address areas needing improvement. Therefore, ensuring judicious antibiotic use, combating AMR, and safeguarding patient health. Figure 1.6 illustrates the flow diagram of the AMS implementation process confirming these standards (NICE AMS Quality Standards, 2016; IDSA, 2016; CQC Insight NHS, 2019; PHE, 2019; CQC, 2023).

**Figure 1.6.** Flow diagram of the AMS bundle (Rasha Abdelsalam Elshenawy et al., 2022).



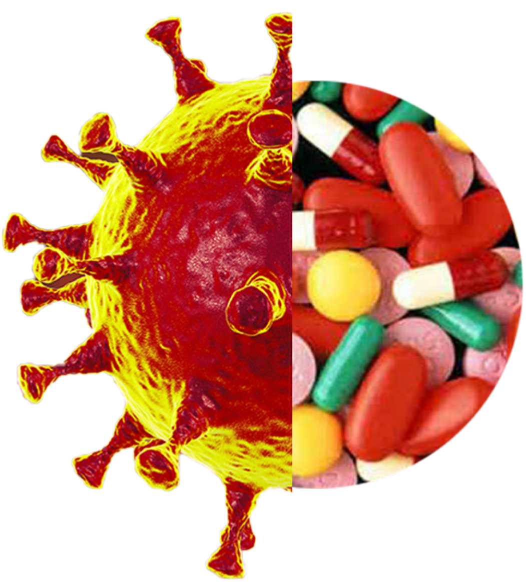

AMS, antimicrobial stewardship; AMR, antimicrobial resistance; and KPIs, key performance indicators.

### 1.1.4. The COVID-19 pandemic's impact on antibiotic use

The global pandemic, instigated by the outbreak of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2; COVID-19) in Wuhan, China, in December 2019, has led to substantial ramifications (Khor et al., 2020). By the 15th of January 2024, WHO had received reports of 632,533,408 confirmed cases of COVID-19 worldwide, along with 6,992,320 deaths (WHO, 2023). A disturbing consequence of the pandemic, according to recent evidence, is that an increasing number of hospital-admitted patients have been receiving empirical antimicrobial therapy, which may not always be suitable, thereby potentially boosting the global prevalence of AMR (Murgadella-Sancho *et al*., 2021). Furthermore, an upward trend has been observed in antibiotic consumption rates in secondary care, gauged as Defined daily dose (DDD) per 1,000 hospital admissions. A substantial surge in these rates was noted between 2019 and 2020, mainly due to a 6% hike in inpatient prescribing (Zhou *et al*., 2020).

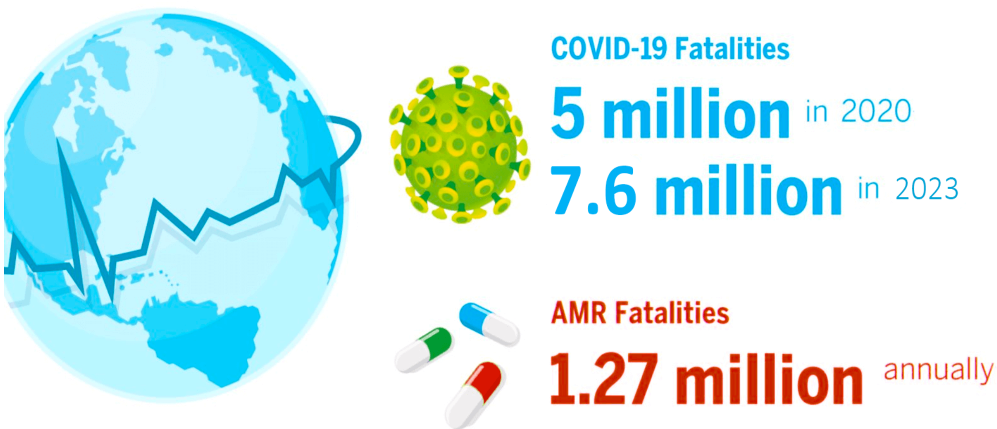
The ESPAUR report, encompassing national statistics on antibiotic prescriptions, resistance patterns, antimicrobial stewardship execution, and awareness initiatives, indicates a decline in antibiotic consumption for bacterial RTIs in 2020 relative to previous years. Exceptions to this trend were a few specific antibiotics, such as piperacillin/tazobactam. Changes in these prescribing patterns are likely connected to the publication of rapid guidance on prescriptions for RTIs in response to COVID-19 (ESPAUR, 2021). Furthermore, an immediate requirement was continuously implementing AMS for URTIs or pneumonia during the pandemic (Khor *et al*., 2020). As depicted in Figure 1.7., the WHO has described AMR as a silent pandemic, advocating for the execution of AMS during the COVID-19 pandemic response throughout the broader healthcare system (Choudhury *et al*., 2022).

**Figure 1.7.** The two pandemics: COVID-19 pandemic and AMR silent pandemic (Abdelsalam Elshenawy *et al*., 2022)



Recent research suggests that the increased use of antimicrobial therapy for hospital patients during the COVID-19 pandemic may have contributed to the rise of resistant infections globally (Murgadella-Sancho *et al.*, 2021). Therefore, it is essential to prioritise AMR and AMS, focusing on the selection of optimal empirical therapies and the appropriate adjustment or discontinuation of antimicrobials based on the presence or absence of bacterial co-infections (Hamidi *et al.*, 2021) (Figure 1.8.).

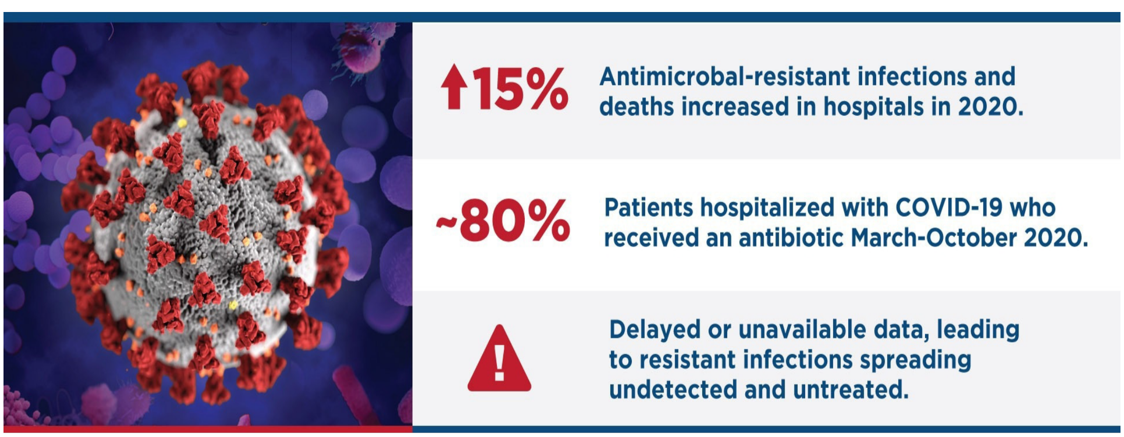
**Figure 1.8.** The global impact of COVID-19 and antimicrobial resistance (Adopted from Lancet, 2022).




COVID-19, coronavirus; and AMR, antimicrobial resistance.

In 2021, the European Centre for Disease Prevention and Control (ECDC) reported that the COVID-19 pandemic resulted in a 15% increase in AMR and hospital deaths in 2020. Additionally, it highlighted the need for further research and action to address this issue (Figure 1.9).

**Figure 1.9.** Impact of the COVID-19 pandemic on antimicrobial usage and antimicrobial resistance (Adopted from ECDC, 2021).




AMR, antimicrobial resistance; and COVID-19, coronavirus.

Therefore, providing empirical data on the pandemic's influence on antimicrobial prescribing is crucial for devising effective strategies to prevent and minimise the impact of future crises. Although the COVID-19 pandemic has significantly impacted antibiotic use, it is essential to fully understand the extent of this impact. There is a need for further evidence of its effects in acute care settings. Hence, the primary objective of this research project is to gain a comprehensive understanding of how the implementation of AMS and antibiotic prescribing practices were affected in response to the COVID-19 pandemic.

## 1.2. Introduction

The increasing prevalence of multi-drug-resistant infections globally poses a significant health threat, escalating morbidity, mortality, and economic impact (WHO, 2019). Antimicrobial stewardship, which champions judicious antibiotic usage, is central to the UK's strategy against AMR (GOV.UK, 2014). AMS focuses on ensuring the right antimicrobial prescriptions and the best antibiotic usage practices, aiming to diminish AMR through specific policies and guidelines (NICE, 2023). In the UK, attention towards AMS started to gain momentum in 2016, leading to encouraging outcomes from its implementation (Duncan et al., 2014). The COVID-19 pandemic has highlighted the necessity for ongoing antimicrobial stewardship. The irrational use of antimicrobials during the pandemic could worsen resistance issues, emphasising the vital need for persistent stewardship efforts globally (Khor et al., 2020).

The irrational use of antimicrobials during the pandemic could worsen resistance issues, emphasising the vital need for persistent stewardship efforts globally (Khor *et al*., 2020). Additionally, the study assessing the impact of COVID-19 on AMS activities revealed significant effects. The pandemic led to a 64% reduction in routine AMS activities, impacting audits, education, and multidisciplinary collaboration (Ashiru-Oredope *et al*., 2021). The long-term consequences of this decrease in AMR are yet to be determined. However, the innovations triggered by the pandemic present potential opportunities to strengthen AMS in the aftermath, requiring further investigation (Ashiru-Oredope *et al*., 2021). There is a significant gap in the literature concerning the implementation of antimicrobial stewardship and prescribing appropriateness in secondary care settings (ESPAUR, 2020).

However, this gap does not necessarily indicate a lack of initiatives or awareness on the issue, as relevant studies may be in progress or not yet published. Notably, there is an absence of research investigating the prevalence of inappropriate antibiotic prescribing in acute care settings during the pandemic in the UK. Additionally, there is a lack of comprehensive empirical studies evaluating antibiotic prescribing and antimicrobial stewardship during this period (Khan *et al.,* 2022). Furthermore, the factors influencing the appropriate antibiotic prescribing during the hospital stay of adult patients remain unexplored (Denny *et al.,* 2020). Given the unprecedented challenges introduced by the pandemic, it's conceivable that the understanding of antibiotic prescribing, AMR and AMS among HCPs might have waned during this time (Nader Nemr *et al*., 2023; Hadi Al Sulayyim *et al.,* 2023; Abdu-Aguye *et al*., 2022). This research aims to address these gaps, intending to develop AMS implementation for healthcare that can guide and inform policymakers.

## 1.3. Research aims and objectives.

### 1.3.1. Aims:

To investigate the implementation of AMS and antibiotic prescribing practices PP and DP, as well as to explore the knowledge, attitudes, and perceptions of health professionals towards antibiotic prescribing and AMS implementation during the COVID-19 pandemic in a secondary care setting in the UK.

### 1.3.2. Objectives:

1. To explore the implementation of AMS in acute care settings at the patient level among adult patients through a systematic review of existing literature from PP and DP from 2000 to 2021.
2. To determine the prevalence of inappropriate antibiotic prescribing at the patient level in adult patients at one NHS Foundation Trust, both PP and DP, in 2019 and 2020 by conducting a retrospective cross-sectional review of patient records.
3. To evaluate the implementation of AMS practices at the patient level among adult patients admitted to one NHS Foundation Trust, both PP and DP, in 2019 and 2020, utilising a retrospective cross-sectional review of patient records.
4. To investigate healthcare professionals' knowledge, attitudes, and perceptions regarding antibiotic prescribing, AMR, and AMS practices at the organisational level through a cross-sectional prospective survey.

### 1.3.3. Research questions:

The following research questions have been formulated for each study:

#### 1.3.3.1. Study one: systematic literature review:

1. How has AMS been implemented in acute care settings as reflected in the literature from 2000 to 2020?

#### 1.3.3.2 Study two: retrospective patient records review study:

1. What is the prevalence of inappropriate antibiotic prescribing among adult patients at the NHS Foundation Trust both PP and DP in an acute care setting?

2. How effectively has AMS been implemented among adult patients admitted to the NHS Foundation Trust both PP and DP in 2019 and 2020 in an acute care setting?
3. Which factors influenced antibiotic prescribing and AMS implementation among adult patients admitted to the NHS Foundation Trust both PP and DP in 2019 and 2020 in an acute care setting?

#### 1.3.3.3 Study three: prospective survey study:

1. What is the level of healthcare professionals' knowledge about antibiotic prescribing, AMR, and AMS practices during the pandemic in an acute care setting?
2. What are the attitudes and perceptions of healthcare professionals towards antibiotic prescribing, AMR, and AMS practices during the pandemic in an acute care setting?
3. Which factors influence healthcare professionals' attitudes toward AMS practices in an acute care setting during the pandemic?

### 1.3.4. Personal interest in this research study:

As an AMS pharmacist with two decades of experience in pharmacy practice within acute care settings, and currently pursuing research studies at UH University, I had the opportunity to work on AMS initiatives at West Hertfordshire Teaching Hospitals NHS Trust during the COVID-19 pandemic. My involvement in AMS ward rounds allowed me to directly interact with infected patients and healthcare professionals in antibiotic prescribing. It became evident that the pandemic significantly impacted antibiotic prescribing practices and the implementation of AMS. This experience sparked my interest in conducting further research in this field.

At the outset of this thesis, there was a lack of empirical data regarding AMS implementation. While a limited number of prevalence studies were conducted, research has demonstrated that antibiotic consumption and antimicrobial resistance surged during the COVID-19 pandemic, consequently impacting AMS efforts. However, no study has yet provided empirical data specifically addressing the implementation of AMS during the pandemic.

This research project addresses a major long-standing global issue, namely antimicrobial resistance, which was exacerbated worldwide during the COVID-19 pandemic. A series of research questions have been examined through a systematic literature review and two empirical studies, one retrospective and the other prospective in design. Additionally, this research project proposes a roadmap for effective AMS implementation in acute care settings.

This thesis is an innovative research effort focused on evaluating the prevalence of inappropriate antibiotic prescribing and implementing antimicrobial stewardship to improve prescribing practices and counteract antimicrobial resistance. It includes a quantitative study of AMS implementation and antibiotic prescribing patterns both pre-pandemic and during the pandemic at Bedfordshire Hospitals NHS Foundation Trust in the UK. Additionally, this thesis explores the knowledge, attitudes, and perceptions of healthcare professionals regarding antibiotic prescribing during the pandemic at one Foundation Trust.

This chapter provides an introductory overview of antimicrobial resistance, antimicrobial stewardship, and the impact of COVID-19 on antibiotic prescribing and AMR. Additionally, it reviews the influence of the pandemic on AMS activities in the UK. The aims, objectives, and research questions of this research project are outlined. The subsequent chapter will discuss the research methodology and offer an overview of the methods used in this research project.

**Summary of this chapter**

This chapter provided the background and introduction to the research project. The next chapter will present the theoretical framework, research paradigm, methodology, and the ethical processes undertaken to conduct this research project.

# Chapter 2

# Methodology and Methods

# Chapter 2: Methodology and Methods

In the previous chapter, the impacts of two pandemics, antimicrobial resistance and the COVID-19 pandemic, on inappropriate antibiotic prescribing were reviewed, along with antimicrobial stewardship strategies and measures. This chapter also presented the rationale for this research project, its aim, and its objectives. Additionally, the AMS toolkit in the UK was reviewed. The next chapter will describe the research methodology and offer an overview of the methods employed in this study.

## 2.1 Introduction

Research, as described by the Oxford online living dictionaries, is "a systematic investigation and analysis of materials and sources to establish facts and formulate new conclusions" (www.dictionary.com, 2023). However, research methodology is defined as a systematic approach underpinning the procedures and methods used to answer a research question (Howell, 2012), while the term “method” is used to describe the means or modes by which data is collected (Howell, 2012). This chapter discusses the research methodology, highlighting research approaches, research paradigms and research designs, and then provides an overview of the methods used in this research. There are three approaches to conducting research: quantitative, qualitative, and mixed methods (Creswell, 2008).

Creswell suggests that traditional qualitative and quantitative research methods should not be viewed as opposing each other, but rather as two ends of a continuum, with mixed methods occupying the middle ground (Creswell & Creswell, 2012). Quantitative research focuses on hypothesis testing, seeking to quantify the relationships between variables using numbers and statistical tests for a deductive analysis of data (Creswell, 2018). The qualitative approach focuses on understanding the meaning and dimensions of a given research problem. Traditionally, qualitative data are words, but other formats of qualitative data are also available. Qualitative data analysis is conducted, leading to themes from which the researcher interprets the data's meaning (Dawadi, Shrestha and Giri, 2021).

## 2.2 Methodology

Research methodology and methods will be discussed in general and with specific reference to this research. The selection of a research approach is influenced by researchers’ philosophical assumptions, in other words, the research paradigm (Creswell & Creswell, 2018). Kuhn defined a research paradigm as “the set of common beliefs and agreements shared between scientists about how problems should be understood and addressed” (Kuhn, 1970). Other researchers argue that the choice of a research approach should be focused on the suitability of the research method in answering the research question regardless of the researcher's philosophical position (Bishop, 2015; Johnson *et al*., 2007) (Figure 2.1).

**Figure 2.1.** Aspects of the methodology and methods in this research project.


### 2.3. Research paradigm:

Paradigm originates from the Greek "pattern", and it was first added to the word "research" by Kuhn (1970), driven by his aspiration to understand the underlying differences between social scientists (Kivunja & Kuyin, 2017). Patton described a paradigm as a "world view, a general perspective, a way of breaking down the complexity of the real world" (Patton, 2015). Paradigms are also viewed as the "philosophical intent or underlying theoretical framework and motivation of the researcher with regard to the research" (Mackenzie & Knipe, 2006).

Paradigms could shape what is considered to be normal science among a particular community of scientists, setting for them the boundaries of their research (Holloway, 1997). There has been conflict among scientists for decades as a result of biases toward their paradigms (Patton, 2015). As a result, there has been long-standing disagreement over whether the only way to reveal reality is through measurements, hence the need for quantitative methods, or whether measurements cannot reveal complex human phenomena, hence the need for qualitative approaches (Patton, 2015).

A research paradigm refers to a set of beliefs, values, assumptions, and methodologies that guide and shape the approach to research within a specific field or discipline (Creswell, 2018). It provides a framework that defines how researchers perceive and interpret the world, the nature of reality, and the ways they investigate and answer research questions. Research paradigms influence the choice of research methods, data collection techniques, data analysis, and the overall structure of a study (Creswell, 2018).

Worldviews are perceived as a researcher's overall perspective on the world and research methodology. Influenced by their field of study, guidance from advisers and faculty, and previous research experiences, these worldviews shape how researchers approach their work. Depending on their specific beliefs, researchers may gravitate towards qualitative, quantitative, or mixed methods in their research approach

(Creswell & Creswell, 2018). Four prevalent worldview research paradigms, as identified by Creswell & Creswell, are positivism, transformative, constructivism, and pragmatism (Creswell & Creswell, 2018).

The philosophy of positivism is tied to the identification of cause and effect, utilising quantitative methodologies (Aliyu, Bello, Kasim, & Martin, 2014; Creswell & Creswell, 2018). On the other hand, constructivist researchers focus on qualitative research to gain insight into participants' viewpoints (Creswell & Creswell, 2018; Neimeyer & Levitt, 2001). The transformative worldview is characterised by research centred on the needs of specific groups, frequently associated with political actions (Creswell & Creswell, 2018). Within the pragmatic worldview, the researcher is driven by problem-solving, employing mixed-method research to grasp the issue (Brierley, 2017; Creswell & Creswell, 2018). The pragmatic paradigm is rooted in a practical, real-world application, a characteristic that aligns with the nature of the current study (Creswell & Creswell, 2018) (Table 2.1). Researchers should select a research paradigm based on the nature of their research questions and the basic philosophical ideas that fit with the objectives of their study. Each paradigm possesses its own understanding of knowledge and research approach, as detailed in Table 2.1.

**Table 2.1.** Brief description of central elements in four research paradigms: four worldviews (Adopted from Creswell, 2018).

| **Postpositivist** | **Constructivism** |
|---|---|
| • Quantitative research<br>• Known as a "scientific method."<br>• Focus on empirical observation and numerical measurements.<br>• Theory verification<br>• Deductive | • Qualitative research approach.<br>• Relay meanings from participants<br>• Prefers open-ended questions.<br>• Focuses on the context of participants and the researcher's role in interpretation.<br>• Theory generation<br>• Inductive |
| **Pragmatism** | **Transformative** |
| • Mixed method research<br>• The researcher selects suitable methods to address the research problem<br>• More than one research method can be used<br>• Focuses on real-world problems<br>• Abductive | • Qualitative research<br>• Focuses on social justice and human rights<br>• Links political and social actions<br>• Focused on change<br>• Inductive |

This chapter substantiates the research rationale, theoretical framework, and research methodology. It outlines the research design and methodologies deployed to address the research questions and achieve the objectives and aims. A synopsis of both retrospective and prospective quantitative studies was presented, and ethical considerations were addressed within this chapter. Both studies were quantitative but some descriptive text arising from an open question in a questionnaire was also analysed.

### 2.4. The postpositivist perspective

Postpositivist philosophy has been a cornerstone in research, aligning more closely with quantitative methods than qualitative ones. This perspective is often referred to as the scientific method or scientific research and is sometimes known as postpositivist research, empirical science, or postpositivism. The term "postpositivism" is used to denote the evolution of thought beyond positivism, challenging the idea of absolute truth in knowledge (Phillips & Burbules, 2000). It acknowledges the limitations of being certain about knowledge claims, especially in the context of studying human behaviour and actions. The roots of postpositivism can be traced back to 19th-century scholars, such as Comte, Mill, Durkheim, Newton, and Locke (Smith, 1983), with its contemporary form elaborated by other scholars (Phillips & Burbules, 2000).

The postpositivist research paradigm adopts a deterministic philosophy, positing that causes are likely to determine outcomes. This approach is evident in research, where the focus is on identifying and evaluating the causes affecting outcomes. It involves reducing complex ideas into a more straightforward, testable format, such as variables in research questions (Creswell, 2018). In postpositivism, knowledge is derived from precise observation and measurement of the objective reality in the external world. For postpositivists, developing numerical measures and studying individual behaviour is crucial (Creswell, 2018). According to postpositivism, the world operates under specific theories that need to be tested and refined to enhance our understanding. The scientific method, favoured by postpositivists, starts with a theory and involves collecting data to support or refute this theory, followed by necessary revisions and further research (Creswell, 2018).

Phillips and Burbules (2000) highlighted several critical assumptions of postpositivist philosophy. They noted that knowledge was seen as conjectural and antifoundational, implying that absolute truth was unattainable and research findings were inherently imperfect and fallible. The research process was characterised by making claims and continually refining or replacing them with more substantiated ones, a common approach in quantitative research that typically began with theory testing. Furthermore, knowledge was formed through data, evidence, and rational analysis, with researchers collecting data through instruments based on participant responses or their observations. Maintaining objectivity is crucial for competent inquiry, necessitating that researchers critically examine their methods and conclusions for bias while adhering to standards of validity and reliability, especially in quantitative research (Phillips and Burbules, 2000). The postpositivist paradigm, evolving from positivist roots, prefers more quantitative methods in research. It represents an advancement in thinking, challenging the concept of absolute truth, particularly in research studies. Additionally, modern scholars have refined postpositivism, acknowledging that it is an intuitive and holistic approach that brings flexibility to research (Maksimović *et al*., 2023).

This thesis is designed to address the research questions and achieve the aims and objectives. In this research project, the postpositivist research paradigm was employed to meet the objectives and address the research questions posed. The rise of multi-drug-resistant infections poses a serious threat to global health, resulting in substantial morbidity, mortality, and economic outcomes. In 2016, the O'Neill review warned of a silent pandemic, projecting 10 million annual deaths from AMR by 2050 if left unaddressed. It was projected that AMR could cause one death every three seconds. This alarming estimate emphasised the urgent need for innovative actions and collaboration in order to avert a catastrophic impact on public health (WHO, 2019).

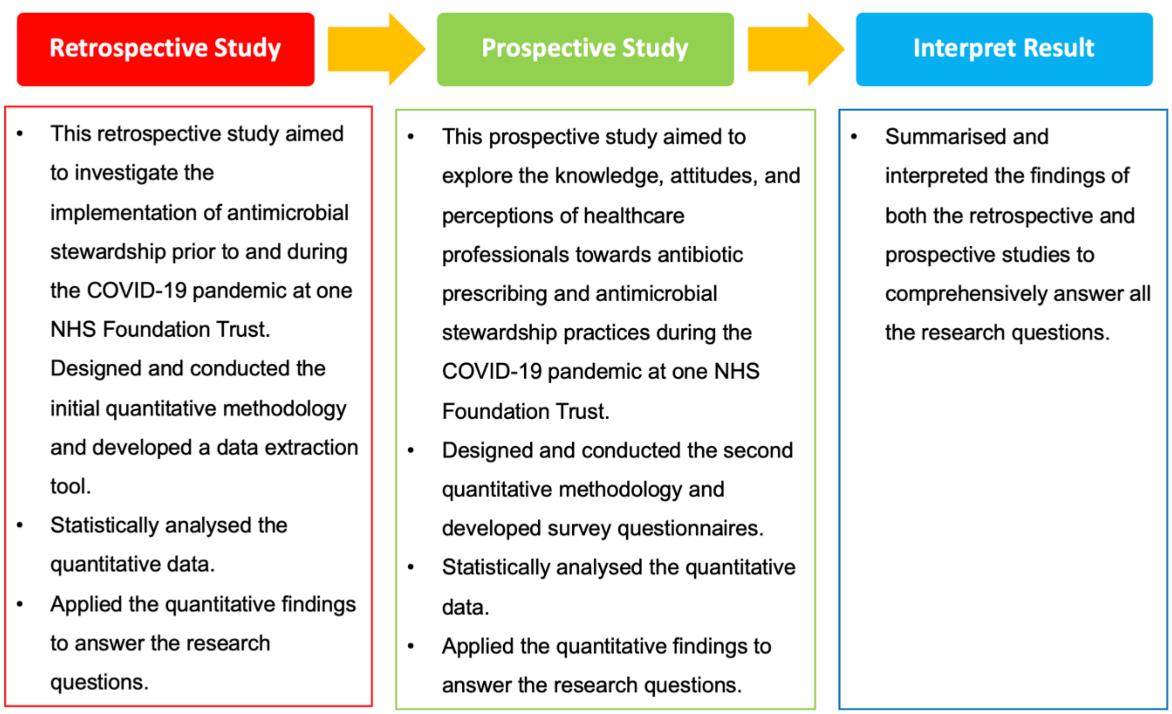
Recognising the severity of this challenge, the WHO has ranked AMR among the top ten global public health threats, urging prompt action to prevent dire outcomes (WHO, 2019). As of 2019, over 1.2 million people worldwide succumbed to AMR-related deaths (Murray *et al*., 2022). In response, antimicrobial stewardship has been recommended as a practical organisational approach to encourage responsible use of antibiotics (NICE, 2015). This research offers in-depth knowledge on the implementation of antimicrobial stewardship and patterns of antibiotic prescribing both prior to and during the COVID-19 pandemic in an acute care setting. This research project evaluates antibiotic prescribing and AMS practices during the pandemic, identifying factors that contribute to inappropriate prescribing. Furthermore, it explores the knowledge, attitudes, and perceptions towards antibiotic prescribing and AMS practices during the COVID-19 pandemic.

The protocol for the research project has been developed to plan the research steps and provide guidance throughout the project. This protocol has been registered with ISRCTN (www.isrctn.com, 2021), which is related to the WHO. Additionally, the research project is registered in the Octopus database (Octopus, 2022).

This research project commenced with a systematic literature review, detailed in Chapter 3. The findings of this review were published in the PMC Public Health journal (Abdelsalam Elshenawy *et al*., 2022). The systematic literature review uncovered a gap in empirical data concerning the implementation of AMS during the COVID-19 pandemic. It is the first of its kind to investigate AMS implementation strategies and measures in acute care settings both prior to and during the pandemic. In response to these findings, both retrospective and prospective studies were undertaken, as shown in Figure 2.2. This necessitates the development of a theoretical framework to enable a more in-depth exploration of AMS implementation in acute care settings, as illustrated in Figure 2.3. After establishing the theoretical framework and research paradigm, the methodology of the study was detailed. Research methodology forms a critical part of performing credible research. Essentially, the methodology chapter should validate the selected design decisions, demonstrating that the chosen methods and techniques are optimally suited to the research goals and objectives and will yield valid outcomes (Bryman et al., 2008).

This research project, conducted at Bedfordshire Hospitals NHS Foundation Trust, consists of two separate quantitative studies. The first, a retrospective study, is critical for evaluating antibiotic prescribing PP in 2019 and DP in 2020. Additionally, it aims to determine the AMS practices PP and DP. This involved a retrospective review of patient medical records. The second quantitative study is a survey aimed at exploring antibiotic prescribing behaviours during the pandemic. The questionnaire is developed using PHE literature on behaviour change. It determines antibiotic prescribing prevalence in acute care settings, incorporating elements of behavioural analysis (PHE, 2018) and the results from the retrospective study. As AMS is a hospital-wide organisational program that requires collaboration among healthcare professionals, this survey study is designed to explore their perspectives on antibiotic prescribing during the COVID-19 pandemic, as shown in Figure 2.2.

**Figure 2.2.** Flowchart of research project methodology: integrating retrospective and prospective studies.



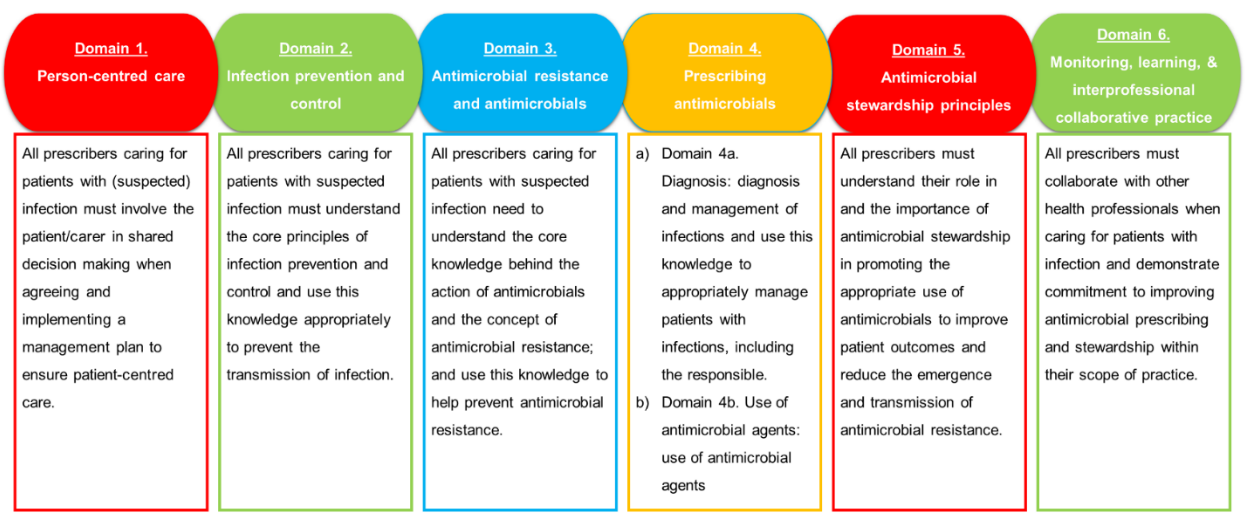

NHS, National Health Service; and COVID-19, coronavirus.

### 2.5. Theoretical framework:

The Antimicrobial Prescribing and Stewardship (APS) competency framework is designed to enhance the quality of antimicrobial treatment and stewardship in real-time. It aims at mitigating the risks associated with inadequate, inappropriate antibiotic prescribing. This significantly elevates patient safety and care quality, maintaining AMS implementation and contributing to the global effort to curb the emergence and spread of AMR (UK.GOV, 2023). The competencies are described as a 'combination of knowledge, skills, motives, and personal traits.' The development of these competencies should help individuals continually improve their performance and work more effectively. The APS Competency Framework can be applied in secondary care settings to support the development of prescribing practices related to antimicrobials and to embody stewardship practices (UK.GOV, 2023).

The framework comprises six domains within the APS Competency Framework. These complement the Royal Pharmaceutical Society (RPS) Competency Framework and, in England, the Infection Prevention and Control Education Framework, as published on NHS England's website (RPS, 2021; NHS England, 2023). Each domain has an overarching statement and corresponding descriptors that detail the activities, knowledge, or outcomes that should be demonstrated. Implementing and assessing practice against the APS Competency Framework can demonstrate compliance with antibiotic prescribing and antimicrobial stewardship practices as per the code of practice in England. The key domains of this framework are illustrated in Figure 2.3.

**Figure 2.3.** The Main Domains of the APS Competency Framework (UK.GOV, 2023).




All aspects of improving antibiotic prescribing and AMS practices that informed this research are detailed in Table 2.2. These will support making recommendations pertaining to the antibiotic prescribing process and the implementation of antimicrobial stewardship in a secondary care setting.

**Table 2.2.** Summary of research design aligned with the APS competency framework.

| | **The Formwork Aspect Involved** |
|---|---|
| **Study 1** | **Domain 1. Person-centred care:** The AMS intervention strategies utilised both before and during the COVID-19 pandemic have been examined in the published literature, such as antibiotic review and prospective audit with feedback.<br><br>**Domain 2. Infection prevention and control:** The AMS intervention strategies used PP and DP, including the antibiogram, infection prevention and control surveillance reports, and multi-drug resistance organisms. Additionally, identify the key national and international initiatives to promote effective infection prevention and control, address the threat of AMR, and effective AMS implementation.<br><br>**Domain 3. Antimicrobial resistance and antimicrobials:** The AMS intervention strategies pertain to the principles of surveillance, antimicrobial use, and the utilisation of surveillance data. Additionally, the AMS intervention measures associated with antibiosis, such as Defined Daily Dose (DDD) and Days of Therapy (DOTs), alongside quality indicators.<br><br>**Domain 4. Prescribing antimicrobials:** The AMS intervention strategies, such as technological support and clinical decision aids, use vital signs and inflammatory markers to guide antibiotic prescribing, such as Procalcitonin, and follow local and national guidelines in antibiotic prescribing.<br><br>**Domain 5. Antimicrobial stewardship principles:** Utilise the principles of AMS, such as 'Start Smart - Then Focus (SSTF)', which includes strategies like IV-to-oral switch, de-escalation, discontinuation, and changing the antibiotic regimen.<br><br>**Domain 6. Monitoring, learning, and interprofessional collaborative practice**<br>• The outcomes and measures of the AMS implementation are highlighted, with a focus on the effectiveness of these strategies in antimicrobial stewardship practices.<br>• The impact of the COVID-19 pandemic on AMS implementation strategies and measures in acute care settings is emphasised.<br>• Utilise collaborative relationships, such as multidisciplinary AMS teams, when managing infections.<br>• Employ antimicrobial stewardship structures and processes implemented by healthcare organisations (for example, AMS committees, monitoring the quantity and quality of antibiotic prescribing, AMS education, audit and feedback, formulary restrictions, guidelines and digital decision-support). |
| **Study 2** | As identified in Study 1, antimicrobial stewardship strategies, measures, and quality improvements were employed both PP and DP, as evidenced in the literature. The subsequent Study 2 investigated AMS implementation in 640 patient records PP in 2019 and DP in 2020 at an NHS Foundation Trust, examining factors affecting antibiotic prescribing and AMS.<br><br>**Domain 1. Person-centred care:** Manages patient expectations or demands for antimicrobials according to the symptoms and primary diagnosis and prescribes the appropriate antibiotics in accordance with local guidelines.<br><br>**Domain 2. Infection prevention and control**: Understand the differences between types of bacteria and their associations with respiratory sites of infection. Additionally, prescribes antibiotics for respiratory tract infections based on the suspected organism and in accordance with local guidelines.<br><br>**Domain 3. Antimicrobial resistance and antimicrobials**<br>• The AMS intervention strategies pertain to the principles of surveillance and antimicrobial use, as well as the utilisation of surveillance data.<br>• Understands the fundamental principles of susceptibility reports and culture results.<br>• Recognise the challenge posed by diagnostic uncertainty in infections due to variations in pathogen epidemiology and utilise the AWaRe categories of antibiotics as outlined by the WHO.<br><br>**Domain 4. Prescribing antimicrobials**<br>**Domain 4a. Diagnosis**<br>• Knows critical features of and diagnostic criteria for specific infections (for example, pneumonia), the best narrow-spectrum antibiotics to prescribe and the length of antibiotic course.<br>• Applies relevant severity scoring tools such as CURB-65 when initiating antimicrobial therapy and interprets results appropriately. |

<table>
<tr><td></td><td>
<ul>
<li>Interprets microbiology results/reports from the laboratory and knows the significance of preliminary pathogen identification.</li>
<li>Reviews vital signs and inflammatory markers where appropriate (for example C-reactive protein (CRP), white cell count (WBC) and procalcitonin (PCT) and other investigations when diagnosing and monitoring the response to treatment of infections and their complications.</li>
<li>Employ additional investigations for diagnosing and monitoring responses to treatment of infections and their complications, such as X-rays in cases of pneumonia.</li>
<li>Considers patient specific factors when diagnosing infections and choosing antimicrobials which may influence the choice of antimicrobial (for example immune function, allergy status, infection severity and risk of antimicrobial resistance – including previous exposure to antimicrobials in hospital-acquired pneumonia), and other factors, such as the risk of previous exposure to antimicrobials or healthcare environments, for example, hospital-acquired pneumonia.</li>
</ul>
Domain 4b. Use of antimicrobial agents
<ul>
<li>Selects appropriate antimicrobial regimens paying due consideration to local and national guidance (for example from NICE and UKHSA, such as SSTF and CARES), including how, and where, to access this.</li>
<li>Selects appropriate antimicrobial regimens according to site of infection and anticipated pathogen groups and understands the concepts of empirical therapy and pathogen-directed therapy.</li>
<li>Understands the key elements of prescribing an antimicrobial, such as Five Rights of antibiotic safety as right patient, drug, dose, time, and duration, pharmacokinetics and how this affects the choice of dosage regimen; how to monitor levels (therapeutic drug monitoring) and adjust doses (for example in obesity, the elderly or renal impairment), and when to consider review/stop dates.</li>
<li>Uses local or national empirical therapy guidelines when prescribing empirical antimicrobial therapy and understands.</li>
<li>Knows the common side-effects, including allergy, drug/food interactions, drug/disease interactions.</li>
<li>Diagnoses and documents patient allergies to antimicrobials accurately.</li>
</ul>
Domain 5. Antimicrobial stewardship principles
<ul>
<li>Documents the clinical indication, degree of diagnostic certainty, route, dosing regimen, duration, and review date.</li>
<li>De-escalation: Switches to the correct antimicrobial when susceptibility testing indicates resistance, or to a narrower spectrum.</li>
<li>Parenteral-to-oral switch: Understands the importance of timely intravenous-to-oral switch and demonstrates the application of appropriate criteria to identify patients eligible for switch.</li>
<li>Conducts post-prescription review of antimicrobial therapy for hospital inpatients on all ward rounds 48 hours after initiation, appropriately selecting and documenting the prescribing decision in accordance with SSTF.</li>
</ul>
Domain 6. Monitoring, learning, and interprofessional collaborative practice
<ul>
<li>Establishes collaborative communication principles and actively listens to other professionals.</li>
<li>Engages the views of others involved in antimicrobial treatment policy decisions, including championing best practice.</li>
<li>Engages regularly in team-based measurement of the quality and quantity of antimicrobial use and prescribing audits.</li>
</ul>
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<tr><td>Study 3</td><td>
As highlighted by Study 2, AMS is an organisational approach necessitating collaboration among healthcare professionals. Furthermore, AMS implementation and antibiotic prescribing behaviour was impacted during the COVID-19 pandemic. Subsequently, Study 3 was conducted to explore the knowledge, attitudes, and perceptions of healthcare professionals towards antibiotic prescribing and antimicrobial stewardship practices during the COVID-19 pandemic.<br><br>
Domain 3. Antimicrobial resistance and antimicrobials
<ul>
<li>Understands that the appropriate use of antimicrobials, including spectrum of activity and treatment duration, reduces the emergence of resistance, and the concept of narrow-spectrum and broad-spectrum antimicrobials, the importance of using narrow spectrum antimicrobials where possible, and the contribution of broad-spectrum antimicrobials to AMR.</li>
<li>Understands clinical situations where broad-spectrum antimicrobials are warranted instead of narrow spectrum, and the burden of antimicrobial resistance to society, the importance of surveillance of epidemiological trends in resistance and the consequences of AMR for individual patient health outcomes.</li>
<li>Understands local AMR epidemiology, resistance and susceptibility patterns and use of guidelines, and the basic principles of</li>
</ul>
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| | |
|---|---|
| | susceptibility reports (antibiograms) and other reporting tools and their interpretation.<br><br>**Domain 4. Prescribing antimicrobials**<br>• Interprets microbiology results/reports from the laboratory and knows the significance of preliminary pathogen identification (for example gram stain) for selecting initial treatment and common methods of testing for antimicrobial resistance.<br>• Selects appropriate antimicrobial regimens paying due consideration to local and national guidance.<br>• Understand the decisions to switch agent (for example from intravenous to oral, narrower to broader spectrum or vice versa) based on microbiological results.<br>• Uses local or national empirical therapy guidelines when prescribing empirical antimicrobial therapy and understands how local microbial/antimicrobial susceptibility patterns impact on the choice of empirical therapy.<br><br>**Domain 5. Antimicrobial stewardship principles**<br>• Avoids the unnecessary use of broad-spectrum antimicrobials.<br>• Promotes best practice approaches to prescribing antimicrobials and ensures adherence to guidelines.<br>• Understands the importance of timely intravenous-to-oral switch and demonstrates the application of appropriate criteria to identify patients eligible for switch.<br>• Conducts post-prescription review of antimicrobial therapy for hospital inpatients on all ward rounds 48 hours after initiation, appropriately selecting and documenting the prescribing decision in accordance with SSTF.<br>• Promotes capacity to search for reliable sources of unbiased/unconflicted information on the best use of antimicrobials.<br><br>**Domain 6. Monitoring, learning, and interprofessional collaborative practice**<br>• Develops trusting and collaborative relationships with other health/social care professionals when managing infections.<br>• Establishes collaborative communication principles and actively listens to other healthcare professionals.<br>• Understands the roles, responsibilities, and other health professionals involved in the prescription as microbiology, the principles of AMS stewardship; and the impact of COVID-19 pandemic on AMS practices.<br>• Engages regularly in team-based measurement of the quality and quantity of antimicrobial use and prescribing audits and understands the significance of sharing results and good practice with all prescribers, as well as informing future antimicrobial surveillance and infection prevention and control measures.<br>• Understands important human factors that can influence antimicrobial prescribing and understands the implications for AMS.<br>• Explore the basic principles of behaviour change in the context of prescribing antimicrobials, how prescribing antimicrobials can be influenced by factors other than clinical need and measures to prevent this and demonstrates good prescribing habits.<br>• Identify the common antimicrobial stewardship structures and processes deployed by healthcare organisations (for example multidisciplinary committees, monitoring quantity and quality of antibiotic prescribing; root cause analysis; education; audit and feedback; prescribing restrictions; antibiogram; drug formularies; guidelines and digital decision-support).<br>• Engages in national antimicrobial stewardship initiatives aimed at supporting national policy and quality improvement. |

AMS, antimicrobial stewardship; COVID-19, coronavirus; DDD, Defined Daily Dose; DOTs, Days of Therapy; SSTF, Start Smart Then Focus; WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; PP, pre-pandemic; DP, during-the-pandemic; CURB-65, Confusion, Urea, Respiratory rate, Blood pressure, 65 years of age and older; NICE, National Institute for Health and Care Excellence; UKHSA, UK Health Security Agency, AWaRe, Access, Watch, and Reserve; and IV, intravenous.

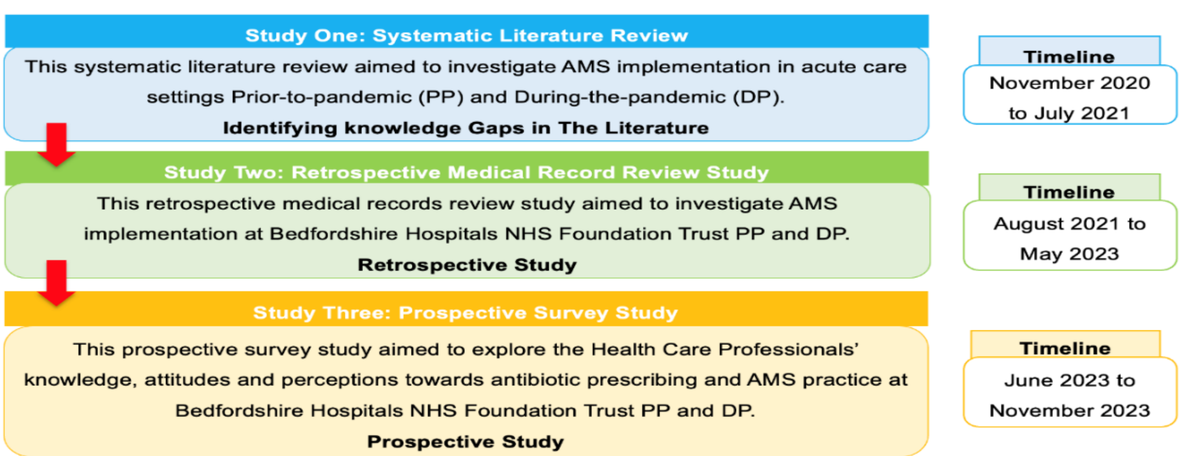
## 2.6 Methods overview

This research project required a combination of retrospective and prospective research methods to achieve its aim and objectives. A comprehensive systematic literature review, designated as Study 1, was conducted to explore the implementation of antimicrobial stewardship in hospitalised adult patients in acute care settings both prior to and during the COVID-19 pandemic. This review explored the strategies, measures, and tools used for AMS implementation in acute care settings. It also identified healthcare professionals, including doctors, pharmacists, and nurses. These insights were subsequently applied in Study 2 to evaluate antibiotic prescribing practices and assess the prevalence of inappropriate antibiotic prescribing in an acute care setting in England. Study 2 investigated AMS implementation in acute care settings prior to and during the pandemic.

This retrospective study involved extracting primary data from 640 electronic patient records, which were then analysed using descriptive and regression analyses with the statistical package for the social sciences (SPSS) software. This study evaluated AMS implementation and the prevalence of inappropriate antibiotic prescribing both PP and DP and identified factors influencing inappropriate antibiotic prescribing in an acute care setting during these periods. As revealed in Study 2, AMS implementation necessitates collaborative efforts among healthcare professionals to ensure the judicious use of antibiotics. It was crucial to explore how antibiotic prescribing behavior was affected during the COVID-19 pandemic.

The subsequent prospective survey study, referred to as Study 3, involved 240 healthcare professionals, including doctors, pharmacists, and nurses. Its design was aligned with the research objectives, drawing on insights from the preceding literature review and the PHE analysis of behavioural changes in antibiotic prescribing within secondary care setting (PHE, 2019). Study 3 further investigated the issues of inappropriate antibiotic prescribing and AMS implementation strategies identified in Study 2. Additionally, it explored healthcare professionals' understanding, attitudes, and perceptions regarding antibiotic prescribing and AMS practices, during the pandemic. The collected anonymous questionnaire responses were analysed through descriptive and regression analyses using the SPSS software. The outcomes of Study 3 also examined the impact of the COVID-19 pandemic on AMS practices. In terms of project design, this research encompasses three sequential studies designed to comprehensively address all the planned objectives, as illustrated in the flowchart (Figure 2.4).

**Figure 2.4.** Description of the research project: three sequential studies.




AMS, antimicrobial stewardship; PP, prior-to-pandemic; DP, during-the-pandemic; and NHS, National Health Service.

### 2.7. Ethical approval and ethical consideration

To enable these studies, an NHS ethical application was submitted to the Research Ethics Committee (REC) and the Confidentiality Advisory Group (CAG) with the aim of securing ethical approval from the Health Research Authority (HRA), in addition to the UH ethical approval. The procedures and results of the application are detailed in Table 2.3.

In this chapter, the chosen research methods for investigating the AMS implementation PP and DP at the Foundation Trust were justified. Existing evidence highlighted the lack of recent studies and limited research focusing on AMS implementation PP and DP. Data collection for this study involved the use of a prospective survey and a retrospective review. Data from the retrospective study are anonymised and then stored in the university's dual secure system. Additionally, the responses from the prospective study were completely anonymised. All data from the studies are anonymised and stored on the University's secured network storage system, which requires a double security check. Following the completion of the PhD, all electronic files will be destroyed.

In this research project, all potential ethical considerations were addressed. Ethical approval was secured from the UH Ethics Committee and the HRA prior to initiating the project at the Bedfordshire Hospitals NHS Foundation Trust.

In England, Wales and Northern Ireland, legal arrangements are in place for considering whether disclosing personal information without consent for health and social care purposes would benefit patients or the public sufficiently to outweigh patients' right to privacy. Examples of these purposes include medical research and the management of health or social care services. Section 251 of the National Health Service Act 2006 (which applies in England and Wales) and the Health and Social Care (Control of Data Processing) Act (Northern Ireland) 2016 allow the common law duty of confidentiality to be set aside for defined purposes where it is not possible to use anonymised information and where seeking consent is not practicable (General Medical Council, 2017). Application to Confidentiality Advisory Group (CAG) was required. However, the Health Research Authority may not approve unless a research ethics committee (REC) has approved the medical research concerned. However, with the new General Data Protection Regulations (GDPR) that came into effect on 25/05/2018, a data subject may wish to opt out of the Section 251 arrangements (HRA, 2018). Unfortunately, in this study, the information governance team excluded patients who had registered with data opt-out. It was not possible to estimate the number of excluded patients who had opted out of data sharing. This limitation affects the comprehensiveness of the study. The GDPR emphasises the importance of lawful, fair, and transparent handling of personal data by organisations. This includes a legal mandate for processing identifiable patient data (HRA, 2018).

In this research project, the process undertaken to secure NHS Ethics approval is detailed in Table 2.3. The initial protocol was prepared to address the research questions, drawing on prior literature in related fields. Prior to submission to the HRA, this protocol was reviewed by several key parties, including the CAG, hospital collaborators, and the Research and Development (R&D) department of both the University and the Foundation Trust. Subsequently, making the necessary amendments. The protocol was also registered with and uploaded to ISRCTN, in accordance with WHO criteria (ISRCTN, 2018) (see Appendix 18).

The research process commenced with the submission of a completed Integrated Research Application System (IRAS) form and research protocol to the University, which granted 'In Principle' sponsorship approval for the project. Following this, a letter of recommendation was procured from a Caldecott Guardian at UH. The subsequent steps included the submission of the fully completed IRAS form and the CAG application form, along with supporting documents, to CAG (as shown in Table 2.3). In March 2022, the initial application was sent to the Brighton & Sussex REC. The protocol was submitted to the HRA via the REC and the CAG on the IRAS system. Unfortunately, the initial application received an unfavourable opinion. Following this, in April 2022, the CAG provisionally approved the application. The CAG requested amendments to certain aspects of the form.

After receiving unfavourable opinions from Brighton REC, the research student, along with the supervisors, devoted significant effort to addressing the comments and providing a response to each one. Furthermore, the research student collaborated with the hospital collaborators from the pharmacy department, including the AMS pharmacist, to further clarify the anonymisation procedures for the data, as well as the details of the data extraction process. Subsequently, the principal supervisor conducted mock meetings with the research student to ensure preparedness for the REC Committee meeting. For further details regarding the responses to the REC comments, please refer to Appendix 23. The IRAS application was updated and resubmitted to the East Midlands - Leicester South REC in July 2022, which subsequently requested additional information. By 10 September 2022, all the necessary documents and information had been resubmitted to the REC, leading to a positive outcome and a favourable opinion (Appendix 24).

Ethical approval for this study was granted by HRA on 29 September 2022., with the REC assigning reference number 22/EM/0161. Subsequently, the researcher submitted all the required documents to UH Ethics, which then issued the UH Ethics approval ethics committee under the reference LMS/PGR/NHS/02975. Furthermore, these HRA approvals and the final IRAS application were submitted to the R&D of the Bedfordshire Hospitals NHS Foundation Trust to assess their capacity and capability for hosting this research project. Unfortunately, this caused a significant 8-month delay in the start date of the retrospective study. The 'Gantt Chart' was updated after that to reflect this delay. Please refer to the attached 'Gantt Chart' in Appendix 2. The research student commenced retrospective data extraction in

October 2022. Table 2.3 shows that each step in this chronology represents a significant milestone in the rigorous ethics approval journey, confirming that the research adheres to the ethical standards required for conducting medical research within the NHS framework.

**Table 2.3.** The undertaken process to secure NHS Ethics for this research project.

| Period | Application | Definitions and Activities | Decision |
|---|---|---|---|
| **NHS Ethics/ Brighton REC Committee/ March 2022** | Application submitted to **London - Brighton & Sussex REC** | • HRA is responsible for a range of committees and services needed to ensure that UK-based research is underpinned by respect for patients and the public.<br>• Research Ethics Committee (REC): Each REC consists of 15 members.<br>• A third of these members have no main professional interest in research and are non – registered health care professionals.<br>• The main objective of REC is to review research proposals and give an opinion on whether the research is ethical.<br>• Integrated Research Application System (IRAS): A single system for applying for approval from HRA and REC.<br>• The Committee meeting was conducted in March 2022. | Unfavourable Opinion |
| **CAG Committee April 2022** | Application submitted to CAG on April 2022 | • Confidentiality Advisory Group (CAG): Provides expert advice to HRA or Secretary of State for Health (known as section 251 support) on the use of confidential patient information in patients who are unable to provide a consent.<br>• It allows the HRA or the Secretary of State to take the final decision.<br>• It promotes and protects the interests of patients and the public but will facilitate the use of confidential patient information in research if there is a need to do so. | Provisional approval for further documents and waiting for REC approval |
| **NHS Ethics July 2022** | Application resubmitted again to **East Midlands - Leicester South REC** | • This Committee meeting has been conducted on 28th July 2022.<br>• The PhD student/PI and Chief Investigator schedules two previously meeting for the Committee preparedness.<br>• They also attended this meeting and answered all questions related to the research study design. | Provisional Outcome, require further information |
| **NHS Ethics September 2022** | Further information submitted to **East Midlands - Leicester South REC** | • The Committee requested additional information about the Clinical Negligence process, and some other information, such as primary outcomes, antimicrobial hospital guidelines that used in the analysis, copy of the systematic literature review and other changes.<br>• The requested further information has been submitted to the Committee on 2nd September 2022, including the clinical negligence flow diagram and other requested information. | Favourable Outcome |
| **HRA Decision** | The final approval letter was released | • The HRA approval letter was provided on 29th September. | HRA approved |
| **UH ethics** | Submitted all the required documents | • The research student applied for the UH ethics, by sending the Protocol, IRAS form, HRA ethical approval letter, Participant Information Sheet, Informed Consent, Participant poster.<br>• The UH ethics is issued, and the research student started the research project at Bedfordshire Hospitals NHS Foundation Trust | UH ethics approval |

HRA, Health Research Authority; REC, Research Ethics Committee; IRAS, Integrated Research Application System; CAG, Confidentiality Advisory Group; PhD, Doctor of Philosophy; PI, Principal Investigator; NHS, National Health Service; and UH, University of Hertfordshire.

## Summary of this chapter

This chapter encompasses details concerning research methods and methodology, as well as ethical considerations. The subsequent chapter presents a systematic literature review conducted to investigate the implementation of AMS in acute care settings prior to and during the COVID-19 pandemic.

# Chapter 3

# Systematic Literature Review

# Chapter 3: Study 1 - Exploring Antimicrobial Stewardship Implementation Prior to and During the COVID-19 Pandemic in Acute Care Settings: A Systematic Literature Review.

## 3.1. Introduction:

This chapter presents a systematic literature review conducted to investigate the AMS implementation in acute care settings prior to and during the COVID-19 pandemic. The review provides valuable insights into the research problem, highlights the role of pharmacists in AMS, and explores both core and supplemental AMS strategies, measures, and quality improvement projects undertaken during this period.

Antimicrobial resistance is a silent pandemic and one of the greatest threats to global health (WHO, 2019). In 2019, it was estimated that more than 1.2 million people worldwide died due to AMR (Murray et al., 2022). AMS comprises a coherent set of actions that promote the effective use of antibiotics, aiming to ensure the optimal selection, dosage, route, and duration of antibiotic treatment (NICE, 2015). Public Health England has emphasised the necessity of AMS implementation to maintain appropriate antibiotic use (PHE, 2015). AMS strategies are crucial in addressing AMR across all healthcare settings. These strategies include various tools, interventions, and activities designed to streamline and enhance antimicrobial use and educate prescribers (ESPAUR, 2021). Epidemiological studies have shown a direct relationship between antimicrobial use and the emergence of resistant strains, advocating a multi-step approach to enhance AMS strategies (Barlam et al., 2016).

The process of prescribing antibiotics involves several steps: diagnosing an infection, starting treatment according to local guidelines, and continually adjusting the therapy based on emerging clinical data (BSAC, 2015). Interventions targeting different points of the antibiotic prescribing pathway have proven clinically effective for hospital inpatients, resulting in increased appropriateness of antibiotic therapy, reduced consumption and duration of antibiotic therapy, and shorter hospital stays (Montrucchio et al., 2019). Evidence suggests that the pandemic has led to an increase in empirical antibiotic prescribing, which may not always be appropriate, potentially contributing to the global rise in resistant infections (Murgadella-Sancho et al., 2021; Zhou et al., 2020). Therefore, considering AMR and AMS, with a focus on the selection of optimal empirical therapies and appropriate de-escalation or discontinuation of antimicrobials, is essential when bacterial co-infection is present or absent (Hamidi et al., 2021).

Previous systematic reviews indicate a co-infection prevalence with resistant bacterial organisms of 24%, with 569 (29%) of 1959 unique isolates identified as resistant (Murgadella-Sancho et al., 2021). Another systematic review and meta-analysis found high antimicrobial consumption among COVID-19 patients (Khan Muhammad et al., 2021). Finding an existing systematic review with similar objectives and using the same databases proved challenging. Akpan et al. thoroughly examined ASPs in hospital settings, specifically focusing on patient outcomes. Their extensive analysis covered 63 studies, comprehensively assessing a wide range of ASP strategies and their effects on antimicrobial usage, expenditure, resistance patterns, infection rates, mortality, length of hospital stay, and readmission rates (Akpan et al., 2016). In another systematic review by Mas-Morey et al., the authors assessed ASPs involving clinical pharmacists in small-to-medium-sized hospitals, encompassing 28 studies primarily from American or Canadian institutions. This review revealed that these ASPs, while not significantly impacting mortality or readmission rates, resulted in substantial cost savings due to reduced or more cost-effective antibiotic usage. The authors emphasised the need for further research and the establishment of standardised methods to assess ASP outcomes. However, their focus remained solely on pharmacists, without including broader AMS implementation strategies and measures in the search criteria (Mas-Morey et al., 2017). Despite these findings, AMS intervention strategies, measures, and quality improvement data have not been extensively published. A critical knowledge gap exists regarding AMS implementation strategies in acute care settings.

This systematic review addressed the research question: “What are the strategies and measures implemented for AMS in acute care settings prior-to-pandemic (PP) and during-the-pandemic (DP)?” The objectives were to (1) review AMS implementation strategies and measures PP and DP; (2) assess the geographic distribution and characteristics of acute care settings implementing these strategies; (3) clearly differentiate between AMS strategies (interventions) and measures (outcomes or metrics used to evaluate the effectiveness of the strategies); and (4) estimate the proportion and types of each strategy and measure reported in the literature.

## 3.2. Method:

### 3.2.1. Search Terms

Prior to the initial search, the review was registered at PROSPERO website (registration number CRD42021242388) (York.ac.uk, 2022) (Appendix 4). The scope of the review was defined by applying the acronym PICOS (Population, Intervention, Comparison, Outcome, Setting), as shown in Table 3.1. A systematic search of databases was conducted using the following keywords and their synonyms (Appendix 7). After this, follow the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines for reporting. The PRISMA 2020 was drawn up and approved by the research team before the commencement of the systematic review (Page *et al*., 2021). The systematic literature review aimed to explore AMS implementation in acute care settings from 2000 to 2021, including the pandemic period. The plan, serving as a guidance document, outlined the review's scope, purpose, and methodological approach. It focused on comparing AMS implementation strategies pre- and post-pandemic within the same studies where possible, to identify effective measures used during crises. This comparison highlighted successful implementation strategies during the pandemic. Ethical approval was not required before the commencement of the review as the use of patients' identifiable data was not intended.

An electronic search of PubMed, OVID journals, CINAHL PLUS, PsycINFO, SCOPUS, Web of Science, Cochrane, and Google Scholar (Wilczynski *et al*., 2004). Choices of databases to be searched were based on insights from the method's section-related reviews. The search was restricted to articles published from January 2000 to March 2021. The AMS strategies and metrics identified within the MEDLINE database through the MeSH term 'antimicrobial stewardship' were employed as search terms for AMS intervention. The search was restricted to English to ensure data accuracy, comprehension, and consistency in analysis. The exact number of excluded non-English papers was not available. Antibiotic use before and during the COVID-19 pandemic was employed as the search term. Settings were specified as acute care settings, AND/OR were used to combine search terms (Table 3.1). The 'snowballing' strategy, going through the reference list of all included studies to obtain further relevant studies, was also employed. The search term combination is detailed in Appendix 7.

**Table 3.1.** The systematic literature review search strategy.

| **Search Strategy** |
|---|
| 1. Antimicrobial resistance OR antibiotic management OR acute care settings OR hospitals. |
| 2. Antimicrobial stewardship OR antimicrobial utilisation OR antimicrobial use OR antimicrobial stewardship strategies OR antibiotic metrics OR antimicrobial stewardship intervention OR antimicrobial stewardship outcomes OR antibiotic use. |
| 3. COVID-19 OR coronavirus OR SARS CoV2 OR severe acute respiratory infection OR pandemic. |
| 4. 1 AND 2 AND 3 |
| 5. Limit 18-65 to yr. = '2000-2021' = lang: 'English' |

COVID-19, Coronavirus; and SARS CoV, Severe Acute Respiratory Syndrome Coronavirus.

The databases searched for this study included PubMed, OVID journals, CINAHL PLUS, PsycINFO, SCOPUS, Web of Science, Cochrane, and Google Scholar. These were selected based on a review of methodologies in other published systematic reviews relevant to this research. Additionally, the researcher's experience from conducting previous systematic reviews informed the choice of databases. A rationale for selecting each database is detailed in Table 3.2. All search results were exported to

Mendeley, which served as a reference manager and facilitated de-duplication. The search was limited to English-language articles.

**Table 3.2.** The rationale behind selecting each database used to conduct the systematic literature review.

| Database | Rational |
|---|---|
| PubMed | Free full-text database that covers MEDLINE and EMBASE journals from life and biomedical sciences, including papers not yet indexed in MEDLINE. |
| Scopus | Freely available; one of the most substantial citations and abstract database of peer-reviewed literature, including journals and conference abstracts. |
| PsycINFO | This weekly updated database is considered the most significant resource in mental and behavioural sciences, including different types of literature, such as dissertation abstracts. |
| CINHAL Plus | Covers a wide range of health topics, including nursing, health and allied medical sciences. |
| Web of Science | Consists of many databases and citations, including Conference Proceedings Citation Index – Social Science & Humanities and MEDLINE. |
| All Ovid journals | Include numerous journals, including health and medical journals. |
| OpenGrey | Consists of grey literature, including research reports, doctoral dissertations, and several conference papers. |

PubMed, Public/Publisher MEDLINE; MEDLINE, Medical Literature Analysis and Retrieval System Online; EMBASE, Excerpta Medica Database; Scopus, A comprehensive abstract and citation database; PsycINFO, Psychological Information Database; and CINAHL Plus, Cumulative Index to Nursing and Allied Health Literature.

### 3.2.2. Studies selection

The selection of studies for this review was based on specific inclusion criteria: (i) Peer-reviewed English articles; (ii) Population of patients prescribed antibiotics aged 18 years and over; (iii) Studies describing the AMS intervention in acute care settings; (iv) Outcomes of AMS strategies, measures, metrics before and during the COVID-19 pandemic; (v) Primary studies; and (vi) Published between 2000 and 2021. The included study designs were observational (retrospective or prospective case-control, case series non-interventional, cross-sectional, cohort) and interventional (quasi-experimental, randomised controlled trials) studies.

However, studies that did not meet these inclusion criteria, those unrelated to the review objectives, abstract-only papers, studies not involving human subjects, and literature and systematic review studies were excluded from this review (Table 3.3).

**Table 3.3.** Criteria for inclusion and exclusion studies in the systematic literature review.

| | Inclusion criteria | Exclusion criteria |
|---|---|---|
| **Participants** | Studies targeting the public/patients' use of antibiotics. HCPs who are responsible for prescribing, dispensing, or administering antibiotics (doctors, pharmacists). | Non-HCPs (patient family or community or nursing or long-term care patients). |
| **Intervention** | Studies describe an intervention to improve antibiotic prescribing or AMS or any other intervention as the use of the parenteral-to-oral switch and the duration of IV and oral antibiotics. | Studies that do not describe an AMS intervention. |
| **Comparison** | Comparison with a control group/a group that carried out usual care without an AMS intervention; comparison between two or more AMS interventions. | |
| **Context** | Interventions carried out in adult inpatient settings in acute care hospitals. | Interventions carried out in nursing homes, care homes or long-term healthcare facilities; community settings; paediatric setting/hospital; and animals/ veterinary practice. |
| **Outcomes** | Primary outcomes: reviewing the AMS implementation before and during the COVID-19 pandemic. | |
| | Secondary outcomes: other AMS measures, metrics, and quality improvement before and during the pandemic. | |
| **Study design** | Randomised Controlled Trials (RCTs), non-randomised trials, Controlled Before-After (CBA) studies, interrupted time series designs, case-control and cohort studies, cross-sectional studies, and qualitative studies. Peer-reviewed articles from recognised scholarly journals. Grey literature sourced from Open Grey, contingent upon verification of rigorous peer review credentials similar to those required for journal articles. | Literature reviews, systematic reviews, meta-analyses, single case studies, case reports, and conference abstracts. |

HCPs, healthcare professionals; AMS, antimicrobial stewardship; COVID-19, coronavirus; RCTs, randomised controlled trials; and CBA, controlled before and after.

### 3.2.3 Data extraction and synthesis

The articles retrieved from the databases were exported into CSV and Excel sheets for screening and identification of the eligible articles by RAE. Titles and abstracts were screened for relevance; duplicates were removed, followed by a screening of the complete articles for possible inclusion by one reviewer (RAE). Another reviewer (ZA) independently reviewed the titles, abstracts, and full studies, confirmed the relevance of studies in meeting the inclusion criteria and excluded studies deemed irrelevant. Three reviewers (ZA and NU) screened the first 60 records to establish the quality of screening at this stage and ascertain that the level of agreement and discrepancies were addressed through mutual consensus among the reviewers. Additional suggestions and amendments to the search teams and relevant keywords were made. There was complete agreement on the relevance of selected studies by RAE, ZA and NU. Data extraction forms were created by the primary reviewer (RAE). It included the author's last name, year of study, country, study design, the AMS intervention strategies, AMS outcome measures, and quality of study analysis (Table 3.4) (Appendix 12).

Three studies were initially piloted to test the form. RAE extracted the data from these three studies into the data extraction tool, and any discrepancies in the extracted data were discussed with the other authors. Data obtained were grouped and summarised into two groups using narrative synthesis, PP and DP (Mino et al., 2023) (Table 3.4.). RAE extracted the data for the included studies. In order to maintain the reliability and validity of the data extraction, another author (AB) independently extracted the data from the included studies into data extraction form. Discrepancies in the extracted data were documented and resolved by discussion or adjudication with a third author (ZA). Meta-analysis could not be performed because of the heterogeneity of the included studies. For all the articles included (as shown in Table 3.4.), the following data were extracted: the author of the study, the year it was conducted (identifying if it was prior to or during the COVID-19 pandemic), the country of the study, the design of the study, the antimicrobial stewardship strategies used, and the measures for antimicrobial stewardship including any quality improvement projects. In this review, the PHE toolkit of AMS was used as a gold standard for analysing AMS implementation. AMS strategies were categorised into AMS core & supplemental strategies according to the AMS toolkit into core and supplemental strategies (PHE, 2015). Additionally, the practical guide for AMS implementation and measures was used in the analysis (BSAC, 2019)

### 3.2.4 Quality assessment

This systematic review necessitated a rigorous quality assessment of the included studies, which featured a variety of designs. The Mixed Methods Appraisal Tool (MMAT) was selected for this evaluation due to its well-documented reliability and efficacy in appraising mixed-method systematic reviews (Souto et al., 2015). Although initial iterations of the MMAT encountered criticism regarding the clarity of questions for qualitative assessments, these shortcomings were addressed in the revised 2018 version, which significantly enhanced its utility (Hong et al., 2018).

The 2018 version of the MMAT, complete with a comprehensive user guide, was utilised because it provides established content validity and practical applicability in mixed-method systematic reviews. This tool was chosen over other options due to its specific enhancements and its alignment with the requirements for evaluating mixed-method studies, rendering it the most appropriate choice for this review. The Mixed Methods Appraisal Tool (MMAT) comprises only five core questions for each type of study design (qualitative, quantitative, and mixed methods). These questions are designed to assess the methodological quality of the studies by evaluating various aspects such as the clarity of the research question, the appropriateness of the methodology, and the coherence of the study design and data collection. This streamlined approach helps in providing a comprehensive yet concise evaluation of the studies' methodological rigour.

After conducting database searches and eligibility screening to identify the final studies, three authors (RAE, NA, and ZA) independently conducted a quality appraisal of each study. Two independent reviewers evaluated a stringent methodology. This was followed by discussions to consolidate findings and ensure the comprehensive nature of the quality assessment. The quality assessment of the studies included in this systematic literature review was performed using the 2018 MMAT tool, as detailed in Table 3.4 below.

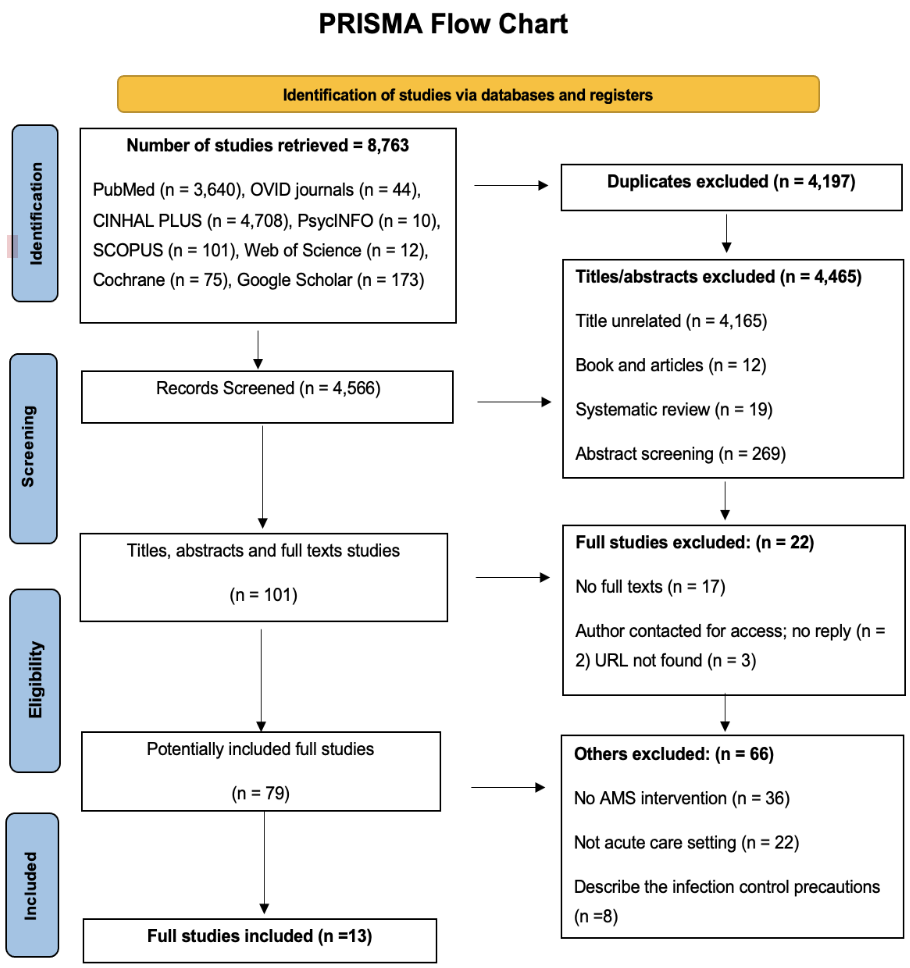
### 3.2.5 Reliability and validity

Reliability is defined as the ability to conduct a search process repeatedly and yield consistent results (Ali & Usman, 2018). Repeatability in systematic reviews means an external researcher can replicate the review process and identify the same set of papers (Ali & Usman, 2018). To enhance repeatability in this study, the PRISMA flow diagram and PRISMA systematic review and meta-analysis protocol checklist were employed. The entire search strategy for each database is detailed in Table 3.4. Consistency in a systematic review ensures that an external researcher searching the same topic produces the same data (Ali & Usman, 2018). In this systematic literature review, the inclusion and exclusion criteria significantly influence the number of studies included in a review. However, in order to ensure validity and reliability, two independent reviewers (RAE and ZA) performed the screening of titles, abstracts, and full texts. Data extraction was also independently conducted by RAE and AB, with their findings compared by adjudicator ZA. Discrepancies were resolved through dialogue until a consensus was reached. The authors (RAE, ZA, and NU) engaged in discussions to consolidate these findings. Additionally, quality assessment was carried out independently by RAE and ZA to ensure a comprehensive evaluation.

## 3.3. Results:

A systematic literature search was conducted from the 9th to the 13th of March 2021 using predefined search terms and updated on the 20th of March 2023 and the 24th of November 2023. This search yielded 8,763 articles, with the screening process outlined in the PRISMA flow diagram (Figure 3.1.) and the included articles summarised in Table 3.4. The initial search produced 8,763 abstracts potentially eligible for inclusion: MEDLINE (n=3,640), all OVID journals (n=44), CINHAL PLUS (n=4,708), PsycINFO (n=10), SCOPUS (n=101), Web of Science (n=12), Cochrane (n=75), and an additional 173 from Google Scholar. After duplicates were removed, 4,566 articles proceeded to title and abstract screening. Of the 101 articles eligible for full-text screening, 79 met the inclusion criteria (Figure 3.1.). Sixty-six articles were excluded for not meeting the inclusion criteria due to lack of AMS intervention (n=36), inappropriate study settings (n=22), or irrelevant outcomes such as infection control precautions (n=8). Ultimately, 13 studies were included in the final analysis (Figure 3.1).

**Figure 3.1.** Systematic literature review results and screening process according to PRISMA guidelines.




PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; OVID, Online Database of Medical Journals; CINAHL PLUS, Cumulative Index to Nursing and Allied Health Literature PLUS; PsycINFO, Psychology Information Database; SCOPUS, A comprehensive abstract and citation database; and AMS, antimicrobial stewardship.

### 3.3.1 Study characteristics

The geographical origin of the 13 studies was as follows: United States (n = 4) (Trivedi and Rosenberg, 2013; Tamma *et al*., 2021; Weston *et al*., 2013 and Mehta *et al*., 2014), United Kingdom (n = 2) (Ashiru-Oredope *et al*., 2021and Williams *et al*., 2021), India (n = 2) (Thakkar *et al*., 2021 and Panditrao *et al*., 2021), Germany (n = 1) (Surat *et al*., 2021), Netherlands (n = 1) (Kallen *et al*., 2021), Jordan (n = 1)

(Ababneh *et al*., 2020), Japan (n = 1) (Moriyama *et al*., 2021), Greece (n = 1) (Spernovasilis *et al.*, 2021). 10 of 13 (77%) studies were conducted before the pandemic. However, only 3 of 10 (23%) studies were conducted during the COVID-19 pandemic (Spernovasilis *et al*., 2021; Ashiru-Oredope *et al*., 2021; Williams *et al*., 2021). The following study designs were identified: retrospective cohort (n = 2) (Surat *et al.,* 2021and Williams *et al*., 2021), cross-sectional (n = 6) (Trivedi and Rosenberg, 2013; (Weston *et al*., 2013; Moriyama *et al*., 2021; Spernovasilis *et al*., 2021; Spernovasilis *et al*., 2021 and Ashiru-Oredope *et al.,* 2021), prospective cohort (n = 2) (Tamma *et al*., 2021 and Thakkar *et al*., 2021), Quasi-experimental study (n= 2) (Mehta *et al*., 2014 and Panditrao *et al*., 2021), and 1 Randomised clinical trial (Kallen *et al*., 2021). The overall quality rating in Table 3.4 is represented by the percentages (%), which indicate the proportion of studies that met specific quality criteria as assessed by the Mixed Methods Appraisal Tool (MMAT). Each percentage shows how many of the included studies satisfied the predefined methodological standards. The results column summarises the overall findings of each study, highlighting key outcomes such as positive, negative, or mixed results based on the research objectives and data analysis. This information provides a snapshot of the study's quality and main conclusions. For example, the studies by Kellen et al. and Ashiru-Oredope et al. (2021) met 100% of the quality criteria, while the study by Panditrao et al. (2021) met 80% of the criteria (Table 3.4).

Table 3.4. A total of 13 articles were included in the synthesis of this systematic literature review.

| Study | Country | Study type | AMS strategies | AMS Measures/Metrics | Overall Quality Rating (%) |
|---|---|---|---|---|---|
| **Prior to COVID-19 Pandemic** | | | | | |
| (Trivedi *et al*., 2013) | United States | Cross-sectional study | - AMS core strategies included formulary restriction, antibiotic review, automatic stop orders, preauthorisation, and prospective review with feedback.<br>- AMS supplemental strategies included education, dose optimisation, dose adjustments, guidelines and clinical pathways, parenteral-to-oral switch, streamlining de-escalation, and antimicrobial order forms. | - Outcomes measured included antimicrobial resistance patterns (39%), antimicrobial utilisation (36%), antimicrobial costs (35%), Clostridium Difficile infection rates (32%), adverse effects (22%), 17% reported monitoring DDD and 13% reported monitoring DOT.<br>- For a positive trend in outcomes data since the initiation of the ASP, including improved antimicrobial use (74%), decreased antimicrobial costs (63%), improved antimicrobial susceptibility patterns (47%), and 38% used computer software to interface with electronic records facilitated AMS. | ***<br>60% |

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|---|---|---|---|---|---|
| (Kallen, *et al.*, 2017) | Netherlands | Randomised clinical trial | - Data extraction and feedback on the overall antibiotic use.<br><br>- Point Prevalence Study of the European Centre for Disease Prevention and Control (PPS-ECDC) was conducted to provide feedback on validated Quality Indicators (QIs) for appropriate antibiotic use (PPS-QI), such as IV-to-oral switch projects (43%) and projects focusing on appropriate treatment for patients with pneumonia (21%) or the appropriate use of restricted antibiotics (19%). | Primary outcome<br><br>The geometric mean Length of Stay (LOS) was 9.5 days (95% CI 8.9–10.1, N=4245 patients) at baseline versus 8.7 days (95% CI 8.1–9.2, N=4195 patients) after intervention while adjusting for dependencies within clusters and potential confounders. After adjusting for the secular trend, the estimated decrease in geometric mean LOS was 0.5 days: 9.5 days (95% CI 8.9–10.1, N= 4245 patients) at baseline versus 9.0 days after intervention (95% CI 8.5–9.6); P<0.001, N= 4195 patients.<br><br>Secondary outcomes<br><br>DOT per 100 admissions decreased from 1320 (95% CI 1253–1387, N= 4245 patients) at baseline to 1185 (95% CI 1119–1252, N= 4195 patients) after the intervention (P<0.001). Similar trends were found for days of IV antibiotics. A larger decrease was found for restricted DOT per 100 admissions (P<0.001). The percentage of patients admitted to the ICU was lower after the intervention (4.8%, N= 201) compared with a baseline (5.9%, N= 251). | *****<br><br>(100%) |
| (Tamma *et al.*, 2021) | United States | Prospective study | Implementation webinars of AMS, antibiotic guidelines, antibiotic time-out, clinical rounds, and antibiotic user guides, identify antibiotic safety and adverse events, antibiotic review, use an innovative strategy of the four moments of antibiotic decision-making framework including make the diagnosis, cultures, empiric therapy, stop, narrow, change to oral antibiotics and duration. | Primary outcome (Unit-Level Antibiotic Use Data):<br><br>- Comparing January-February with November-December 2018, antibiotic use decreased from 900.7 to 870.4 DOT per 1000 PD (−30.3 DOTs; 95%CI, −52.6 to −8.0 DOT; P = .008).<br><br>- Fluoroquinolone use decreased from 105.0 to 84.6 DOT per 1000 PD across all units between January-February and November-December (−20.4 DOT; 95%CI, −25.4 to −15.5 DOT; P = .009).<br><br>Secondary outcome (C difficile identification):<br><br>- The number of hospital-onset C difficile Laboratory-identified events per 10 000 PD across the Safety Program cohort was 6.3 for quarter 1, 5.3 for quarter 2, 6.0 for quarter 3, and 5.1 for quarter 4 in the 2018 calendar year in the participating units. The incidence rate of hospital-onset C difficile Laboratory-identified events decreased from quarter 1 to quarter four by 19.5% (95%CI, −33.5%to −2.4%, P = .03). | ***<br><br>(60%) |

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| (Surat *et al.*, 2021) | Germany | Retrospective study | - AMS multidisciplinary committee and regular ward rounds.<br>- Formulary restriction of specific antibiotics (e.g., tigecycline and colistin).<br>- Creation of selective antibiotic resistogram profiles.<br>- Electronic access to antimicrobial prescribing guidelines and mobile applications.<br>- Introduction of both the surveillance data on antimicrobial resistance and antibiotic consumption rate.<br>- In accordance with the current effective clinical practice guidelines for antimicrobial prophylaxis, the standard prophylactic regime changed from cefuroxime to cefazolin (depending on the procedure, it may differ).<br>- Further targets involved the following antibiotic groups: meropenem, which AMS strived to reduce its usage, and fluoroquinolones, which involved a drastic change in the hospital's general antibiotic policy. | Primary outcome (The primary endpoint was defined as the total DOT for intraabdominal infections): An overall reduction in the total days on antibiotic therapy (ABT) from a mean of 6.1 days to 4.8 days (p = 0.02) was noted in the antimicrobial stewardship program (ASP) period, decreasing the days of therapy per 100 patient days (DOT/100PD) from 47.0 to 42.2 (p = 0.035).<br>Secondary outcome (The secondary endpoints included the appropriateness (indication and documentation) of the postoperative antibiotic therapy (PAT), the empiric selection of antibiotics and the frequency of antibiotic changes):<br>- The rate of patients receiving postoperative antibiotic therapy decreased from 56.8% to 45.2% (p= 0.002) in the ASP period.<br>- A trend of change in the duration of postoperative antibiotic therapy from 8.1 to 7.2 days (p=0.08) was observed.<br>- The individual assessments of postoperative therapy revealed significantly less inappropriate (no indication) postoperative antibiotic therapy, shortened treatment durations (not significant) and an influence on the choice of antibiotics, with the use of more narrow-spectrum antibiotics. | ***<br>(60%) |
| (Weston et al., 2012) | United States | Cross-sectional study. | - Antibiotic restriction, by using new restriction methods, such as front-end back end, automatic stop orders, ID consult required, verbal approval required.<br>- Antibiotic guidelines and clinical pathways, antimicrobial order forms, streamlining or de-escalation, dose optimisation, parenteral-to-oral switch, and closed formulary. | - Combining the results of both surveys, 31 out of 44 (70%) institutions had formal ASP in place. 13 institutions indicated on either survey that they did not have a formal ASP program. 25/38 institutions who responded to the second survey had an existing ASP. | **<br>(40%) |
| Mehta *et al.*, 2014) | United States | Quasi-experimental study. | Prior authorisation and prospective audit with feedback | - The change from prior authorisation to prospective audit with feedback was associated with a significant increase both in the use of the affected antimicrobials and in the overall use of all antimicrobial agents. | ****<br>(80%) |

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| | | | | - Broad-spectrum anti-gram-negative agents that still required prior authorisation during both time periods continued to decline in use after the change in ASP.<br><br>- The overall change in stewardship approach was associated with a significant increase in hospital LOS.<br><br>- During the pre-intervention period, the use of broad-spectrum anti-gram-negative antibiotics was declining at a rate of −4.00 DOT/1,000-PD per month. However, during the post-intervention period, use increased by 0.80 DOT/1,000-PD per month, indicating that the change in ASP was associated with a slope change of 4.80 DOT/1,000-PD per month ($P < .001$).<br><br>- After decreasing during the two years before the ASP change, the use of cefepime and piperacillin/tazobactam significantly increased following the transition to prospective audit with feedback by 3.21 DOT/1,000-PD per month ($P = .003$).<br><br>- Overall use of all systemic antimicrobial agents significantly increased after the change in the ASP method ($P < .001$).<br><br>- Vancomycin use declined before the intervention but significantly increased after the intervention ($P = .005$). The use of non-audited antimicrobials significantly increased after the change in ASP methods ($P < .001$), and the slope during the postintervention period continued to decline at −1.87 DOT/1,000-PD per month.<br><br>- The LOT of all systemic antimicrobials declined before the intervention by −2.30 LOT/1,000-PD per month, and, despite a significant increase in slope ($P = .029$), use continued to decrease after the intervention by −0.33 LOT/1,000-PD per month. | |
| (Moriyama *et al.*, 2021) | Japan | Cross-sectional study | - Prospective audit and feedback protocol were observed in 23 (59.0%) hospitals when using broad-spectrum antimicrobials.<br><br>- Preauthorisation was observed in 4 (10.3%) hospitals for using broad-spectrum antimicrobials. - Notification protocols support form was present in | - The number of hospitals with preauthorisation and notification protocols, respectively, using the investigated antibiotics were as follows: broad-spectrum antimicrobials overall 4 (10.3%) and 37 (94.9%); carbapenem 2 (5.1%) and 34 (87.2%); 3rd generation cephalosporin 0 (0%) and 0 (0%); 4th generation cephalosporin 0 (0%) and 10 (25.6%); piperacillin/tazobactam 0 (0%) and 17 (43.6%); and intravenous quinolone 3 (7.7%), and 18 (46.2%). | ***<br><br>(60%) |

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| | | | 37 (94.9%) for use of broad-spectrum antimicrobials. | - Regarding preauthorisation and notification protocols, there were no significant differences between small/middle-sized hospitals and large hospitals.<br><br>- The numbers for hospitals that had intervention procedures within 7 d and 28 d, respectively, for each investigated antibiotic were as follows: broad-spectrum antimicrobials overall 17 (43.6%) and 34 (87.2%); carbapenem 16 (41.0%) and 34 (87.2%); 3rd generation cephalosporin 1 (2.6%) and 11 (28.2%); 4th generation cephalosporin 7n(17.9%) and 20 (51.3%); piperacillin/tazobactam 12 (30.8%) and 23 (59.0%); and intravenous quinolone 13 (30.8%) and 22 (56.4%). Intervention procedures to use broad-spectrum antimicrobials within 7 d were statistically more frequent in small/middle-sized hospitals than in large hospitals with findings as follows: overall, OR = 5.7, 95% CI = 1.4–23.5, p = 0.023; carbapenem, OR = 4.7, 95% CI = 1.1–19.1, p = 0.049; piperacillin/tazobactam, OR = 7.3, 95% CI = 1.3–39.9, p = 0.018; and intravenous quinolone, OR = 8.8, 95% CI = 1.6–48.2, p = 0.008. | |
| (Thakkar *et al.*, 2021) | India | Prospective study | - The pre-existing components of the hospital antimicrobial stewardship program included the generation of antibiograms, formulation/ education and dissemination of antibiotic policies for surgical prophylaxis, community and hospital-acquired infections and auditing antibiotics for surgical prophylaxis.<br><br>- Prospective audit and feedback for the restricted antimicrobials.<br><br>- Antibiotic restriction using the justification form. | - Around 1.4% of admitted patients were put on restricted antimicrobials. The total days of therapy (DOT) were 41.5/1000 inpatient days.<br><br>- Unjustified use of antimicrobials was reported in 13% and recommendations of the AMS for de-escalation were accepted in 89% by the treatment team.<br><br>- There was no significant difference between antimicrobial DOT of the restricted antimicrobials between 2018 and 2019.<br><br>- The colistin susceptibility rates remained stable compared to the previous years. | *<br><br>(20%) |
| (Panditrao *et al.*, 2021) | India | Quasi-experimental study. | <u>- Baseline Phase:</u> from April–June 2017<br><br>Routine prospective audit and feedback was undertaken.<br><br><u>- Intervention Phase:</u> from July–December 2017<br><br>The following interventions were added: | - There was a reduction in the cumulative DDD/1000 PD for all antimicrobials in the intervention phase compared with baseline (baseline phase 1326.3 DDD/1000PD vs. intervention phase 1313.5 DDD/1000PD).<br><br>- There was no change in the average number of antimicrobials per individual patient stay in the hospital | ****<br><br>(80%) |

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| | | | Timeout, Correction of doses, continued education for rational use of antimicrobials, and Care bundle approach for prevention of hospital-acquired infections (HAIs). | between the baseline and intervention phases; P = 0.59).<br><br>- DOT/1000PD declined from 1112.3 in the baseline phase to 1048.6 days in the intervention phase, while LOT/1000 PD changed from 956.0 in the baseline phase to 936.3 during the intervention phase.<br><br>- There was a decrease in DDD/1000 PD for antimicrobials such as piperacillin/tazobactam, imipenem, meropenem, clindamycin, levofloxacin, and amikacin, while there was an increase in DDD/1000 PD of vancomycin, colistin, cefoperazone/sulbactam, metronidazole and teicoplanin.<br><br>- There was a decrease in the percentage of carbapenem use in the intervention phase compared with the baseline phase (26.3% vs. 20.9%), whereas there was an increase in the use of polymyxins, particularly colistin (11.1% vs. 6.2%) and glycopeptides (vancomycin and teicoplanin) (12.3% vs 11.0%). | |
| (Ababneh *et al.*, 2020) | Jordan | Cross-sectional study | This study quantified antimicrobial use in inpatient settings as part of antimicrobial stewardship program surveillance. | - In terms of DDDs, carbapenems (ertapenem, meropenem, imipenem) were the most commonly used agents in a total of 28.0 DDD/100 admissions, followed by glycopeptides (vancomycin, teicoplanin) in a total of 26.8 DDD/100 admissions, piperacillin-tazobactam with 20.5 DDD/100 admissions and ceftriaxone with 14.2 DDD/100 admissions, fluoroquinolones (ciprofloxacin and levofloxacin) in a total of 11.2 DDD/100 admissions.<br><br>- The highest prescription rate of antibiotics was in the internal medicine wards (49.8 DDD/100 admissions), followed by surgery wards (33.2 DDD/100 admissions), intensive care unit (20.6 DDD/100 admissions), paediatrics (10.5DDD/100 admissions), oncology (10.4DDD/100 admissions).<br><br>- Regarding DOTs, piperacillin-tazobactam was the most commonly used agent (27.6 DOT/100 admissions), followed by carbapenems (27.2 DOT/100 admissions), glycopeptides (24.7 DOT/100 admissions), fluoroquinolones (12.4 DOT.100 admissions), and cefazolin (11.4 DOT/100 admissions). | ***<br><br>(60%) |

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| **During the COVID-19 Pandemic** | | | | | |
| (Spernovasilis *et al.*, 2021) | Greece | Cross-sectional study | - Prospective audit and feedback strategy,<br>along with a case-based education of treating doctors.<br>- Antibiotic review after 24 hours, 72 hours and seven days. | - Doctors believed that the prospective audit and feedback ASP strategy is more effective and educational than the preauthorisation ASP strategy (70.3% and 77.7%, respectively).<br>- Most respondents (90.6%) agreed that the implementation of an ASP improves the patients' outcomes compared to the absence of such a programme.<br>- Less than 25% of participants agreed that the prospective audit and feedback strategy of the current ASP should change.<br>- More than 80% of respondents agreed that in-person consultation is the preferred practice for the ASP and education. | ***<br>(60%) |
| (Ashiru-Oredope *et al.*, 2021) | United Kingdom | Cross-sectional study | - Audits and Regular surveillance of antimicrobial use/<br>- Point Prevalence Surveys.<br>- Quality improvement initiatives.<br>- Education, AMS meetings, multidisciplinary team and ward rounds.<br>- Writing non-COVID-19 guidelines.<br>- IV to oral switches.<br>- AMS surveillance activities.<br>- Technology (virtual meetings, virtual platforms, remote working and ward rounds).<br>- Introduction of novel biomarkers (e.g., Procalcitonin) for differentiating viral and bacterial infections.<br>- The use of hospital electronic prescribing systems facilitated<br>- AMS activities by antimicrobial pharmacists, allowing them to target their activities, for example, the | - From qualitative open questions: respondents highlighted core AMS work, e.g., reviewing and writing non-COVID-19 guidelines, as being the most affected.<br>- Respondents were concerned about increased antibiotic use, delayed IV-to-oral switches (IVOST), and prolonged antibiotic durations.<br>- The respondents also were concerned that cases of Clostridioides difficile Infection (CDI) were rising in some hospitals.<br>- Stock shortages were also identified as difficult to manage due to overwhelmed supply chains for antibiotics, antivirals and, in some cases, personal protective equipment (PPE).<br>- Positive COVID-19 outcomes included: technology being increasingly used as a tool to facilitate stewardship, e.g., virtual meetings and ward rounds.<br>- Another positive outcome was the increased introduction of novel biomarkers (e.g., procalcitonin) for differentiating viral and bacterial infections.<br>- The use of hospital electronic prescribing systems facilitated AMS activities by antimicrobial pharmacists.<br>- There has also been a positive increase in the multidisciplinary team. | *****<br>(100%) |

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| | | | identification of patients receiving excessive amounts of antibiotics.<br><br>- Infection prevention control.<br><br>- Clinics/outpatient consults and Outpatient parenteral antibiotic therapy (OPAT).<br><br>- Changing current inpatient processes, such as COVID-19 patients receiving a senior review more quickly.<br><br>- Prescribing indicators/targets reporting and Antibiotic Kit Review (ARK).<br><br>- AMS committee meeting (formal or informal). | - Increased awareness of antimicrobial guidelines and improvements seen in infection prevention. | |
| (Williams *et al*., 2021) | United Kingdom | Retrospective study | - Seventy-three (33%) patients in the negative PCT group were on antibiotics 48 h following diagnosis of COVID-19 compared with 126 (84%) patients in the positive PCT group (P<0.001), suggesting good compliance with the guideline | Primary outcome:<br><br>- Patients in the negative PCT group received significantly fewer DDDs of antibiotics (both total and per alive day) compared with patients in the positive PCT group (median DDD 3.0 vs 6.8; P<0.001).<br><br>- A significant relationship between PCT and total DDDs remained after accounting for confounders; on average, a patient with PCT >0.25 ng/mL had almost three-fold more DDDs of antibiotics compared with patients with PCT 0.25 ng/mL [coefficient 2.72, 95% confidence interval (CI) 2.03e3.62; P<0.001].<br><br>Secondary outcomes:<br><br>- Sixty-two (28%) patients in the negative PCT group died compared with 54 (36%) patients in the positive PCT group (P.0.021), and 19 (9%) patients in the negative PCT group were admitted to the ICU compared with 28 (19%) patients in the positive PCT group (P.0.007).<br><br>- Meropenem was the only carbapenem used in the study population. With specific reference to meropenem consumption, positive PCT was associated with a three-fold increase in the odds of receiving any meropenem during the course of hospital admission (odds ratio 3.16, 95% CI 1.50e6.65; P = 0.002). | ****<br><br>(80%) |

*Though this study was published during the COVID-19 pandemic, it was conducted before the pandemic, and the AMS has implemented PP.

The quality assessment that was conducted using the MMAT tool 2018. The MMAT tool has five questions. * (20%) Means only one question answered yes. ** (40%) means two out of five questions answered yes. *** (60%) means three out of five questions answered yes. **** (80%) means four questions answered yes. ***** (100%) means all questions answered yes.

AMS, antimicrobial stewardship; DDD, Defined Daily Doses; DOT, Days of Therapy; ASP, antimicrobial stewardship program; PPS-ECDC - Point Prevalence Study of the European Centre for Disease Prevention and Control; Qis, quality indicators; PPS-QI - Point Prevalence Surveys; LOS, length of stay; ICU, intensive care unit; ABT, antibiotic therapy; PAT, postoperative antibiotic therapy; LOT, length of therapy; HAIs, Hospital-Acquired Infections; COVID-19, coronavirus; IVOST, IV to oral switches; CDI, Clostridioides Difficile Infection; PPE, personal protective equipment; OPAT, Outpatient Parenteral Antibiotic Therapy; ARK, Antibiotic Review Kit; PCT, procalcitonin; and CI, Confidence Interval.

### 3.3.2. Antimicrobial stewardship strategies prior to and during the COVID-19 pandemic.

Strategies and interventions aimed at improving appropriate prescription of antibiotics in all acute care settings. They are considered an essential part of “antimicrobial stewardship”. According to the literature, there are many antimicrobial stewardship tools, interventions and activities (collectively termed “strategies”) that can be used to streamline and improve antimicrobial use and educate prescribers (Dellit *et al*., 2017). For more details about AMS strategies, please see Appendix 9 and Appendix 10. In this systematic literature review, a range of AMS strategies has been classified according to the AMS implementation guidelines of the Infectious Disease Society of America (IDSA) and the AMS practical guide from the BSAC into core and supplemental strategies (IDSA, 2017 and BSAC, 2018).

Prior to the pandemic, regarding the core strategies, the ‘AMS Multidisciplinary Team’ was found in ten studies (Trivedi *et al*., 2013 and Ababneh *et al*., 2020), and the ‘Prospective Audit & Feedback’ strategy was found in nine studies (Trivedi *et al*., 2013; Kallen *et al*., 2021; Surat *et al*., 2021 and Ababneh *et al*., 2020). However, ‘Antibiotic Review’ was noticed in seven studies (Trivedi *et al*., 2013; Tamma *et al*., 2021; Weston *et al*., 2013; Mehta *et al*., 2014; Thakkar et al., 2021; and Ababneh *et al*., 2020). For AMS supplemental strategies, ‘Formulary Restriction & Pre-authorisation’ strategy was found in seven studies (Trivedi *et al*., 2013; Kallen *et al*., 2021; Surat *et al*., 2021; and Thakkar *et al*., 2021), ‘Dose Optimisation’ strategy was found in seven studies (Trivedi *et al*., 2013; Surat *et al*., 2021; Mehta *et al*., 2014; Thakkar et al., 2021; and Ababneh *et al*., 2020), ‘Streamlining/timely De-escalation’ strategy was found in five studies (Trivedi *et al*., 2013; Surat *et al*., 2021; Weston *et al*., 2013; Thakkar *et al*., 2021; and Panditrao *et al*., 2021), ‘Parenteral to Oral Conversion’ was found in five studies (Trivedi *et al*., 2013; Tamma *et al*., 2021; Weston *et al*., 2013; and Thakkar *et al*., 2021), and ‘Guidelines and Clinical Pathways’ strategy was found in six studies (Trivedi *et al*., 2013; Tamma *et al*., 2021; Weston *et al*., 2013; Panditrao *et al*., 2021; and Ababneh *et al*., 2020), ‘Antibiotic Order Form’ was found in two studies (Trivedi *et al*., 2013; and Weston *et al*., 2013), ‘Education’ was found in six studies (Trivedi *et al*., 2013; Weston *et al*., 2013; Thakkar *et al*., 2021; and Panditrao *et al*., 2021), ‘Computerised Decision Support’ was found in two studies (Trivedi *et al*., 2013; and Weston *et al*., 2013), and ‘Laboratory Surveillance’ was found in four studies (Trivedi *et al*., 2013; Surat *et al*., 2021; Mehta *et al*., 2014; and Thakkar *et al*., 2021) (Table 3.6).

During the COVID-19 pandemic, concerning the core AMS strategies, each 'AMS Multidisciplinary Team', 'Prospective Audit and Feedback' strategy, and 'Antibiotic Review' were found in two studies (Spernovasilis *et al*., 2021; and Ashiru-Oredope *et al*., 2021). For AMS supplemental strategies, the 'Dose Optimisation' strategy was found in only one study (Spernovasilis *et al.*, 2021). However, each 'Streamlining/timely De-escalation and Parental-to-oral Conversion' was found in one study (Ashiru-Oredope *et al*., 2021). Additionally, 'Guidelines and Clinical Pathways' found in three studies (Spernovasilis *et al*., 2021; and Williams *et al.*, 2021), 'Education' was found in two studies (Spernovasilis *et al*., 2021; and Ashiru-Oredope *et al*., 2021), 'Computerised Decision Support' was found in one study (Williams *et al*., 2021), and 'Laboratory Surveillance and Feedback' found in two studies (Spernovasilis *et al*., 2021; and Williams et al., 2021).

### 3.3.3. Identifying key measures for antimicrobial stewardship outcomes

Measurement of prescribing performance is essential to evaluate the impact of AMS implementation in clinical practice and its demonstrable benefits for patients. The British scientist mentioned in his Popular Lecture, "If you cannot measure it, you cannot improve it" Lord Kelvin 1824-1907 (Kelvin and Gerstein, 1889). Improving antimicrobial use must be measured by Identifying the measurable elements/metrics that can be used to evaluate the outcomes of AMS. These metrics can be used for many purposes, such as quality assurance, improvement, and comparisons/benchmarking either intra-hospital or Inter-hospital. Establishing what to measure is one of the essential steps to maintain sustainability in AMS intervention (Dellit *et al*., 2017; WHO, 2019).

Measuring stewardship can be divided into four categories: antimicrobial consumption, process measures, outcome measures, and financial (WHO, 2019). Before 2019, there were no reliable means for measuring antimicrobial usage or correlating usage to resistance until 2019, when the WHO promoted measurable tools that can be used worldwide to accurately reflect antimicrobial usage, such as the DDD. WHO defined DDD as the assumed average maintenance dose per day for the antibiotic used for its main indication in adults (WHO, 2019).

In order to estimate the total number of days of antimicrobial therapy, healthcare personnel divide the total grams of each antimicrobial used for a given period by the WHO-defined DDD for the individual antimicrobials. Because DDD is a standardised unit of measure, it allows comparisons with antimicrobial usage in other hospitals and countries (WHOCC, 2019). Each hospital should select suitable measures/metrics that maintain the effective implementation of the AMS. It is essential to be aware of each measure's advantages and disadvantages to maintain a proper selection. For more details about AMS outcome measures and metrics, Appendix 10 presents measures for antimicrobial stewardship, detailing structural and process indicators for quality improvement, along with outcome measures to assess AMS effectiveness (Table 3.5).

**Table 3.5.** Summary of findings about antimicrobial stewardship implementation prior to and during the COVID-19 pandemic.

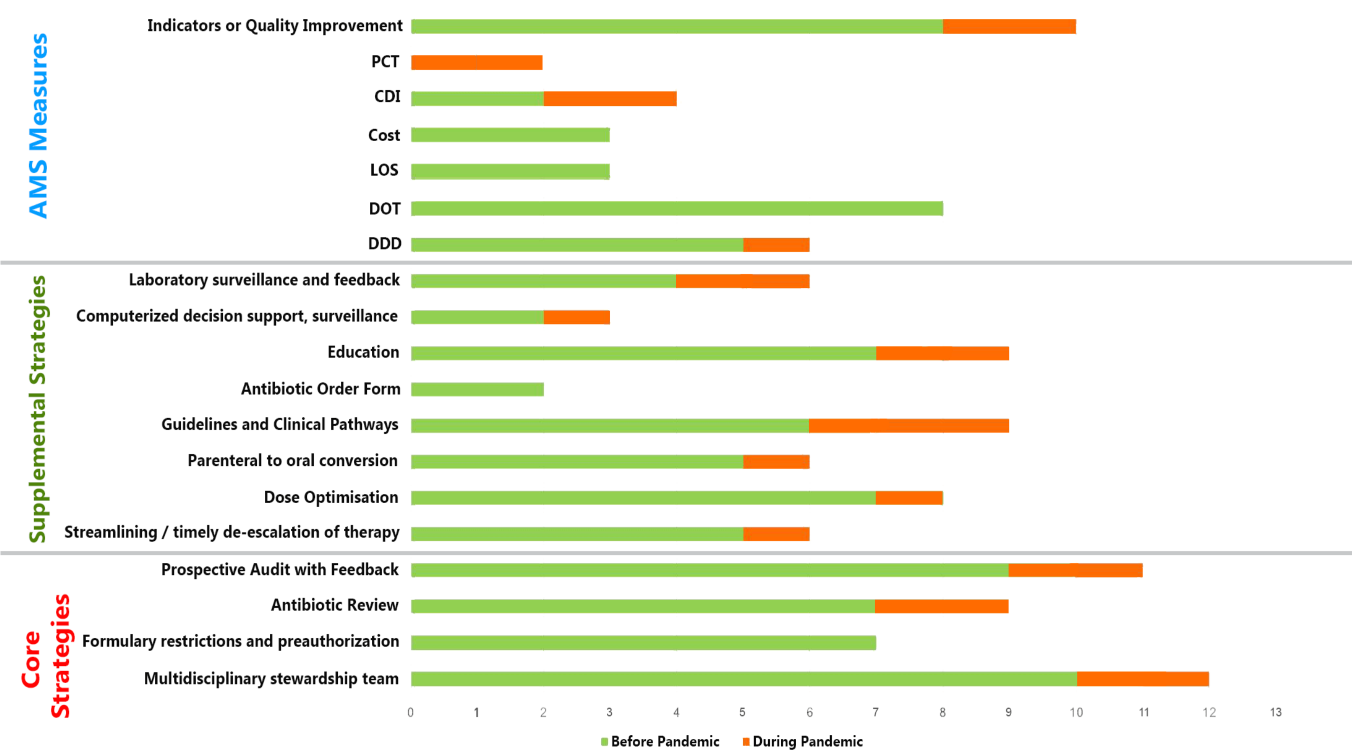
| Study | | | Antimicrobial Stewardship (AMS) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | AMS Strategies | | | | | | | | | AMS Measures | | | | | | | | | |
| | | | AMS Core Strategies | | | | AMS Supplemental Strategies | | | | | | | | | | | | | | |
| | Before-the-pandemic | During-the-pandemic | Multidisciplinary stewardship team | Formulary restrictions and preauthorisation | Antibiotic Review | Prospective Audit with Feedback | Streamlining / timely de-escalation of therapy | Dose Optimisation | Parenteral to oral conversion | Guidelines and Clinical Pathways | Antibiotic Order Form | Education | Computerised decision support, surveillance | Laboratory surveillance and feedback | DDD | DOT | LOS | Cost | CDI | PCT | Indicators or Quality Improvement |
| Trivedi (2013) [19] | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ | | ✓ |
| Kallen (2017) [20] | ✓ | | ✓ | ✓ | | ✓ | | | ✓ | | | ✓ | | | ✓ | ✓ | ✓ | | | | ✓ |
| Tamma (2021) [21] | ✓ | | ✓ | | ✓ | | | | ✓ | ✓ | | ✓ | | | | ✓ | | | ✓ | | ✓ |
| Surat (2021) [22] | ✓ | | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | | ✓ | | ✓ | ✓ | ✓ | ✓ | | | | ✓ |
| Weston (2012) [23] | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | | | | | ✓ |
| Mehta (2014) [24] | ✓ | | ✓ | ✓ | ✓ | ✓ | | ✓ | | | | | | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| Moriyama (2021) [25] | ✓ | | ✓ | ✓ | | ✓ | | | | | | | | | | | | ✓ | | | |
| Thakkar (2021) [26] | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | ✓ | | ✓ | | ✓ | | | | | |
| Panditrao (2021) [27] | ✓ | | ✓ | | ✓ | ✓ | ✓ | ✓ | | ✓ | | ✓ | | | ✓ | ✓ | | | | | ✓ |
| Ababneh (2020) [28] | ✓ | | ✓ | | ✓ | ✓ | | ✓ | | ✓ | | | | | ✓ | ✓ | | | | | ✓ |
| Spernovasilis (2021) [29] | | ✓ | ✓ | | ✓ | ✓ | | ✓ | | ✓ | | ✓ | | ✓ | | | | | | | |
| Ashiru-Oredope (2021) [30] | | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | ✓ | | ✓ | | | | | | | ✓ | ✓ | ✓ |
| Williams (2021) [31] | | ✓ | | | | | | | | ✓ | | | ✓ | ✓ | ✓ | | | | ✓ | ✓ | ✓ |

AMS, antimicrobial stewardship; DDD, Defined Daily Dose; DOT, Days of Therapy; LOS, length of stay; CDI, Clostridioides difficile Infection; and PCT, procalcitonin.

Prior to the COVID-19 pandemic, DDD was noticed in five studies (Trivedi *et al.*, 2013; Kallen *et al.*, 2021; Surat *et al.*, 2021; Panditrao *et al.*, 2021; and Ababneh *et al.*, 2020). Additionally, the days of therapy (DOT) were found in eight studies (Trivedi *et al.*, 2013; Surat *et al.*, 2021; Mehta *et al.*, 2014; Thakkar *et al.*, 2021; and Ababneh *et al.*, 2020). The Length of Stay (LOS) was found in three studies (Kallen *et al.*, 2021; Surat *et al.*, 2021; and Mehta *et al.*, 2014), and Cost was found in three studies (Trivedi *et al.*, 2013; Mehta *et al.*, 2014; Moriyama *et al.*, 2021). Furthermore, the Clostridioides Difficile Infection (CDI) was found in two studies (Trivedi *et al.*, 2013; Tamma *et al.*, 2021). However, Indicators of Quality Improvement were found in eight studies (Trivedi *et al.*, 2013; Mehta *et al.*, 2014; Panditrao *et al.*, 2021; Ababneh *et al.*, 2020). Appendix 11 provides examples of measures used to evaluate the efficacy of Antimicrobial Stewardship implementation. During the COVID-19 pandemic, DDD was found in only one study (Williams *et al.*, 2021), CDI was found in two studies (Ashiru-Oredope *et al.*, 2021; Williams *et al.*, 2021), and Procalcitonin (PCT) was found in one study (Williams *et al.*, 2021). Indicators or Quality

Improvement were found in two studies (Ashiru-Oredope *et al*., 2021 and Williams *et al*., 2021) (Table 3.6) (Figure 3.2.).

**Figure 3.2.** AMS before and during the COVID-19 pandemic in acute care settings (Total studies 13).

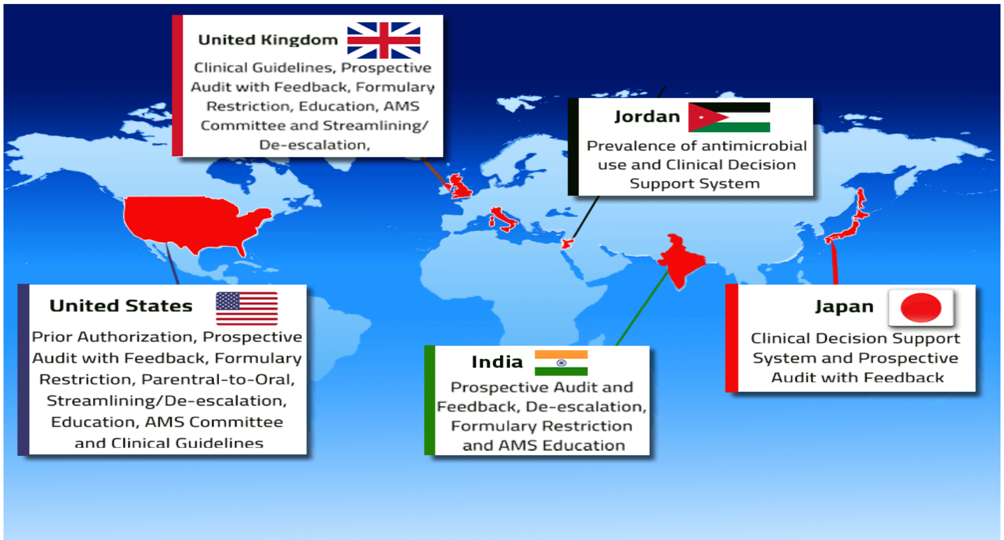



PCT, procalcitonin; CDI, Clostridioides Difficile Infection; LOS, length of stay; DOT, Days of Therapy; and DDD, Defined Daily Dose.

### 3.3.4. Pharmacists' contribution to AMS prior to and during the pandemic

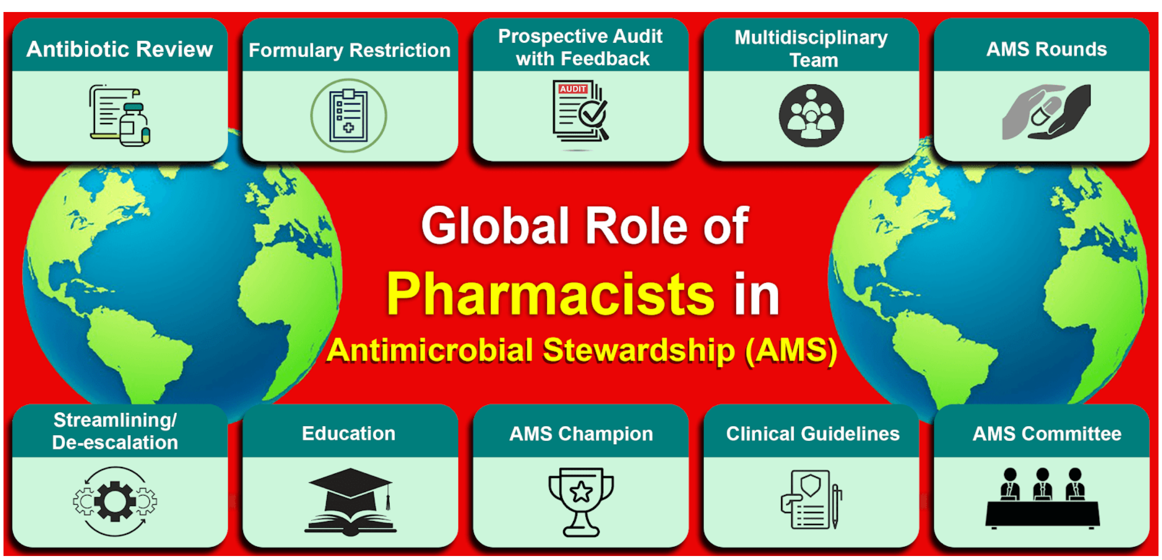
One interesting outcome highlighted by this systematic literature review is the pharmacist's role in co-leading AMS implementation in acute care settings worldwide. Among the 13 studies reviewed, the involvement of pharmacists was noted in seven of them. In the United Kingdom, particularly during the pandemic, pharmacists were instrumental in updating clinical guidelines, conducting prospective audits, participating in AMS committees, AMS rounds, antibiotic reviews, and de-escalation (Ashiru-Oredope *et al*., 2021). Similarly, in the United States, pharmacists played a significant role in prior authorisation, prospective audits, formulary restriction, serving on AMS advisory committees, and in clinical guideline development and de-escalation (Trivedi *et al*., 2013; Mehta *et al*., 2014; Tamma *et al*., 2021). The roles of pharmacists in Jordan, India, and Japan were also notable, especially in clinical decision support, formulary restriction, AMS education, and prospective audits with feedback (Ababneh et al., 2020; Moriyama et al., 2021; Thakkar et al., 2021). Figure 3.3 below shows a map highlighting the global contributions of pharmacists to AMS in acute care settings, both prior to and during the pandemic.

**Figure 3.3.:** Map highlighting pharmacists' AMS global contributions in the acute care settings (Adapted from Goff et l., 2020).




Additionally, the roles of pharmacists in the implementation of AMS strategies, as identified from the data extraction table, were gathered from the seven previously mentioned studies included in the systematic literature review over the last 20 years. These roles covered a range of AMS-related strategies: antibiotic review, restriction, prospective audit, participation in AMS rounds, involvement in multidisciplinary teams, educational contributions, antibiotic de-escalation, updating clinical guidelines, and serving on AMS committees. These findings are summarised in Figure 3.4.

**Figure 3.4.** Summary of the roles of pharmacists in AMS implementation (Adapted from Goff et., 2020).



## 3.4. Discussion:

This systematic review analysed data from over 63,921 patients who received antibiotics in acute care settings between 2000 and 2021. Overuse and irrational use of antimicrobials were significant problems, impacting patient safety, increasing antibiotic resistance, and economic burden (ECDC, 2019; Dadgostar, 2019). Most respiratory tract infections, especially URTIs, are viral but often treated with antimicrobials (Li et al., 2016). AMS interventions reviewed in US IDSA guidelines and BSAC guidelines highlight core strategies to reduce antimicrobial exposure, costs, and improve clinical outcomes (Dellit et al., 2017; BSAC, 2018; Mehta et al., 2014). Two core ASP strategies have emerged: front-end strategies, which involve an approval process for making antimicrobials available ('Formulary Restrictions and Pre-authorisation'), and back-end strategies, which involve reviewing antimicrobial use after therapy has been initiated ('Prospective Audit with Intervention and Feedback'). A review of these strategies found that back-end strategies, although more labour-intensive, are more widely practised, more readily accepted by clinicians, and provide more educational opportunities, leading to a more sustained impact on improving antimicrobial prescribing quality (BSAC, 2019). The front-end strategy was used in 54% of studies PP, while the back-end strategy was used in 85% of all studies and two studies DP (Spernovasilis et al., 2021; Ashiru-Oredope et al., 2021).

A multidisciplinary AMS team was present in 92% of the included studies, highlighting its importance in AMS structure and governance. The core team typically includes an infectious disease physician, a clinical microbiologist, and a clinical pharmacist with expertise in infection, with additional members like specialist nurses and quality improvement managers (BSAC, 2019). Before COVID-19, a study across US hospitals emphasised the importance of effective communication with the AMS team for successful implementation (Tamma *et al*., 2021). In 2022, Lebanon's first study on the post-prescription review and feedback AMS programme showed a significant reduction in therapy days and hospital stay length, with an 88% recommendation acceptance rate (Llewelyn *et al*., 2022). During COVID-19, a UK study noted increased multidisciplinary work and enhanced pharmacist contributions to AMS (Ashiru-Oredope et al., 2021). The AMS team's role was crucial in performing gap analyses of antimicrobial use and developing implementation plans (BSAC, 2019). A study conducted in Pennsylvania compared the 'Pre-authorisation' AMS strategy with the 'Prospective Audit with Feedback' approach, finding a significant increase in the use of affected antimicrobials and overall antimicrobial use.

The antibiotic review emerged as an effective AMS strategy both pre-pandemic and during the pandemic, identified in 69% (9 of 13) of included studies. Typically conducted after 24 hours (Day 1) of prescribing antibiotics, it involved reviewing doses and considering an 'IV-to-oral switch'. Reviews on Day 4 and Day 7 assessed appropriateness based on microbiological culture results and therapy duration, respectively (BSAC, 2019). Reviews conducted 48-72 hours post-prescription were performed by microbiology (Surat et al., 2021) or the AMS multidisciplinary committee (Thakkar et al., 2021). The team antibiotic review form (TARF) significantly reduced antibiotic use by 30.3 DOT per 1000 PD (P = 0.008) and decreased hospital-onset C. difficile events by 19.5% (P = 0.03) (Tamma et al., 2021). In the UK, 58 acute hospital organisations followed the Start Smart—Then Focus guidance, requiring prescribers to review antibiotics every 48-72 hours (UKHSA, 2023). The Antibiotic Review Kit (ARK) intervention aimed to reduce antibiotic use by promoting decisions to stop rather than start antibiotics, achieving a mean reduction in use of 4.8% per year (Seaton et al., 2020). A study in Greece focused on carbapenem prescriptions, emphasising appropriate indication, dosage, age, and duration, along with carbapenem-sparing antibiotics when suitable. The programme used prospective audit and feedback, with an infectious diseases (ID) specialist and fellow providing in-person consultations within 72 hours of carbapenem prescription requests (Spernovasilis et al., 2021). Queries and suggestions were made for 52.1% of 94 patients in the baseline phase and for 38.7% of 243 patients in the intervention phase (Panditrao et al., 2021). This approach could benefit hospitals with limited resources in developing countries.

The 'Streamlining/timely De-escalation of Therapy' strategy was identified in five studies PP and one DP (Ashiru-Oredope et al., 2021). Implemented with a 48-hour antimicrobial timeout, it involved re-evaluating patients' antimicrobial regimens and adjusting according to their clinical condition. This strategy was part of 'Prospective Audit and Feedback', with data-recording teams monitoring timelines and doctors responsible for each patient (Panditrao et al., 2021). The 'Antibiotic De-escalation' strategy in community-acquired pneumonia (CAP) was notably affected by COVID-19 (Ashiru-Oredope et al., 2021). Both 'Dose Optimisation and IV-to-oral Conversion' strategies showed significant outcomes, with p-values of 0.03 and 0.04 respectively, in a multi-centre study of 422 general acute care hospitals in California, USA (Trivedi et al., 2013). During the pandemic, dose optimisation, particularly for carbapenems, became crucial, focusing on appropriate indications, dosages, and treatment durations, along with carbapenem-sparing antibiotics (Trivedi et al., 2013; Spernovasilis et al., 2021). In the UK, increased antibiotic use, including broad-spectrum antibiotics and delayed IV-to-oral switches, raised concerns during the pandemic (Ashiru-Oredope et al., 2021).

'Guidelines and Clinical Pathways' were widely used, applied in 69% of cases both PP and DP. Effective organisational collaboration in implementing AMS guidelines during the pandemic was noted (Ashiru-Oredope et al., 2021; Williams et al., 2021). Adherence to updated guidelines from NICE, WHO, and FIP was crucial in preventing inappropriate antimicrobial prescribing. Local guidelines, adapted based on antibiograms, played a significant role in reducing antimicrobial resistance (Surat et al., 2021). In Scotland, the challenge of bacterial co-infection with SARS-CoV-2 necessitated careful antimicrobial stewardship. A point prevalence survey in April 2020 across 15 acute hospitals found relatively low antibiotic prescribing rates in SARS-CoV-2 hospitalised patients, reflecting effective national AMS initiatives. However, broad-spectrum antibiotic use in critical care highlighted the need for ongoing infection control and stewardship efforts (Khor et al., 2020).

Education played a critical role in promoting AMS before the pandemic. A study across US hospitals implemented educational activities and webinars to foster collaboration with clinical microbiology labs, integrate nurses into stewardship activities, and address antibiotic allergies. The AMS educational programme, ‘Building Stewardship: A Team Approach Enhancing Antibiotic Stewardship in Acute Care Hospitals’, offered by the AHRQ, was highly effective, focusing on ASPs, implementation strategies, and operational issues like pharmacodynamics and electronic surveillance (Mehta et al., 2014). AHRQ’s educational components were innovatively used as posters, discussion points on clinical rounds, or for developing local guidelines (Tamma et al., 2021). During the pandemic, AMS education featured in only one study, highlighting the need for structured AMS education to manage crises effectively (Ashiru-Oredope et al., 2021). AMS educational programmes within health systems, designed for AMS leaders and top management, significantly aid AMS implementation, equipping systems to respond effectively to future emergencies (Majumder et al., 2020).

Measuring prescribing performance is crucial for assessing the impact of AMS implementation and its benefits for patients. Identifying measurable metrics to evaluate AMS outcomes is essential, serving as KPIs, quality assurance tools, and benchmarking tools within and between hospitals (Th et al., 2018; WHO, 2019). Monitoring trends in antimicrobial use and resistance within a hospital over several years and identifying small changes over a one-month period are vital. This helps adapt empiric treatment according to local resistance trends, demonstrates changes in practice over time, and identifies wards with high antimicrobial usage to define targeted interventions (BSAC, 2019). Surveillance of antimicrobial use and resistance is essential at hospital, local, regional, national, and global levels (WHO, 2022; ECDC, 2022; Choi et al., 2021; WHO, 2018; PHE, 2018; Patel et al., 2020). Quality improvement projects during the COVID-19 pandemic assisted clinicians in selecting the appropriate antibiotic, dose, duration, and route to optimise clinical outcomes while minimising resistance (Ashiru-Oredope et al., 2021; Williams et al., 2021). Linking ASPs with hospital patient safety and quality initiatives and using appropriate quality improvement committees for follow-up are crucial (Trivedi et al., 2013). A single-centre study showed AMS measures optimised antibacterial use in intra-abdominal infections, reducing geometric mean length of stay (LOS) by 0.8 days in a multicentre trial in the Netherlands (Kallen et al., 2021). AMS quality indicators are essential for maintaining preparedness for emergencies (ESPAUR, 2022). During the pandemic, Sheffield Teaching Hospitals NHS Foundation Trust evaluated a PCT-based guideline, facilitating AMS measures and surveillance (Williams et al., 2021). LOS and cost were examined in three studies pre-pandemic (PP), showing significant increases after AMS strategy changes (Mehta et al., 2014; Moriyama et al., 2021). In included studies, DDD and DOT were used in 53% PP and 28% DP. KPIs like AMR local indicators by UKHSA among NHS hospitals showed significant AMS outcomes (Ashiru-Oredope et al., 2021; WHO, 2019). CDI rate measured AMS outcomes, reducing hospital-onset CDI rates (Tamma et al., 2021). During the pandemic, CDI rates increased across NHS acute trusts in England (Ashiru-Oredope et al., 2021).

An AMS Dashboard is crucial for addressing antibiotic prescribing challenges, allowing real-time visualisation and immediate action, especially during emergencies like COVID-19 (Khor et al., 2020). NHS England's antibiotic quality premium monitoring dashboard supports monitoring Integrated Care Systems' performance (NHS England, 2021). ECDC provides an AMS dashboard showcasing antimicrobial consumption metrics across Europe (ECDC, 2023). Advanced technology, such as AI in dynamic dashboards, can identify gaps and propose AMS interventions (Health Education England, 2023). Integrating antibiogram results with dashboards and disseminating them hospital-wide is beneficial (William et al., 2021).

Pharmacists were pivotal in implementing AMS strategies in the USA and UK before the COVID-19 pandemic. They were involved in multidisciplinary teams, antibiotic reviews, formulary restrictions, and dose adjustments. In the UK, pharmacists focused on quality improvement projects, adhering to national key performance indicators, and conducting AMS audits (Ashiru-Oredope et al., 2021). In the USA, the Agency for Healthcare Research and Quality Safety Program saw pharmacists leading infection management efforts, emphasising teamwork and communication (Trivedi et al., 2013; Mehta et al., 2014; Tamma et al., 2021). Contributions from pharmacists in Jordan, India, and Japan were notable, especially in clinical decision support, formulary restriction, AMS education, and prospective audits with feedback (Ababneh et al., 2020; Moriyama et al., 2021; Thakkar et al., 2021). During the pandemic, UK pharmacists integrated technology into virtual stewardship efforts and used diagnostic tests like procalcitonin to distinguish bacterial from viral infections. The pandemic impacted routine AMS activities for 65% of UK pharmacists, highlighting their dual role in pandemic response and AMS (Ashiru-Oredope et al., 2021). Updating clinical guidelines became essential, and pharmacists ensured these revisions aligned with evolving pandemic needs and ongoing AMS requirements.

### 3.5 Strengths and limitations

This systematic review investigated the implementation of AMS in acute care settings prior to and during the COVID-19 pandemic. Unlike previous reviews that assessed AMS in hospitalised patients, this review uniquely focused on core and supplemental AMS strategies and measures in secondary and acute care settings during these periods. Additionally, findings suggest that effective antibiotic use, particularly during emergencies or pandemics, is best achieved through organisational collaboration. It involved a narrative synthesis approach to identify crucial elements of AMS strategies and measures in the acute settings, during both PP and DP periods and identified several research gaps. This systematic review has certain limitations. The exclusive search of published databases may have overlooked unpublished yet relevant studies, and restricting the language to English potentially excluded significant studies in other languages. Although this is the first review to assess AMS implementation prior to and during the COVID-19 pandemic, the scarcity of studies using AMS strategies and measures limited the comprehensiveness of the analysis and affected the comparability of findings.

## 3.6 Opportunities for future research

This review highlighted several research gaps in the existing literature, emphasising the need for further studies to examine the impact of the COVID-19 pandemic on antibiotic prescribing and the implementation of AMS in acute care settings. The limited representation of AMS measures and quality improvement initiatives in current studies points to a substantial need for additional research. Upcoming studies should focus on developing standardised methodologies for implementing and evaluating AMS, thereby improving the comparability of results across different studies. There is also a pressing need to investigate the factors influencing AMS implementation during emergencies or crises, such as the COVID-19 pandemic. Additionally, future research should delve into understanding and exploring the knowledge, attitudes, and perceptions related to antibiotic prescribing, AMR, and AMS practices in acute care settings during the pandemic.

## 3.7. Conclusion

This systematic literature review explored AMS strategies in acute care settings, highlighting the need for ongoing AMS advocacy post-pandemic. Key learnings from COVID-19 stress the importance of multidisciplinary teams for effective AMS and starting with core strategies in new programs. Hospitals should choose AMS tools matching their resources to optimise antibiotic use and combat AMR. Core strategies, such as prospective audits, have been effective during the pandemic. Educational strategies, clinical pathways, and national prescribing indicators are vital for AMS's success. Innovative methods, such as procalcitonin-guided prescribing, show promise. Pharmacists are central in AMS, leading program implementation, education, and metric monitoring. Standardising AMS measures and integrating decision support systems are crucial for effective AMS planning and future crisis preparedness.

**Summary of this chapter**

This chapter has discussed the overall findings of the systematic literature review study conducted in this research project. The next chapter will present the findings from the subsequent retrospective medical records review study, also derived from this research.

# Chapter 4

# Retrospective Medical Records Review

# Chapter 4: Study 2 - Investigating Antimicrobial Stewardship Implementation Prior to and During the COVID-19 Pandemic in a Secondary Care Setting: A Retrospective Medical Records Review.

The previous chapter explored the AMS implementation in acute care settings in the previous 20 years. This included an exploration of AMS strategies and measures prior to and during the COVID-19 pandemic. In Chapter 3, the focus shifted to the most widely used core and supplemental AMS strategies, examining their clinical relevance. The initial study, an extensive systematic literature review, played a pivotal role in developing the data collection methodology for Study 2. Additionally, this review was instrumental in identifying the key stakeholders, such as doctors, pharmacists, and nurses, who were surveyed in the third study. In this chapter, the evaluation of antibiotic prescribing and AMS implementation prior to and during the pandemic in 2019 and 2020 is presented. This assessment utilises the AMS strategies and measures identified in the systematic literature review discussed in the previous chapter.

## 4.1. Introduction

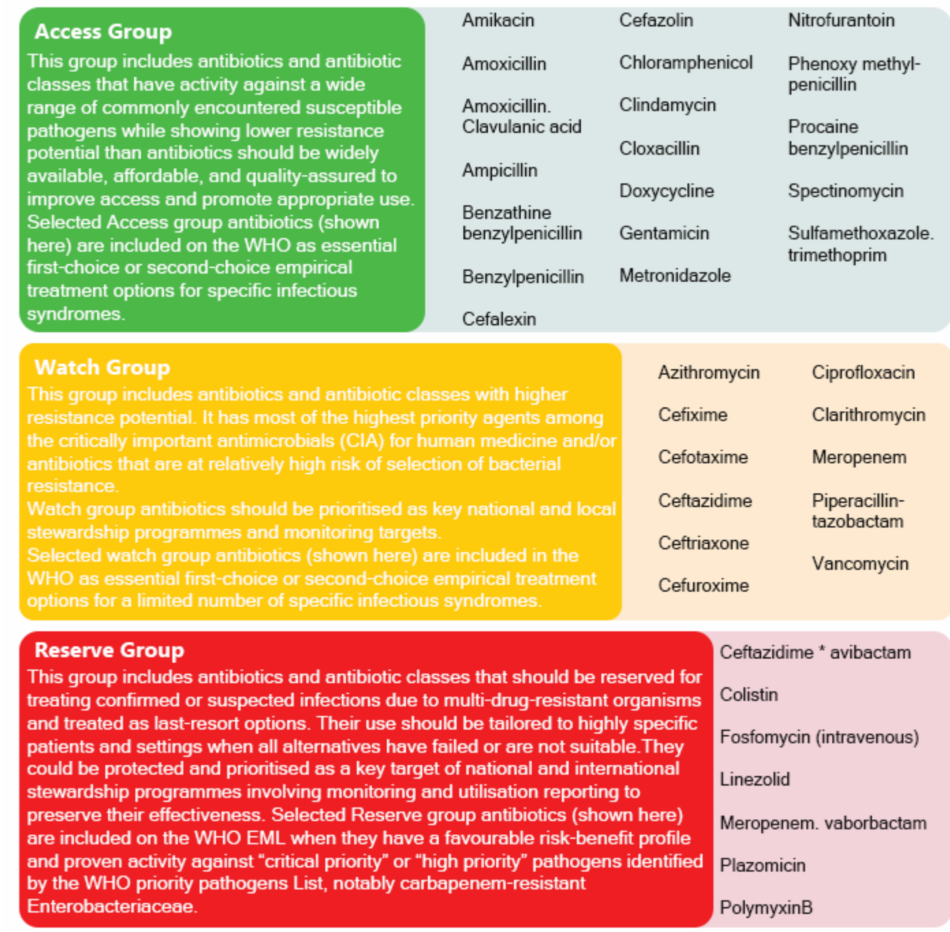
The increasing prevalence of multi-drug-resistant infections poses a severe global health risk, escalating morbidity, mortality, and economic impact. The WHO has classified antimicrobial resistance (AMR) as a top global health threat, with 1.2 million deaths attributed to AMR-related causes (Murray et al., 2022). Antimicrobial stewardship (AMS) is crucial to the UK's Five-Year Antimicrobial Resistance Strategy, aiming to enhance patient care and reduce the spread of AMR (Department of Health and Social Care, 2019). The 'Start Smart, Then Focus' toolkit by UKHSA promotes responsible antibiotic use and timely reviews (GOV.UK, 2023). During the COVID-19 pandemic, increased antimicrobial therapy contributed to a rise in resistant infections (Murgadella-Sancho et al., 2021). As healthcare systems return to pre-pandemic modalities, maintaining a focus on AMR remains crucial (ESPAUR, 2021).

The World Health Organisation (WHO) has actively contributed to this endeavour by developing the AWaRe classification system (WHO, 2023) (Figure 4.1). This framework is instrumental in guiding the global implementation of AMS and promoting responsible antibiotic usage, aligning with the strategic objectives outlined in the UK's Five-Year AMR Strategic Plan (Department of Health and Social Care, 2019). This alignment emphasised an integrated international commitment to addressing and mitigating the challenges posed by AMR (Tejpar *et al.*, 2022). In the AWaRe tool, antibiotics are divided into three categories: Access, Watch, and Reserve. Each category is based on its respective effect on AMR. The ‘Access’ antibiotics are characterised by their narrow spectrum of activity, typically resulting in fewer side effects, a reduced likelihood of antimicrobial resistance selection, and lower costs (WHO, 2023). They are strongly recommended for empiric treatment of common infections and should be readily available.

Conversely, 'Watch' antibiotics carry a higher risk of promoting antimicrobial resistance and are primarily prescribed for patients with more severe conditions, predominantly within hospital settings (Figure 4.1). To monitor progress, NHS Trusts can use Fingertips indicators for ‘Access’, ‘Reserve’, and ‘Watch’ antibiotics (PHE, 2019). Vigilant monitoring of these antibiotics is vital to prevent their overuse. 'Reserve' antibiotics, however, are considered the last resort and should be employed only when dealing with severe infections caused by multidrug-resistant pathogens. Their use should be reserved for critical situations. The AWaRe classification highlights the importance of restricting the use of 'Watch' and 'Reserve' category antibiotics (Figure 4.1). By 2023, the WHO aims for at least 60% of all antibiotic consumption to come from the Access group (WHO, 2023). An inevitable consequence of the pandemic has been the increase in inappropriate antibiotic use, which contributes to rising AMR rates (Subramanya *et al*., 2021). This is despite WHO guidelines that advise against the use of antibiotics unless there's strong evidence of a secondary bacterial infection (WHO, 2020). Surprisingly, it was found that 70% of COVID-19 patients were administered antimicrobials (WHO, 2020). Consequently, the inappropriate use of antibiotics during the COVID-19 pandemic may exacerbate the global challenge of AMR (Nandi *et al.*, 2023).

This research aims to examine the use of antibiotics in the initial and subsequent treatment stages of RTIs, including pneumonia, both PP to and DP at one English NHS Foundation Trust. In order to provide an in-depth understanding of the impact of the pandemic on antibiotic prescribing, data from eight seasonal time points in 2019 and 2020 will be used. The objectives of this study are as follows: (1) to determine the proportion of inappropriately prescribed antibiotics PP and DP; (2) to evaluate AMS implementation between PP and DP periods; (3) to identify factors influencing antibiotic prescribing and AMS implementation in both PP and DP phases.

**Figure 4.1.** AWaRe classification of antimicrobials (Adopted from WHO, 2023).




## 4.2. Methods

### 4.2.1. Study Design:

A cross-sectional retrospective study was conducted to estimate the proportion of inappropriate antibiotic prescribing among adult patients aged 25 years and older admitted to Bedfordshire Hospitals NHS Foundation Trust. This secondary care provider, formed from the merger of Luton and Dunstable University Hospital and Bedford Hospital in April 2020, serves approximately 400,000 individuals within Luton, South Bedfordshire, and parts of Hertfordshire and Buckinghamshire. Established as a foundation trust in 2006, the hospital network now comprises approximately 742 beds, combining resources and expertise from both entities.

#### 4.2.2. Sample Size

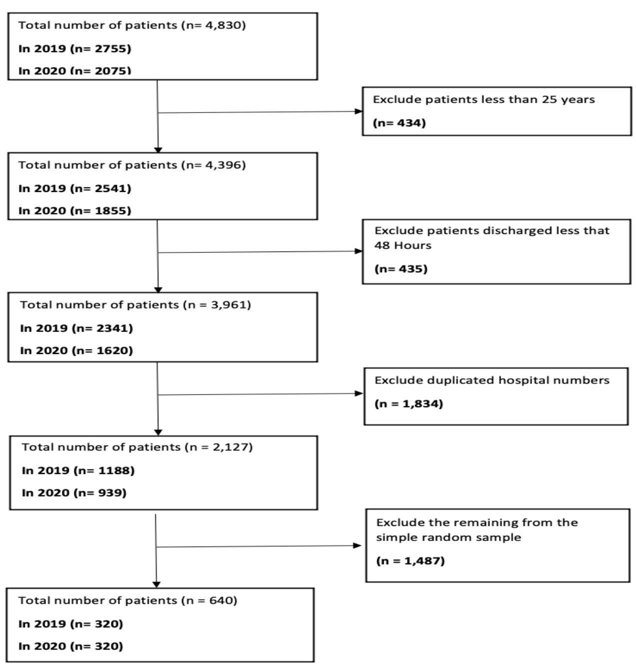
The study's sample size was carefully determined based on Public Health England's estimate that 20% of all antibiotics prescribed in the UK might be inappropriate (PHE, 2018). Using Minitab statistical software, the sample size was calculated with the aim of achieving an appropriate antibiotic prescribing rate of 70%-80%. This calculation factored in the overall population size, a 10% margin of error, and a 95% confidence interval. The target sample size was designed to allow comparison between pre-pandemic (PP) and during pandemic (DP) periods. The estimated baseline prevalence of inappropriate prescribing (20%) was used as a reference. The sample size was set at 320 records for each period, totalling 640 records. Data were collected from medical records in two hospitals, with each hospital providing 160 records PP and 160 records DP. Considering the seasonal variation in antibiotic prescribing, the sample was further divided into four seasons, with 80 records from each season per hospital. This approach ensured a comprehensive and representative dataset for analysing antibiotic prescribing trends throughout the year, enhancing the robustness of the study's findings. The systematic sampling method ensured representativeness, providing a solid basis for evaluating antibiotic prescribing trends and practices.

In this retrospective research, patient-identifiable data was accessed without explicit consent. Post HRA approval, the research student communicated with the AMS pharmacist within Trust to initiate the study. The AMS pharmacist liaised with the coding team to prepare a list of RTI diagnoses using the ICD-10 system, corresponding to the study's timeline. In compliance with the National data opt-out, which enables patients to opt-out from the use of their data for research purposes, the AMS pharmacist at the Trust liaised with the Information Governance team to ensure the removal of NHS numbers of patients who opted out from the study population (NHS Digital, 2018). Unfortunately, in this study, the information governance team excluded patients who had registered with data opt-out. It was not possible to estimate the number of excluded patients who had opted out of data sharing. This limitation affects the comprehensiveness of the study. Post-data extraction, the AMS pharmacist within the Trust anonymised the dataset before handing it to the research student. Anonymised data collection and processing was fair and lawful in line with General Data Protection Regulation (GDPR) principles, Caldicott Guardian, and Trust protocols (National Data Guardian for Health and Care, 2018).

For public and patient involvement, the study protocol was sent to representatives of the East of England Citizens' Senate, an organisation representing patients and carers. They provided an extensive review and valuable feedback. The feedback from the East of England Citizens' Senate centred on enhancing the study protocol, particularly emphasising the need for medical explanations that are easier to understand, improved data security measures, patient-centred summaries, and the integration of patient-centred outcome measures using simple, plain language and attractive colours. The student researcher effectively integrated these suggestions by including clear definitions and a glossary, writing more details about the data protection, confidentiality, and anonymisation procedures and preparing public-facing posters in an accessible format, as an example of this approach is the poster on comparative risk analysis: higher vs. lower risk of community-acquired pneumonia in patients admitted with respiratory tract infections, which utilises colours and straightforward language. This is presented at the end of this chapter (Figure 4.10). Another example of a public poster for the overall research project is shown in Appendix 47. For database registration, this study has been officially registered with the ISRCTN registry. The ISRCTN registry is a primary registry acknowledged by the WHO and the International Committee of Medical Journal Editors (ICMJE), accepting all clinical research studies (ISRCTN, 2022). Moreover, it was registered in Octopus, the global primary research record (Octopus, 2022).

For sampling, the systematic method was employed to consistently select patient medical record data from a larger dataset of the Trust (Thomas, 2022). Initially, data from 4,830 records (2,755 from 2019 and 2,075 from 2020) were extracted. After applying inclusion and exclusion criteria and eliminating duplicate records, the numbers were narrowed down to 1,188 for 2019 and 939 for 2020. Subsequently, a random selection of 80 records for each of the four-time points in 2019, as well as 80 records from 2020, was conducted using Excel's Random function. This resulted in a total of 640 patient records, as shown in Figure 4.2. The systematic sampling method ensured equal representation across the patient population and was consistently applied across all eight seasonal time points, spanning from Spring 2019 to Winter 2020. This approach streamlined the sampling process while ensuring a comprehensive representation of the patient population.

**Figure 4.2.** Data Filtering Algorithm for Extracting a Representative Sample of 640 Patient Medical Records from 2019 and 2020.



#### 4.2.3. Ethics Approval

Ethical approval for this study was granted by the Health Research Authority (HRA), with the Research Ethics Committee (REC) assigning reference number 22/EM/0161. In compliance with this approval, the study protocol underwent review and received approval from the University of Hertfordshire (UH) ethics committee under the reference LMS/PGR/NHS/02975.

#### 4.2.4. Study Population

A stratified sampling strategy was employed to ensure maximum diversity among the included medical records (MRs). To calculate the percentage of appropriate antibiotic prescribing before the pandemic in 2019 and during the pandemic in 2020, empirical and pathogen-targeted prescribed antibiotics were compared with the local antimicrobial guidelines for adult patients aged 25 years and over. The inclusion criteria comprise the following: (i) adult patients aged 25 years and older; (ii) pregnant women and immunocompromised patients; (iii) patients admitted to the Trust; (iv) patients admitted in 2019 and 2020; and (v) patients prescribed antibiotics for respiratory tract infections (RTIs). However, patients who spent less than 48-72 hours in the Accident and Emergency (A&E) department, patients who were not prescribed antibiotics, and children were excluded from this study.

Patient selection was based on electronic health record (EHR) entries identified by their respective ICD-10 codes for RTIs. This encompassed a range of conditions, including both specific and indeterminate diagnoses. Specific conditions included community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), chronic obstructive pulmonary disease (COPD) infective exacerbation without pneumonia, and COVID-19 pneumonia. Alongside these, indeterminate diagnoses such as upper respiratory tract infections (URTIs), lower respiratory tract infections (LRTIs), or pneumonia were grouped under the 'unspecified' category for RTIs. The primary diagnosis of RTIs was pivotal in determining the initial or empirical antibiotics prescribed to patients.

#### 4.2.5. Data Collection

Data was collected from the patient's electronic medical records within the Trust in accordance with the study's inclusion and exclusion criteria. The data collection process for each patient's medical record took about 45 minutes. Data was gathered from eight-time points, with four-time points PP: (i) March (Spring 2019); (ii) June (Summer 2019); (iii) September (Autumn 2019); and (iv) December (Winter 2019). Additionally, four-time points occurred DP: (i) March (Spring 2020) - the first wave of COVID-19; (ii) June (Summer 2020) - the first lockdown; (iii) September (Autumn 2020) - the second wave of COVID-19; and

(iv) December (Winter 2020) - the vaccination rollout. A research student extracted the data from the patient's electronic medical records within the Trust, adhering to the study's inclusion and exclusion criteria (Appendix 29).

#### 4.2.6. Data Extraction

A data extraction tool was employed to obtain the necessary data from patients' medical records (Table 4.1.). A Mind Map was created to aid in organising the data extraction tool in relation to the antibiotic use process and the PHE toolkit for AMS (Appendix 21). The hospital fostered a welcoming atmosphere, providing a two-year honorary contract, access to a secure NHS email, and Trust secure email facilities complete with a temporary username and password for the purpose of data gathering.

Comprehensive training was also afforded to facilitate adept navigation of the hospital's system and the medication management programme. In order to extract data from patients fitting the inclusion criteria, access to three electronic systems in each hospital was required. For instance, at Luton and Dunstable University Hospital, data was extracted from three electronic systems; the Evolve system provided information on antibiotic prescribing upon admission (prescribing stage); the JAC hospital system supplied data on medications expected to be dispensed to the patient (transcribing stage); and the ICE electronic system collated all data related to the patient's discharge. Conversely, at Bedford Hospital, data was gathered from three alternative systems; the Viper hospital system, an integrated hospital information management system and medical records database; the MedChart medicines management system, a pharmacy medication administration system; and the ICE System, which offered an integrated network of communication within the hospital, including details on culture results, lab results, and x-ray investigations.

Prior to commencing 'data extraction', the research student completed training modules for all these systems and subsequently gained access to them. The framework for the antibiotic-use process was utilised, encompassing five stages: 1) prescribing, 2) transcribing, documenting, 3) dispensing, 4) administering, and 5) monitoring (www.usp.org, 2013). Only the first two stages were applied, with the remaining stages falling outside the scope of this study. The AMS Data Extraction Tool was prepared, encompassing demographic information, primary diagnosis, Start Smart criteria, Then Focus criteria, AMS interventions, investigations, and patient outcomes (Figure 4.1).

#### 4.2.7. Pilot Study

The research student undertook the pilot study. Data were extracted from 10 medical records for each time point for 80 patient medical records in 2019 and 2020 (Appendix 29 and Appendix 30). This pilot study aimed to provide more description of the data and examine the feasibility of the data extraction tool in answering the research questions. It was expected to include both descriptive and statistical data.

The result of the pilot study indicated that the data extraction form was sufficient to address all the study objectives. Due to the small sample size of the pilot study, not all statistical analyses were applied. It was impossible to undertake statistical tests for relationships (associations and correlations). More data were required to calculate the prevalence of antimicrobial resistance, CDIs, and antibiotic safety issues, as every patient had one or more of them according to their prognosis. Data generated and extracted from the pilot test will not be included in the actual study analysis.

### 4.2.8. Validity and Reliability

The research student developed the data extraction tool based on the literature. Items within the data extraction tool were identified and agreed upon through discussions with the supervision team members. The research student assessed AMS implementation according to the PHE Toolkit. To ensure the validity of the data extraction tool, an AMS pharmacist at the Trust and the research student independently assessed approximately 1% of the sample (five records) for appropriateness.

The assessments of appropriateness were checked for reliability and validity by examining the percentage of agreement in the data extracted independently. A standardised data extraction tool was utilised, including demographic information, antibiotics used on admission, clinical diagnosis, co-morbidities, antibiotics used after culture, discharge date, and selected laboratory results (Table 4.1). Inter-rater reliability was determined by examining the percentage of agreement in the data extracted independently. Agreements of ≥80% were indicators of the data extraction tool's reliability. Any disagreements were resolved through dialogue. This process ensured the tool's reliability and validity for assessing AMS implementation.

**Table 4.1.** Data extraction tool from the individual patient medical record.

| | |
|---|---|
| **Patient Demography** | |
| Patient Study ID number: | Patient hospital number: |
| Patient age: | Sex: |
| **Start Smart** | |
| Allergies: | Date of admission: |
| Main diagnosis/Clinical Indication: | Medical history / Co-morbidities: |
| Name of Initial antibiotic: (dose, frequency, route, and duration) | Is the duration/stop date documented (Y/N)? |
| Is complies with local guidelines (Y/N)? | Did culture send to Mic prior to Abx (Y/N) |
| **Clinical investigations:**<br>• X-Ray finding:<br>• Blood culture results:<br>• WBCs count:<br>• CRP result:<br>• D Dimer result:<br>• PCT result:<br>• Urea result: | Other relevant clinical information:<br>• Symptoms on admission<br>• Confusion (Y/N):<br>• Others: |
| **Then Focus** | |
| Is abx clinically reviewed? (Y/N) | If yes, what is the review day, e.g., D1, D2, D3...? |
| If yes, who reviewed the Antibiotics?<br>• Prescribing Doctor<br>• Pharmacist<br>• Both of them | What type of AMS intervention:<br>• Continue Antibiotics<br>• Escalation<br>• De-Escalation<br>• IV-to-Oral Switch<br>• Stop Antibiotics<br>• No Intervention |
| **Antibiotic change (Escalation/De-escalation)** | |
| What are the cultural results? | What is culture sensitivity results (S/R/I/NA)? |
| What is the name of the antibiotic changed after the culture results? | Is the changed antibiotic appropriately selected (Y/N)? |
| **IV-to-Oral Switch** | |
| Name of changed Oral Antibiotics? | Is the changed antibiotic appropriately selected (Y/N)? |
| **Abx Stop** | |
| When the antibiotic has been stopped? | Is antibiotic stop complying with the local guidelines (Y/N)? |
| **Infection Control / Healthcare-associated infection (If the patient developed Secondary infection)?** | |
| MRSA bacteremia (Y/N) CDI (Y/N) | COVID-19 (Y/N) |
| **Antibiotic Safety Alert** | |
| Is there any antibiotic allergic reaction? (Y/N)? | Is the antibiotic prescribed comply with the 5Rs, i.e. Right drug, dose, duration, route, and frequency)? |
| **Patient Outcome** | |
| What is the patient outcome(Discharged=1, Deceased=2)? | If discharged, what is the discharge date? |
| What is the Length of Stay (LOS)? | |

ID, Identification; Y/N, yes/no; WBCs, white blood cells; CRP, C-reactive protein; PCT: procalcitonin, D1, D2, D3: Day 1, Day 2, Day 3; AMS, antimicrobial stewardship; MRSA, Methicillin-Resistant Staphylococcus Aureus; CDI, Clostridioides Difficile Infection; MDRO, Multi-Drug-Resistant Organism; COVID-19, coronavirus Disease 2019; LOS, length of stay; Abx, antibiotics; and S/R/I/NA, sensitive/resistant/intermediate/not available.

#### 4.2.9. A key guide for retrospective data coding and analysis

The key code for this study is outlined in Table 4.2., guiding the retrospective data coding and analysis. The research evaluates the appropriateness of antibiotic prescribing guidelines (Bedfordshire, 2020). It compares prescriptions to these guidelines to assess the prevalence of inappropriate prescribing both prior to the pandemic in 2019 and during it in 2020. Additionally, the study examines the initially prescribed antibiotics based on the "five rights" (right antibiotic, right time, right dose, right route and right duration) (RPS, 2019). The analysis also incorporates the AWaRe classification of antibiotics (www.who.int, 2022), allergy considerations (Phillips *et al*., 2019), SSTF (GOV.UK, 2021), and antibiotic review (BSAC, 2018). The key guide used in data analysis is shown in Table 4.2.

**Table 4.2.** A key guide for retrospective data coding and analysis.

| Key Approaches | Description |
|---|---|
| **Inappropriate Antibiotic Prescribing Classification**<br><br>**(Nowakowski et al., 2019)** | Reasons for inappropriate antibiotic prescriptions were categorised into six approaches according to Guidelines, Indication, Dose, Duration, Frequency, and Route of Administration:<br>● 'Guideline-based inappropriateness', the diagnostic code was compared against local treatment guidelines.<br>● 'Indication-based inappropriateness' occurred when there was no indication for the antibiotic prescription or an incorrect choice of antibiotic was made.<br>● The other four approaches of inappropriateness – 'Dose, Duration, Frequency, and Route of Administration' – inappropriateness was classified when antibiotics prescribed with incorrect dose, duration, frequency, or route. |
| **Antimicrobial Stewardship: Start Smart - Then Focus**<br><br>**(Gov.UK, 2023)** | The Start Smart – Then Focus antimicrobial stewardship toolkit presents various options for antimicrobial prescribing decisions and stewardship interventions:<br>● The "Start Smart" steps involve obtaining clear evidence of infection, taking a thorough drug allergy history, and initiating prompt effective antibiotic treatment within one hour of diagnosis, among other steps.<br>● The "Then Focus" steps involve reviewing the clinical diagnosis and documenting a clear plan of action for the "antimicrobial prescribing decision."<br><br>This toolkit recommends five interventions; stop, switch from intravenous to oral administration, continue and review again; change (if possible, to antibiotics with a narrower spectrum of activity); or move to outpatient intravenous antibiotic therapy. |
| **AWaRe Antibiotic Classification**<br><br>**(www.who.int, 2022)** | The World Health Organisation (WHO) updated the Essential Medicines List (EML) by classifying key antibiotics into three categories to promote responsible use, optimise access, and combat antibiotic resistance. The categories are:<br>● **'Access':** These antibiotics, such as amoxicillin, cefalexin, and doxycycline, are first- or second-choice options for common infections. They should be available at all times, as they are effective and affordable. This category aims to improve access and affordability.<br>● **'Watch':** Antibiotics like fluoroquinolones, third generation cephalosporins, and macrolides have a higher risk of selecting for antibiotic resistance. They should be used cautiously and prescribed only for specific infections |

| | |
|---|---|
| | when no Access alternatives are available. The Watch category aims to monitor the use of these antibiotics and reduce their overuse.<br>● **'Reserve':** The 'last resort' antibiotics, such as colistin, carbapenems, and polymyxins, are reserved for use when other options have failed or are unavailable. They are critical for treating multidrug-resistant infections and should be preserved to ensure continued effectiveness. The Reserve category aims to limit their use, preventing further resistance development.<br>This categorisation helps guide appropriate antibiotic use, improve access to essential antibiotics, encourage responsible prescribing practices, and reduce the emergence and spread of antibiotic-resistant bacteria. |
| **Five Rights of Antibiotic Safety**<br><br>**(Royal Pharmaceutical Society, 2019)** | Adherence to the Five Rights of Antibiotic Safety is crucial for healthcare professionals to minimise the risk of errors and ensure the safe, efficacious use of antibiotics for their patients. These rights encompass:<br>● **'Right Antibiotic':** It is essential to select the appropriate antibiotic for each patient, based on local antibiotic guidelines.<br>● **'Right Dose':** Accurate dosing is crucial, and doses should be determined in accordance with local guidelines or the British National Formulary (BNF).<br>● **'Right Duration':** Aligning the duration of antibiotic treatment with local guidelines is necessary to achieve optimal therapeutic outcomes.<br>● **'Right Route':** Ascertaining the route of administration and verifying its appropriateness for the patient, in accordance with local guidelines, is vital for ensuring safe and effective treatment.<br>● **'Right Time':** Timely administration of the prescribed medication, while maintaining a consistent schedule, is of paramount importance for delivering the most effective treatment to the patient. |
| **Coding of allergy**<br><br>**(Phillips et al., 2019)** | The documentation of allergy and adverse drug reaction (ADR) status was coded into three groups:<br>● **'Allergy':** Referring to a hypersensitivity reaction to the antibiotic;<br>● **'Side Effect':** Indicating ADR or side effects associated with the antibiotic; or<br>● **'No documentation':** Representing the absence of allergy and ADR information in the patient's medical record.<br>These classifications were based on the data available in the allergy field of the patient's medical record. |
| **Antibiotic Review**<br><br>**(The British Society for Antimicrobial Chemotherapy, 2018)** | The days of antibiotic review post-admission were coded as follows:<br>● **'2-3 days'** (48-72 hour period) post-admission: Review the dose and the possibility of an IV-to-Oral switch;<br>● **'4-5 days'** post-admission: Review appropriateness, considering microbiological culture results, laboratory findings, and radiological investigations; and<br>● **'7 days'** post-admission: Review the duration of antibiotic therapy. |

WHO, World Health Organisation; EML, Essential Medicines List; IV, Intravenous; AMS, antimicrobial stewardship; ADR, adverse drug reaction; and BNF, British National Formulary.

In this study, the prevalence of inappropriate antibiotic prescribing was evaluated based on the local antimicrobial prescribing guidelines. Inappropriate antibiotic prescribing was assessed by comparing prescriptions to hospital antimicrobial guidelines, both PP and DP. The appropriateness of antibiotic prescribing according to local guidelines was assessed for both empirical antibiotic selection ('Start Smart') and the antibiotics prescribed post-review ('Then Focus'). Additionally, AMS implementation was assessed using the AMS Toolkit from UKHSA (ESPAUR, 2021). The decisions made following this review were utilised to determine the type of AMS intervention and the appropriateness of antibiotic prescribing in relation to the local guidelines (Cartuliares *et al*., 2023).

### 4.2.10. Data analysis

The hypotheses for this chapter's research were multifaceted. Firstly, it was hypothesised that the prevelance of inappropriate antibiotic prescribing would show significant variation between 2019 and 2020. Secondly, it was anticipated that the implementation of AMS, as per the PHE Start Smart, Then Focus toolkit, would vary significantly between both years. Additionally, it was hypothesised that the distribution of co-morbidities would differ significantly between the 2019 and 2020 groups. Factors associated with AMS, such as laboratory tests, investigations, culture results, and day of antibiotic review, were also expected to show significant associations. Lastly, it was hypothesised that COVID-19 would have a significant impact on AMS, length of stay, and patient outcomes.

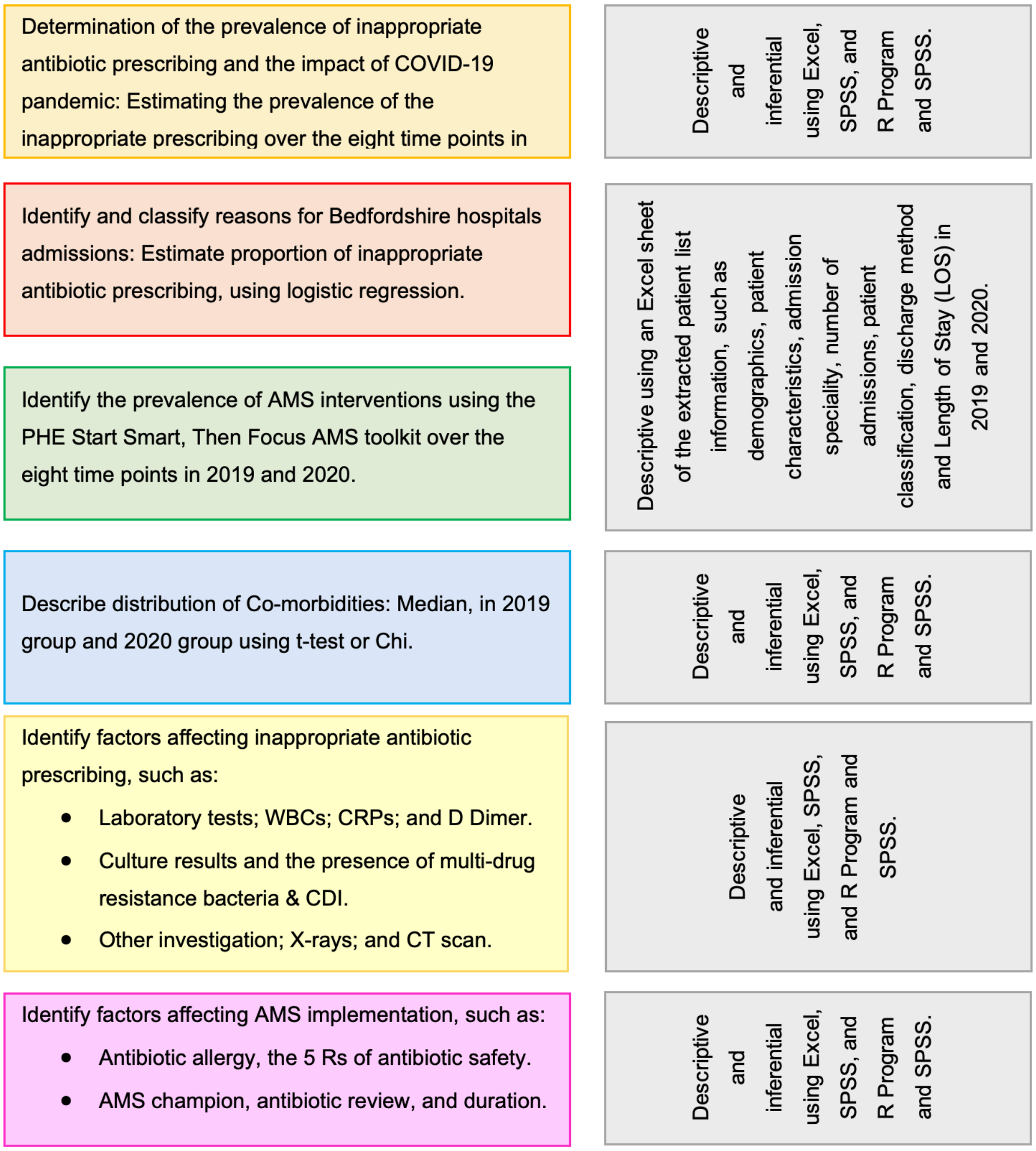
To test these hypotheses, various statistical methods were employed. Descriptive statistics summarised patient characteristics, admission specialties, and the number of admissions, including means, medians, and standard deviations. Inferential statistics, such as Chi-Square tests, compared categorical variables, including the distribution of co-morbidities and reasons for hospital admissions between 2019 and 2020. T-tests compared the means of continuous variables, such as laboratory test results and length of stay, between the two groups. Additionally, SPSS analysis was conducted for inferential statistics to identify factors associated with AMS and the impact of COVID-19 on AMS, patient outcomes, and length of stay. This comprehensive approach, outlined in the framework of data analysis, ensured a robust examination of the various aspects of AMS implementation and its outcomes, providing valuable insights into the effectiveness of AMS practices and the influence of the COVID-19 pandemic.

The sample size and characteristics significantly influenced the validity and reliability of the hypotheses tested in this research. The study utilised a sample size of 640 patient records, with 320 records each from 2019 (pre-pandemic) and 2020 (during-the-pandemic). This sample was systematically selected to ensure representativeness and robustness in analysing antibiotic prescribing trends and AMS implementation. The large sample size allowed for adequate statistical power to detect significant differences and associations across the time points and between the two groups. The systematic sampling method ensured that the data was representative of the broader patient population, enhancing the generalisability of the findings. Despite the limitation of excluding patients who opted out of data sharing, the overall sample size and selection methodology provided a solid foundation for testing the research hypotheses and drawing reliable conclusions about the impact of AMS practices and the effects of the COVID-19 pandemic on antibiotic prescribing and patient outcomes. Figure 4.3 presents the framework for retrospective data analysis, focusing on evaluating inappropriate antibiotic prescribing and AMS implementation across eight time points in 2019 and 2020. It includes classifying hospital admissions, analysing co-morbidities, and identifying factors associated with AMS using descriptive and inferential statistics. The framework also assesses the impact of COVID-19 on AMS, length of stay, and patient outcomes.

In this study, the prevalence of inappropriate antibiotic prescribing was evaluated based on local antimicrobial prescribing guidelines. The appropriateness of antibiotic prescribing was assessed by comparing the prescribed antibiotics to hospital antimicrobial guidelines for both the pre-pandemic and during-pandemic periods. Specifically, the study examined the empirical antibiotic selection ('Start Smart') and the antibiotics prescribed post-review or pathogen-directed antibiotic selection ('Then Focus'). Additionally, AMS implementation was assessed using the AMS Toolkit from UKHSA (UKHSA, 2023). The decisions made following this review were utilised to determine the type of AMS intervention and the appropriateness of antibiotic prescribing in relation to the local guidelines (Bedfordshire, 2020).

Descriptive analyses were conducted. Data on categorical or binary variables were presented as numbers (n) and proportions (%), while continuous variables with non-normal distributions were summarised using mean and standard deviation (SD). The 'Start Smart' approach data, including age, sex, allergies, indication, comorbidities, and duration, were described using numbers (n) and percentages (%) and further analysed via logistic regression. Similarly, the 'Then Focus' approach data, covering WBCs, CRP, serum creatinine, chest X-rays, day of antibiotic review, and type of AMS intervention, were presented in numbers (n) and percentages (%) and underwent advanced analysis via logistic regression. Data analysis was conducted using Excel and SPSS tools, ensuring comprehensive and robust insights. For advanced statistical analysis, IBM SPSS Statistics version 22.0 (www.IBM.com, 2020), RStudio version 2022, and R version 4.2.2 (R-project.org, 2016) were utilised. The data analysis framework for this retrospective study was shown in Figure 4.3. Statistical tests used included t-tests for comparing means, Chi-Square tests for categorical data, and logistic regression to calculate adjusted odds ratios (ORs) of factors affecting 'Start Smart' initial antibiotic prescribing PP and DP (2019 and 2020). Additionally, the study assessed the 'Then Focus' criteria of antibiotic prescribing, comparing data from 2019 (n=320) and 2020 (n=320). The proportion of the five rights of antibiotic safety was compared between 2019 and 2020 during the COVID-19 pandemic. The implementation rate of antimicrobial stewardship interventions was also measured before the COVID-19 pandemic (n=320) and during the pandemic (n=320).

**Figure 4.3.** Framework for retrospective data analysis.




AMS, antimicrobial stewardship; PHE, Public Health England; WBCs, white blood cells; CRPs, C-reactive proteins; CT, Computed Tomography; CDI, Clostridioides Difficile Infection; SPSS, statistical package for the social sciences; and 5 Rs: five rights of antibiotic safety.

## 4.3. Results

### 4.3.1. Clinical and demographic characteristics

A retrospective analysis was conducted on the patient medical records of 640 patients from the Trust, with the demographics of these individuals presented in Table 4.3. This comprehensive analysis of various variables revealed no statistically significant differences between the years 2019 and 2020. The ages of patients admitted for RTIs during this period ranged from 25 to 99 years. A slight shift was noted in gender distribution: in 2019, females represented 49.4% (158) of cases, which increased marginally to 49.7% (159) in 2020.

In terms of patient outcomes, the data showed that the mortality rate — the proportion of patients who passed away or died — remained constant at 15% over the two-year study period. A comparison of the *p*-Value for patient demographics and outcomes between PP in 2019 and DP in 2020 indicated no significant changes. The mean age differed slightly (PP: 74.3, DP: 76.2; P=0.127), with no notable changes in gender distribution (female P=0.886, male P=0.525) or outcomes for deceased (P=0.886) and discharged patients (P=0.525), as illustrated in Table 4.3.

**Table 4.3.** Characteristics of the patient demographics admitted prior to the COVID-19 pandemic (n=320) and during the pandemic (n=320), in 2019 and 2020.

| **Patient characteristics** | | **Prior to Pandemic 2019** ***n* (%)** | **During the Pandemic 2020** ***n* (%)** | ***P*-Value** |
|---|---|---|---|---|
| **Age (Range= 25-99)** | Mean (SD) | 74.3 (16.0) | 76.2 (15.5) | 0.127 |
| **Gender** | Female (%) | 158 (49.4) | 159 (49.7) | |
| | Male (%) | 162 (50.6) | 161 (50.3) | |
| **Patient Outcome** | Deceased (%) | 48 (15.0) | 50 (15.4) | 0.886 |
| | Discharged (%) | 272 (85.0) | 270 (84.4) | |

Table 4.4 presents patients' LOS in 2019 and 2020. The average LOS was 13.7 days in 2019 and decreased to 12.3 days in 2020. The LOS varied from one day to a maximum of 119 days in 2019.

**Table 4.4.** Length of stay in 2019 and 2020 (Days).

| | 2019 | 2020 |
|---|---|---|
| **Mean** | 16 | 15 |
| **Median** | 11 | 10 |
| **Range** | 1-119 | 1-97 |
| **Standard Deviation** | 16 | 13 |

### 4.3.2. Prevalence of Inappropriate Antibiotic Prescribing Using Start Smart - Then Focus

The prevalence of adherence to local guidelines indicated that approximately 50% of patients received appropriate empirical antibiotics or met 'The Start Smart Criteria' upon admission, with no significant difference between the PP and DP periods. However, the prevalence of non-adherence to guidelines in the pathogen-directed antibiotic or 'Then Focus Criteria' notably increased during the pandemic in 2020. Inappropriate antibiotic prescribing rose from 36% PP to 64% DP.

The term "Start Smart" denotes the initial stage of antibiotic administration or empirical therapy (GOV.UK, 2019). The discrepancy in the appropriateness of antibiotic prescribing prior to and during the COVID-19 pandemic seems statistically insignificant. Age and gender do not appear to impact antibiotic prescribing patterns significantly. However, the age group of 66-85 years represented the largest segment of the study population, with 156 individuals (48.8%) PP in 2019 and 148 (46.3%) DP in 2020. The extraction of allergy/adverse drug reaction (ADR) status was categorised as ‘allergy’, ‘side-effect’, or ‘no documentation’. This classification was based on the data recorded in the allergy/ADR field, along with any supporting information found in the EHR (Phillips *et al*., 2019). A difference in the documentation of side effects was observed only between 2019 and 2020, with an odds ratio (OR) of 7.23 (95% CI 1.54 to 53.37, *p*-Value =0.023).

Additionally, several factors influenced this initial antibiotic prescribing or empirical therapy ‘Start Smart’, including the initial diagnosis ‘indication’. For example, CAP was the predominant diagnosis in approximately 126 (39.4%) PP and 136 (42.5%) DP. Uncertain diagnoses, including URTIs, LRTIs, and Pneumonia, impact the selection of appropriate antibiotics at admission. These unclear or non-specific diagnoses accounted for 28.8% PP and 22.8% DP. Regarding COPD, a statistically significant difference was observed between PP and DP, with an odds ratio (OR) of 0.42 (0.19-0.90, p=0.029). Interestingly, within the data procured from the study population, the severity risk assessment, CURB-65 score for CAP, was only reported in three patient records (NICE, 2016).

The presence of unclear diagnoses, such as URTIs, LRTIs, and pneumonia, influences the appropriate choice of antibiotics at the time of admission. Additionally, the analysis revealed a statistically significant difference in the incidence of COVID-19 pneumonia between 2019 and 2020, with an odds ratio (OR) of 20.24 (95% CI 5.82-128.19, *p*-Value=0.001).

Concerning adherence to empirical antibiotic treatment guidelines, it was observed that guidelines for empirical therapy were followed by 50% of the RTI study population in 2019 and 51% DP in 2020. In comparing comorbidities prior to and during the pandemic, significant differences were observed in several conditions. Heart failure demonstrated a notable increase with an odds ratio (OR) of 2.06 (95% CI 1.23-3.52, *p*-Value=0.007). Hypercholesterolemia also showed a significant difference with an OR of 1.90 (95% CI 1.14 to 3.20, *p*-Value=0.014). In contrast, kidney diseases exhibited a lower OR of 0.52 (95% CI 0.32 to 0.84, *p*-Value=0.008). Similarly, liver diseases revealed an increased OR of 3.55 (95% CI 1.41-9.82, *p*-Value =0.010), while asthma had a reduced OR of 0.50 (95% CI 0.25 to 0.95, *p*-Value=0.038). Regarding the duration of antibiotic therapy, there were no significant differences in the duration, whether shorter (≤3 days) or longer (≥6 days), between PP and DP (Table 4.5).

**Table 4.5.** Adjusted ORs of factors affecting the 'Start Smart' initial antibiotic prescribing PP and DP (2019 and 2020).

| | | **Prior to Pandemic - 2019 *n* (%)** | **During the Pandemic - 2020 *n* (%)** | **Adjusted OR (95% CI)** |
|---|---|---|---|---|
| **Age** | 25-45 | 22 (6.9) | 22 (6.9) | - |
| | 46-65 | 52 (16.3) | 46 (14.4) | 1.13 (0.49-2.68, *p*=0.775) |
| | 66-85 | 156 (48.8) | 148 (46.3) | 1.35 (0.62-3.04, *p*=0.455) |
| | >85 | 90 (28.0) | 104 (32.4) | 1.75 (0.77-4.08, *p*=0.186) |
| **Gender** | Female | 158 (49.4) | 161 (50.3) | - |
| | Male | 162 (50.6) | 159 (49.7) | 0.98 (0.67-1.42, p=0.910) |
| **Allergy** | Allergy | 18 (5.6) | 17 (5.3) | - |
| | No allergy | 254 (79.4) | 258 (80.6) | 1.00 (0.46-2.20, *p*=1.000) |
| | Not documented | 46 (14.4) | 29 (9.1) | 0.58 (0.23-1.45, *p*=0.243) |
| | Side effect | 2 (0.6) | 16 (5.0) | 7.23 (1.54-53.37, *p*=0.023)* |
| **Indication** | CAP | 126 (39.4) | 136 (42.5) | - |
| | COPD Infective Exacerbation | 30 (9.4) | 14 (4.4) | 0.42 (0.19-0.90, *p*=0.029)* |
| | COVID Pneumonia | - | 44 (13.8) | 20.24 (5.82-128.19, *p*<0.001)*** |

| | | | | |
|---|---|---|---|---|
| | HAP | 67 (20.9) | 52 (16.2) | 0.74 (0.46-1.20, *p*=0.221) |
| | LRTI | 30 (9.4) | 23 (7.2) | 0.77 (0.39-1.51, *p*=0.452) |
| | Pneumonia | 56 (17.5) | 42 (13.1) | 0.92 (0.53-1.60, *p*=0.769) |
| | URTI | 6 (1.9) | 8 (2.5) | 1.61 (0.46-5.85, *p*=0.455) |
| | VAP | 5 (1.5) | 1 (0.3) | 0.20 (0.01-1.38, *p*=0.156) |
| **Comorbidities** | Hypertension | 143 (44.7) | 148 (46.2) | 1.17 (0.80-1.72, *p*=0.414) |
| | Hypotension | 13 (4.0) | 14 (4.4) | 1.20 (0.49-2.91, *p*=0.689) |
| | Atrial Fibrillation | 61 (19.0) | 64 (20.0) | 1.02 (0.64-1.63, *p*=0.922) |
| | Heart failure | 32 (10.0) | 63 (19.6) | 2.06 (1.23-3.52, *p*=0.007)** |
| | Hypercholesteremia | 40 (12.5) | 58 (18.1) | 1.90 (1.14-3.20, *p*=0.014)* |
| | Diabetes Mellitus | 65 (20.3) | 54 (16.9) | 0.76 (0.47-1.22, *p*=0.256) |
| | Hypothyroidism | 24 (7.5) | 20 (6.2) | 0.81 (0.40-1.63, *p*=0.555) |
| | Kidney Diseases | 75 (23.4) | 46 (14.4) | 0.52 (0.32-0.84, *p*=0.008)** |
| | Liver Diseases | 8 (2.5) | 19 (5.9) | 3.55 (1.41-9.82, *p*=0.010)* |
| | Malignancy | 50 (15.6) | 43 (13.4) | 0.95 (0.57-1.57, *p*=0.850) |
| | Osteoarthritis | 31 (9.7) | 40 (12.5) | 1.06 (0.58-1.93, *p*=0.843) |
| | Asthma | 35 (10.9) | 21 (6.5) | 0.50 (0.25-0.95, *p*=0.038)* |
| | COPD | 42 (13.1) | 40 (12.5) | 1.38 (0.76-2.49, *p*=0.289) |
| | Dementia | 25 (7.8) | 23 (7.2) | 0.81 (0.41-1.59, *p*=0.538) |
| | Epilepsy | 10 (3.1) | 13 (4.1) | 1.32 (0.49-3.65, *p*=0.580) |
| | Depression | 12 (3.7) | 20 (6.2) | 1.81 (0.77-4.39, *p*=0.178) |
| **Duration** | <=3 Days (Short) | 168 (52.5) | 164 (51.3) | - |
| | >=6 Days (long) | 152 (47.5) | 156 (48.7) | 1.16 (0.82-1.66, *p*=0.400) |

HPN, hypertension; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; COVID, Coronavirus; HAP, hospital-acquired pneumonia; LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection; and VAP- ventilator-associated Pneumonia. Notes: ***P < 0.001; **0.001≤ P <0.01; *0.01≤ P <0.05.

Table 4.6. provides an overview of factors impacting the 'Then Focus' antibiotic prescribing or pathogen-directed therapy in patients with RTIs prior to and during the COVID-19 pandemic (ESPAUR, 2023). No significant differences were observed in laboratory tests, such as white blood cell (WBC), C-reactive protein (CRP), and serum creatinine. The incidence of positive chest X-ray results indicating pneumonia was higher in 2020 compared to 2019, showing a statistically significant difference with an odds ratio of 1.75 (95% CI 1.04 to 2.97, *p*-Value = 0.037). For the timing for antibiotic review post-admission, it was noted that reviews were typically conducted within 48-72 hours of admission. There was no significant difference in the timing of these reviews between 2019 and 2020, with an odds ratio of 1.02 (95% CI 0.97 to 1.08, *p*-Value = 0.461). Regarding the AMS interventions, significant changes were observed in only two interventions. The 'Continue Antibiotics' AMS intervention showed a significant difference during the pandemic, with an odds ratio of 3.36 (95% CI 1.30-9.25, p=0.015). Additionally, there was a notable significant increase in the 'De-escalation' AMS intervention, evidenced by a statistically significant odds ratio of 2.77 (95% CI 1.37-5.70, *p*-Value =0.005) (Table 4.5).

In terms of adherence to local antibiotic treatment guidelines in the 'Then Focus' approach, it was found that antibiotic choices made post-review adhered to these guidelines in 64% of the RTIs study population PP in 2019. This rate of adherence or appropriateness dropped to 36% DP in 2020. In contrast, interventions such as escalation, the switch from intravenous to oral antibiotics, and the discontinuation of antibiotics did not exhibit statistically significant shifts, with the *p*-Values exceeding the 0.05 significance level. The odds ratios for these interventions were 0.97 (0.48-1.96, *p*-Value=0.928) for the 'IV-to-oral Switch' and 0.86 (0.44-1.71, p=0.659) for 'Stopping Antibiotics', respectively (Table 4.6). In accordance with local guidelines, the percentage of inappropriate antibiotic prescriptions rose from 36% in 2019 (PP) to 64% in 2020 (DP).

**Table 4.6.** Adjusted ORs of factors affecting the 'Then Focus' criteria of antibiotic prescribing prior to the COVID-19 pandemic (n=320) and during the pandemic (n=320) (in 2019 and 2020).

| | | Prior to Pandemic – 2019 n (%) | During the Pandemic - 2020 n (%) | Adjusted OR (95% CI) |
|---|---|---|---|---|
| WBCs | | 12 (3.8) | 11 (3.4) | |
| CRP | | 82 (25.6) | 78 (24.4) | 1.00 (1.00-1.00, *p*=0.595) |
| Serum Creatinine | | 126 (39.4) | 123 (38.4) | 1.00 (1.00-1.00, *p*=0.860) |
| Chest X-rays | Pneumonia % | 39 (12.2) | 54 (16.9) | 1.75 (1.04-2.97, *p*=0.037)* |
| | No Pneumonia % | 82 (25.6) | 65 (20.3) | - |
| | Not done % | 199 (62.2) | 201 (62.8) | 1.26 (0.86-1.85, *p*=0.231) |
| Day of Antibiotic Review | Mean (SD) | 4.2 (2.8) | 4.4 (2.9) | 1.02 (0.97-1.08, *p*=0.461) |
| Type of AMS intervention | Change Antibiotic (Substitution) | 25 (7.8) | 20 (6.3) | - |

| | | | | |
|---|---|---|---|---|
| | Continue Antibiotics | 14 (4.4) | 19 (5.9) | 3.36 (1.30-9.25, *p*=0.015)* |
| | De-escalation | 37 (11.6) | 81 (25.3) | 2.77 (1.37-5.70, *p*=0.005)** |
| | Escalation | 65 (20.3) | 76 (23.8) | 1.50 (0.76-2.99, *p*=0.248) |
| | IV-to-Oral Switch | 70 (21.9) | 58 (18.1) | 0.97 (0.48-1.96, *p*=0.928) |
| | Stop Antibiotics | 94 (29.4) | 59 (18.4) | 0.86 (0.44-1.71, *p*=0.659) |
| | No Intervention | 15 (4.6) | 7 (2.2) | - |

WBCs, white blood cell; CRP, C-reactive protein; and AMS, antimicrobial stewardship.

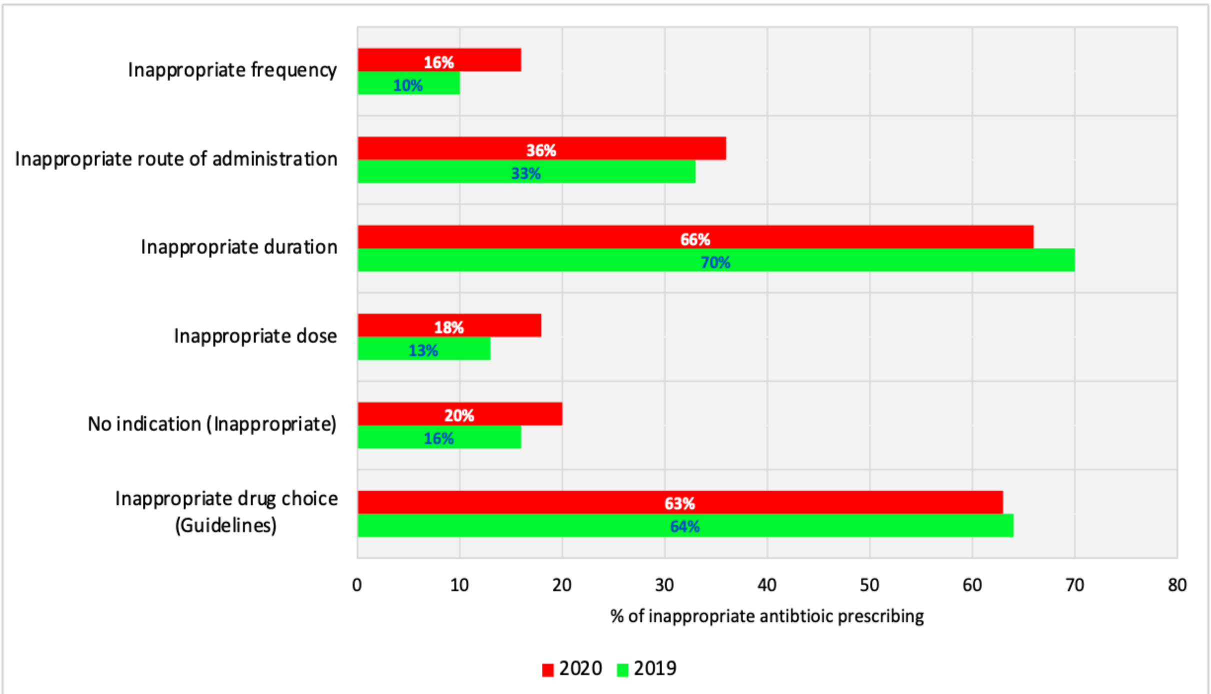
Notes: ***P < 0.001; **0.001≤ P <0.01; *0.01≤ P <0.05.

#### 4.3.3. Proportion of Inappropriate Anti-Infective Prescribing Using the 'Five Rights of Antibiotic Safety'

According to the Institute for Safe Medication Practices (ISMP) and Institute for Healthcare Improvement (IHI), the 'Five Rights of Antibiotic Safety' are essential for ensuring proper anti-infective use in acute care settings (ISMP, 2017; RPS, 2021). These rights encompass the right patient, drug, dose, time, and duration (IHI, 2020). This study evaluated adherence to the 'Five Rights of Anti-Infectives' for the years 2019 and 2020. As illustrated in Figure 4.4 below, there were significant shifts in the proportions of inappropriate anti-infective prescribing during this period.

The inappropriate route of anti-infective administration saw a slight increase from 33% in 2019 to 36% in 2020 (Abdelsalam Elshenawy et al., 2023). Similarly, instances of inappropriate dosing rose from 13% in 2019 to 18% in 2020. However, the proportion of inappropriate duration prescriptions showed improvement, decreasing from 70% in 2019 to 66% in 2020. Conversely, prescriptions made without clear indications increased from 16% in 2019 to 20% in 2020. Interestingly, the selection of the anti-infective, in accordance with antimicrobial guidelines, remained relatively stable, hovering around 63-64% across both years. These findings highlight a concerning rise in inappropriate anti-infective prescribing patterns, especially during the 2020 COVID-19 pandemic.

**Figure 4.4.** Proportion of inappropriate anti-infective prescribing: a comparison of 2019 and 2020 during the COVID-19 pandemic using the 'five rights of antibiotic safety'.




### 4.3.4. Prevalence of inappropriate antibiotic prescribing by INDICATION

#### 4.3.4.1. Antibiotic prescribing in CAP

The analysis indicated an over-diagnosis trend in pneumonia cases. In 2019, CAP represented about 40% (128 out of 320) of the prescribing reasons, increasing slightly to 42% in 2020. For CAP, the severity and corresponding treatment method are determined using the CURB-65 score, as shown in Figure 4.5. This scoring system includes five prognostic indicators, each contributing one point: **C**onfusion, **U**rea levels above 7 mmol/litre, **R**espiratory rate over 30 breaths per minute, **B**lood pressure under 90mmHg systolic or 60mmHg diastolic, and **A**ge 65 or older. In adults, CAP severity assessment involves clinical judgment, supported by mortality risk scores like CURB65. A score of 0 or 1 indicates low severity, 2 points to moderate severity, and a score between 3 and 5 reflects high severity. The CURB-65 Risk Assessment Framework for community-acquired pneumonia is shown in Appendix 34.

The local antimicrobial guidelines, in conjunction with NICE, dictate that antibiotic prescribing for CAP is contingent upon the CURB-65 score (Bedfordshire, 2020). As such, the selection of antibiotics is escalated concomitant with an increase in the CURB-65 score (Bestpractice.bmj.com, 2020). However, within the data procured from the study population, the CURB-65 score was only reported in three instances. This scarcity of data may potentially influence the appropriateness of antibiotic prescribing for patients diagnosed with CAP (NICE, 2020). The clinical pathway, risk assessment, and antimicrobial management of CAP in an acute care setting are detailed in Appendix 34. Upon analysing the assembled data and the CURB-65 score, it was discerned that age of 65 or above, confusion, and hypotension were the most salient factors escalating the risk severity of CAP.

Moreover, key symptoms upon admission, such as shortness of breath (SOB), fever, and cough, experienced an uptick in 2020 compared to 2019. For instance, incidences of SOB rose to 33% (106 out of 320) in 2020, as opposed to the pre-pandemic level of 22.5% (72 out of 320) in 2019. Furthermore, the presence of other clinical conditions could influence the prescribing of antibiotics for CAP. Notably, respiratory conditions such as COPD, Asthma, and COVID-19 significantly impacted antibiotic prescribing patterns in 2020. Conditions that compromise the immune system, such as cancer, also play a crucial role. Lastly, incidents such as accidental falls can exacerbate the severity of illness and consequently affect the appropriateness of antibiotic prescribing. However, it's important to note that these findings necessitate further investigation to fully understand this complex issue (Table 4.5).

#### 4.3.4.2. Antibiotic Prescribing in HAP

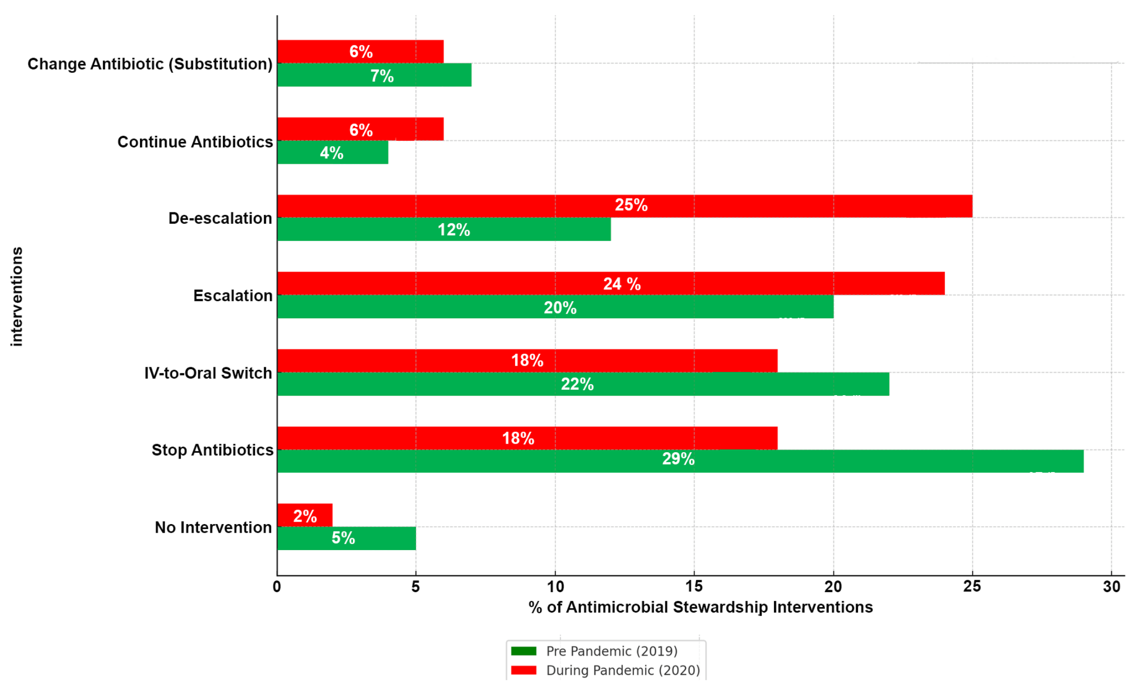
Hospital-acquired pneumonia was identified as the second most common diagnosis in the study group. This type of pneumonia develops at least 48 hours after hospital admission. It is not in the incubation phase at the time of admission, as noted in the NICE 2019 prescribing considerations. The local antimicrobial guidelines categorise HAP into two types: ‘Early-onset HAP’, occurring 48 to 96 hours post-admission without previous antimicrobial treatment, and ‘Late-onset HAP’, which appears after five days from admission or after prior antimicrobial therapy. The selection of antibiotics for HAP depends on its classification, with choices becoming more complex as the patient's hospital stay lengthens. The study showed a decrease in HAP incidence from 21% (67 out of 320 cases) in the previous period to 16% (52 out of 320 cases) in 2020, as shown in Table 4.6. The prevalence of early-onset HAP was relatively low at 5% (5 out of 106 cases), while late-onset HAP was significantly more common, accounting for 95% of cases. This study further disclosed a high prevalence of HCAIs among the study population, estimated at 94% (603 out of 640). Concerning these cases, 62% (376 out of 603) involved the inappropriate prescription of antibiotics. This area warrants further academic exploration to identify effective strategies for preventing and curtailing HCAIs. These strategies should include the employment of evidence-backed infection prevention and control measures.

Interestingly, this study highlighted the presence of unspecific diagnosis plays a substantial role in instances of unsuitable antibiotic prescribing and the implementation of AMS programmes. For example, the analysis found that unclear diagnoses, specifically in cases of LRTIs, URTIs, or pneumonia, constituted 24% (153 out of 640) of all cases. These diagnostic uncertainties were linked to 72% of unsuitable antibiotic prescribing decisions in this group, as shown in Table 4.6. The 'Then Focus’ AMS toolkit was used to investigate the predictors of inappropriate targeted antibiotic(s) prescribing, and the findings are presented in Table 4.7. In terms of adherence to the local antibiotic guidelines, the prevalence of inappropriate antibiotic prescribing was 22.1% and 21.2% in 2019 and 2020, respectively. A single variable was found to be significantly associated (*p-Value* < 0.05) with inappropriate antibiotic prescribing, as shown in Table 4.7., which is the use of the X-Ray investigation for pneumonia (*p-Value*= 0.037, OR = 1.75, 95% CI = 1.04-2.97). However, CRP laboratory test was insignificant (*p-Value*= 0.595).

### 4.3.5. Antimicrobial Stewardship Interventions

The Start Smart – Then Focus antimicrobial stewardship toolkit presents various options for antimicrobial prescribing decisions and stewardship interventions. The present study observed a significant difference among AMS interventions in all seasons, as demonstrated by Figure 4.5. The bar chart below presents a comparison of antimicrobial stewardship interventions in the years prior to and during the COVID-19 pandemic, specifically in 2019 and 2020. From the bar chart, we can see that the percentage of cases with 'No intervention' intervention decreased slightly during the pandemic, from 5% to 2%. There was a noticeable decline in the practice of 'Stop Antibiotics', from 29% PP to 18% DP. The 'IV-to-Oral Switch' also saw a small decrease from 22% to 18%. On the other hand, the 'Escalations' intervention increased from 20% to 24%. Notably, the rate of "De-escalation' nearly doubled, rising from 12% to 25%, and the practice of "Continuing antibiotics' intervention went up from 4% to 6%. The frequency of "Changing antibiotics, or substitution", showed a minor decrease from 7% to 6% (Figure 4.5).

**Figure 4.5.** Antimicrobial stewardship interventions prior to the COVID-19 pandemic (n=320) and during the pandemic (n=320) (in 2019 and 2020).



### 4.3.6. The WHO Access, Watch, Reserve (AWaRe) classification

A heatmap was generated to visually display the antibiotics prescribed for RTIs before and during the COVID-19 pandemic. The WHO Access, Watch, Reserve (AWaRe) classification was employed as the gold standard for antibiotic classification (WHO, 2023). Table 4.7. shows the heatmap for antibiotic consumption in 2019 and 2020 based on AWaRe criteria, indicating a significant increase in antibiotic consumption in 2020 compared to 2019. According to the WHO AWaRe Tool's categorisation, 10 antibiotics had been classified under the 'Access' group, 11 as 'Watch' antibiotics, and 3 as 'Reserve' category antibiotics, as depicted in Figure 4.6. The research examined the antibiotics that had been prescribed for RTIs to 640 patients who were admitted between 2019 and 2020. In this heatmap, each row represented a different antibiotic, while each column corresponded to a specific month within the seasons from 2019 to 2020.

The colour intensity in each cell of the heatmap corresponded to the frequency of prescriptions for each antibiotic used in treating RTIs, including pneumonia and COVID-19-positive cases, among the 640 patients admitted during those years. This visualisation became particularly informative, considering that COVID-19 could lead to secondary bacterial infections necessitating antibiotic treatment. Darker colours indicated higher rates of prescriptions, thus providing a visual representation of the prescribing trends over time.

The heatmap employed a colour-coded system to illustrate the levels of antibiotic consumption across several seasonal months, from March 2019 to December 2020. Antibiotics were categorised into three groups based on AWaRe classification, which aims to promote the proper use of antibiotics to combat resistance (WHO, 2023). In this heatmap figure, the consumption of antibiotics was delineated into four levels based on their values, with the highest recorded value being 86 and the lowest being 0. The categories were defined as follows: 0 indicated no antibiotic usage, 1–9 denoted minimal antibiotic consumption, 10–29 signified a moderate level of antibiotic usage, and 30 and above represented the highest level of antibiotic consumption (Figure 4.6). The categorisation of data in Figure 4.7 was derived from a literature review and the clinical relevance of antibiotic prescribing trends.

The "Access" category encompassed essential antibiotics that were to be widely available. In this category, amoxicillin/clavulanic acid exhibited a substantial increase, beginning at 67 in March 2019 and peaking at 86 in September 2020, indicating high usage. Flucloxacillin also showed an increase from 2 in March 2019 to 5 in June 2020, suggesting moderate use.

The "Watch" group consisted of antibiotics with a higher potential for resistance and were to be used more cautiously. In this study, azithromycin usage surged from zero in March 2019 to 19 in June 2020, displaying a high level of use. Clarithromycin began at 21 in June 2019 and rose to 32 by December 2020. Ciprofloxacin and levofloxacin also experienced increases in their consumption levels over the study period. Piperacillin/tazobactam maintained a consistently high consumption level, remaining at 29 in both March 2019 and March 2020. Meropenem showed a modest rise from 2 in March 2019 to 5 in December 2020.

Within the "Reserve" category, which contains antibiotics reserved for treating infections caused by multidrug-resistant organisms, linezolid sustained a high consumption level of 3 in March 2019 with no significant increase throughout 2020. Aztreonam and ceftazidime/avibactam displayed minimal increases in usage.

Notably, there was an increase in the total usage of antibiotics within the 'Access' category, which reached 305 in 2019 before slightly decreasing to 298 in 2020. In contrast, usage within the 'Reserve' category decreased, falling from 9 to 3. Meanwhile, the 'Watch' category experienced a considerable increase in 2020, with usage escalating to 386, up from 259 in the previous year (R. Elshenawy *et al.*, 2023).

**Table 4.7.** Heatmap for antibiotic use in 2019 and 2020 according to AWaRe criteria.

**WHO Access, Watch, Reserve (AWaRe) classification for antibiotics evaluation and monitoring before and during the COVID-19 pandemic**

| Access | Mar-19 | Jun-19 | Sep-19 | Dec-19 | Mar-20 | Jun-20 | Sep-20 | Dec-20 |
|---|---|---|---|---|---|---|---|---|
| Amoxicillin | 2 | 1 | 2 | 3 | 6 | 6 | 0 | 1 |
| Amoxicillin/clavulanic acid | 67 | 61 | 56 | 76 | 25 | 70 | 86 | 66 |
| Benzylpenicillin | 1 | 0 | 2 | 0 | 3 | 0 | 0 | 0 |
| Doxycycline | 1 | 1 | 3 | 2 | 1 | 2 | 0 | 1 |
| Flucloxacillin | 2 | 2 | 3 | 2 | 0 | 5 | 2 | 1 |
| Gentamicin | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 |
| Metronidazole | 3 | 7 | 2 | 0 | 4 | 4 | 2 | 4 |
| Sulfamethoxazole/Trimethoprim | 0 | 1 | 1 | 0 | 4 | 2 | 0 | 0 |
| Clindamycin | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cephalexin | 0 | 0 | 2 | 1 | 1 | 0 | 0 | 0 |
| **Watch** | | | | | | | | |
| Azithromycin | 0 | 1 | 2 | 0 | 13 | 19 | 3 | 11 |
| Ceftazidime | 2 | 2 | 0 | 0 | 0 | 1 | 0 | 0 |
| Ceftriaxone | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 |
| Cefuroxime | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Ciprofloxacin | 3 | 3 | 1 | 8 | 7 | 5 | 9 | 5 |
| Clarithromycin | 14 | 21 | 26 | 33 | 32 | 21 | 25 | 32 |
| Levofloxacin | 12 | 9 | 8 | 11 | 14 | 13 | 14 | 23 |
| Meropenem | 2 | 0 | 1 | 1 | 5 | 4 | 4 | 5 |
| Piperacillin/Tazobactam | 29 | 30 | 15 | 16 | 29 | 21 | 22 | 25 |
| Teicoplanin | 0 | 0 | 1 | 0 | 3 | 0 | 0 | 0 |
| Vancomycin | 1 | 4 | 0 | 1 | 0 | 1 | 0 | 0 |
| **Reserve** | | | | | | | | |
| Aztreonam | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| Cefazidime/Azobactam | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| Linezolid | 3 | 2 | 1 | 1 | 0 | 0 | 1 | 1 |

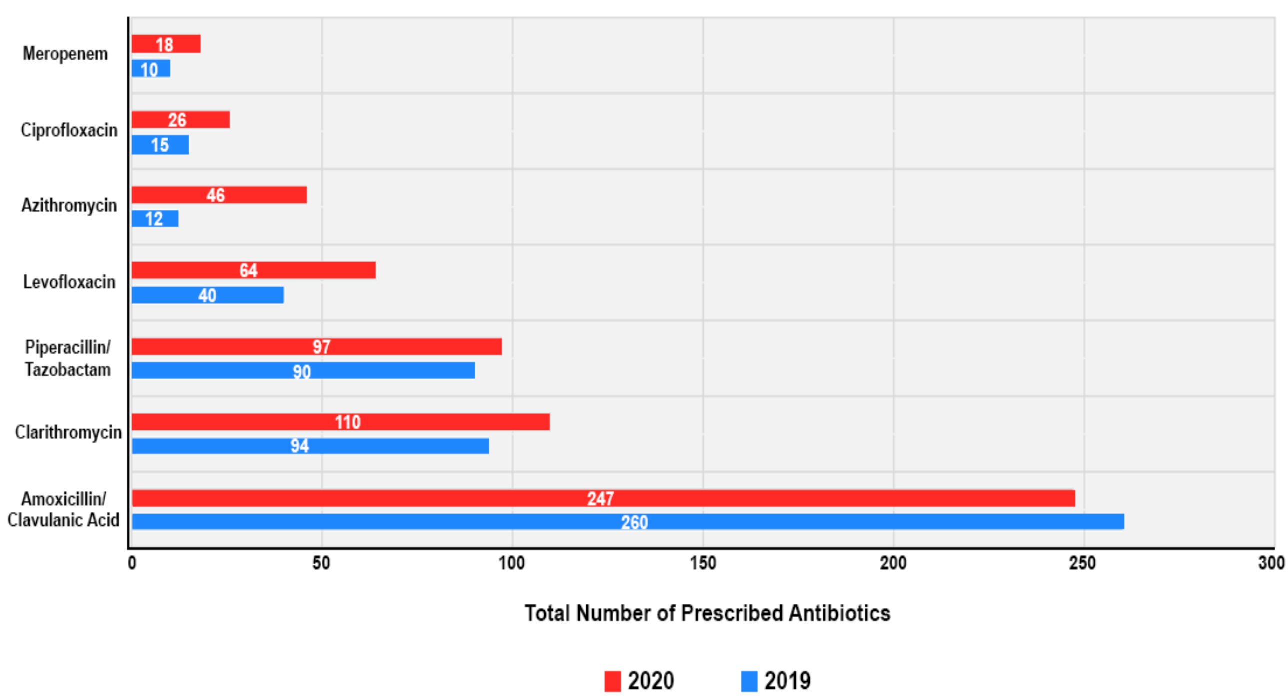
| | |
|---|---|
| (grey) | 0: Absence of antibiotic usage |
| (green) | 1 - 9: Minimal antibiotic consumption |
| (orange) | 10 - 29: Moderate level of antibiotic usage |
| (red) | 30 and above: High level of antibiotic consumption |

### Top seven prescribed antibiotics prior to and during the COVID-19 pandemic

Figure 4.6 shows the use of the seven most prescribed antibiotics in both pre-pandemic and during-pandemic periods, further detailed in Supplement 1. In 2019, amoxicillin/clavulanic acid was the most frequently prescribed antibiotic, accounting for 260 instances. This trend persisted in 2020 with 247 instances, maintaining its top position. Although there was a slight decrease in the total number of amoxicillin/clavulanic acid prescriptions in 2020, its percentage as the top prescribed antibiotic relative to other antibiotics increased notably.

In 2020, compared to 2019, there was an increase in prescriptions for most of the other antibiotics. For instance, clarithromycin saw an increase from 94 prescriptions in 2019 to 110 in 2020. Piperacillin/tazobactam also witnessed a slight rise, from 90 instances in 2019 to 97 in 2020. Additionally, 2020 saw increased prescriptions of levofloxacin, azithromycin, and ciprofloxacin compared to 2019. Levofloxacin prescriptions grew from 40 in 2019 to 64 in 2020. Azithromycin had a surge, jumping from 12 in 2019 to 46 in 2020. Ciprofloxacin also displayed a rising trend, going from 15 in 2019 to 26 in 2020. Meropenem's usage modestly increased in 2020, from 10 to 18 instances.

**Figure 4.6.** Seven commonly prescribed antibiotics prior to and during the COVID-19 pandemic.



### 4.3.7. Factors affecting inappropriate antibiotic prescribing and AMS implementation

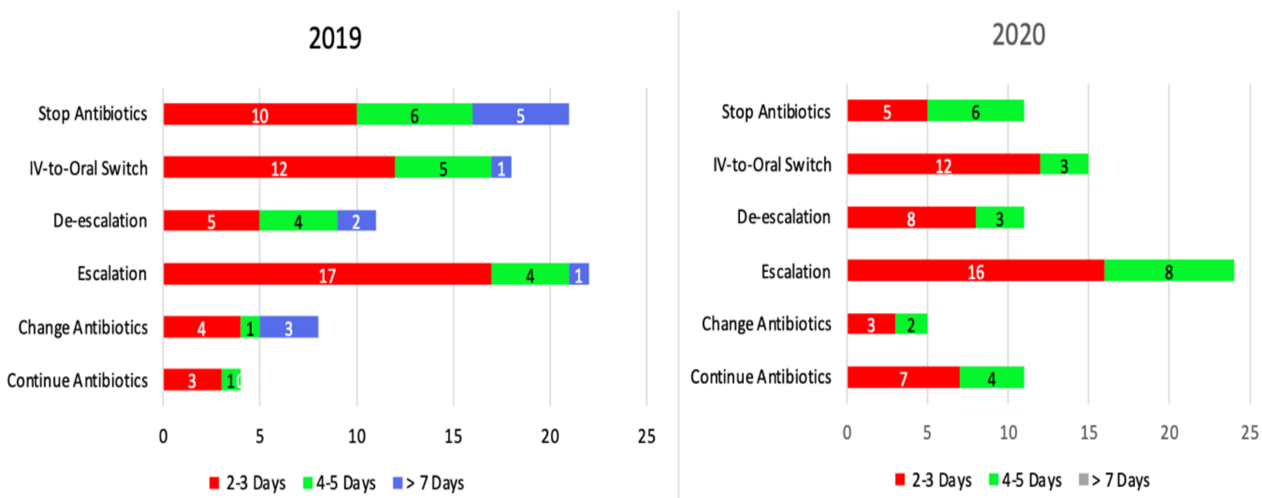
#### 4.3.7.1. Antibiotic review

The results indicate that there was no significant difference in the days of antibiotic review between 2019 and 2020 ($P = 0.461$, OR = 1.02, 95% CI = 0.97-1.08) (Table 4.8.). Antibiotic reviews were classified into three categories based on the review day: 2-3 Days, 4-5 Days, and 7 Days or more (BSAC, 2018). A review in the 48-72 hours of admission (2-3 Days) category was applied in order to review the dose and possibility of an 'IV-to-Oral Switch'.

The 4-5 Days category was used to review appropriateness considering microbiological, culture results, laboratory and radiological investigations). However, a review after the 7-day category was implemented to review the duration of antibiotic therapy.  In Figure 4.7., it was found that 2-3 Days of antibiotic review was used in 2019 more than in 2020, 91 and 51, respectively.

The most common AMS interventions used in the 48-72 hours review were 'Escalation and IV-to-Oral Switch'. For the 4-5 day review, 'Stop Antibiotics and IV-to-Oral Switch' were the most frequently used AMS interventions PP, with 6 and 5 instances, respectively. The most frequently used intervention DP in the 4–5-day review was 'Escalation and Stop Antibiotics', with 8 and 6, respectively. However, the seven-day review category was only found PP in 2019, with 'Stop Antibiotics' being the most frequently applied AMS intervention in this category.

**Figure 4.7.** Antibiotic review (days) and AMS interventions.



#### 4.3.7.2. Shorter versus longer antibiotic duration per local guidelines

A key finding of this study was the assessment of the appropriateness of initial or empirical antibiotic prescribing according to local guidelines. Appropriate prescribing was evaluated by comparing the prescriptions with local antimicrobial guidelines for both PP and DP periods (BSAC Stewardship, 2018; (Bedfordshire, 2020). Of the total 640 patients admitted in 2019 and 2020, 463 received antibiotics for ≤5 days, 109 for 6-7 days, and 68 for periods exceeding 8 days. This categorisation was derived from local antimicrobial guidelines, a review of the literature, and the clinical relevance of antibiotic duration practices. The study also focused on analysing the differences between shorter and longer courses of appropriate antibiotic therapy for various RTIs. For instance, with CAP, local guidelines (Bedfordshire, 2020) recommend an antibiotic treatment duration ranging from 5 days (shorter duration) to longer durations of 6-7 days and >8 days. Similarly, in cases of COPD infective exacerbation, a shorter antibiotic course of ≤5 days was assessed against longer durations of 6-7 days and >8 days.

Table 4.8 presents a comparison of appropriate antibiotic prescribing: shorter versus longer durations of antibiotic treatment prior to and during the COVID-19 pandemic in 2019 and 2020. For conditions, such as HAP, VAP, COPD infective exacerbation, and COVID-19 pneumonia, a 'Shorter Duration' of ≤5 days was shown to be as effective as 'Longer Durations' of 6-7 days and >8 days. There was no significant difference in the appropriateness of shorter versus longer antibiotic durations among the three RTI categories, with the exceptions of CAP, which showed a p-value of 0.02, and 'Unspecified' RTIs, which had a p-value of 0.07. Furthermore, the majority of patients were appropriately prescribed antibiotics for shorter durations of ≤5 days, representing 164 (35.4%) of the cases.

**Table 4.8**. Comparison of appropriate antibiotic prescribing: shorter versus longer duration of antibiotic treatment prior to and during the COVID-19 pandemic in 2019 and 2020 (*n*=640).

| | **Indication (*n*,%)** | **Duration of antibiotic use** | | | ***p*-Value** |
|---|---|---|---|---|---|
| | | **≤ 5 Days *n*=463** | **6-7 Days *n*=109** | **> 8 Days *n*=68** | |
| | | ***n* (%)** | ***n* (%)** | ***n* (%)** | |
| Appropriateness of antibiotics | CAP (262, 409%) | 84 (18.1) | 25 (22.9) | 14 (20.6) | 0.02 |
| | HAP (119, 18.6%) | 45 (9.7) | 11 (10.1) | 7 (10.3) | 0.7 |
| | VAP (6, 0.9%) | 3 (0.6) | 1 (0.9) | 1 (1.5) | 0.6 |
| | COPD infective exacerbation (44, 6.9%) | 17 (3.7) | 5 (4.6) | 1 (1.5) | 0.6 |
| | COVID pneumonia (47, 7.3%) | 8 (1.7) | 1 (0.9) | 1 (1.5) | 0.4 |
| | Unspecified (162, 25.3%) | 7 (1.5) | 2 (1.8) | 0 (0) | 0.07 |
| | Overall (640, 100%) | 164 (35.4) | 45 (41.3) | 24 (35.3) | 0.5 |

CAP, community-acquired Pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia; and COPD, chronic obstructive pulmonary disease.

#### 4.3.7.3. Intravenous-to-Oral Antibiotic Switch (IVOS)

Certain antimicrobial agents, including amoxicillin 500mg IV, clarithromycin 500mg IV, flucloxacillin 1g IV, and levofloxacin 500mg IV, were switched to oral regimens with equivalent doses and potencies. On the other hand, some antimicrobials were switched to corresponding oral regimens but with different dosages. For instance, amoxicillin with clavulanic acid 1.2g IV, ciprofloxacin 200-400mg IV, and metronidazole 500mg were altered to amoxicillin 500mg with clavulanic acid 125mg oral, ciprofloxacin 250-500mg oral, and metronidazole 400mg oral, respectively. However, piperacillin with tazobactam 4.5g IV was replaced with a different oral regimen, amoxicillin 500mg with clavulanic acid 125mg (Table 4.9).

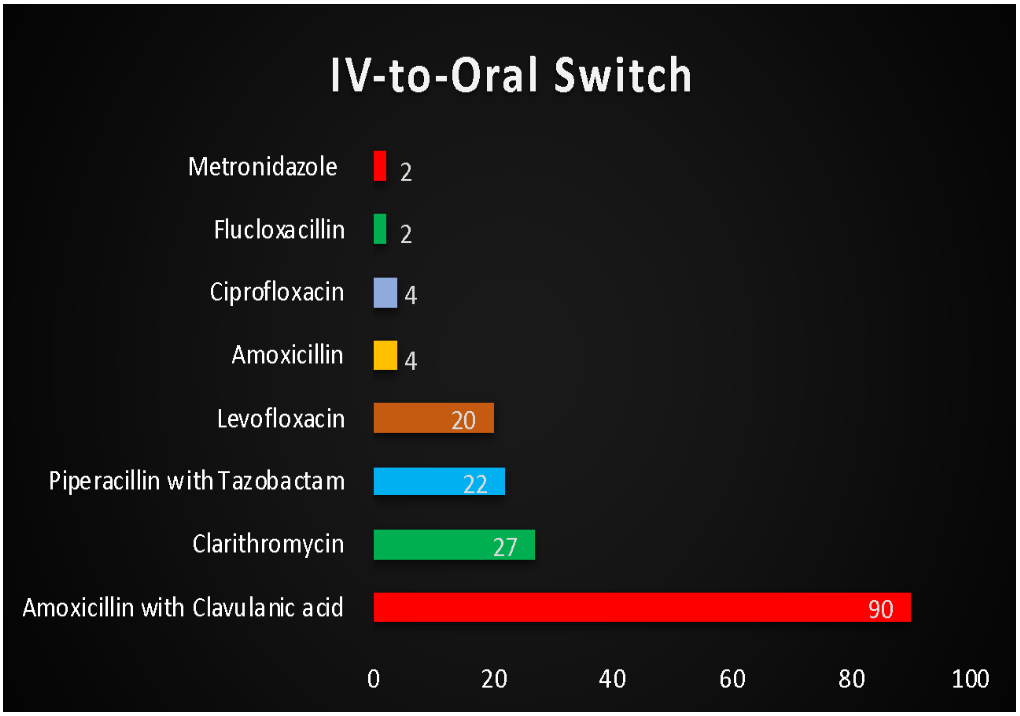
**Table 4.9.** IVOS changes in respiratory tract Infections in 2019 and 2020.

| Current IV Therapy | Oral option |
|---|---|
| Amoxicillin 500mg-1g tds | Amoxicillin 500mg-1g tds |
| Amoxicillin with Clavulanic acid 1.2g tds | Amoxicillin 500 with Clavulanic acid 125mg tds |
| Ciprofloxacin 200-400mg bd | Ciprofloxacin 250-500 bd |
| Clarithromycin 500mg bd | Clarithromycin 500mg, bd |
| Flucloxacillin 1g qds | Flucloxacillin 1g qds |
| Levofloxacin 500mg bd | Levofloxacin 500mg bd |
| Piperacillin with Tazobactam 4.5g tds | Amoxicillin 500 with Clavulanic acid 125mg tds |
| Metronidazole 500mg tds | Metronidazole 400mg tds |

Od, once a day; bd, 2 times /day; tds: 3 times/day; and qds, 4 times/day.

Figure 4.8. illustrates the most prevalent antibiotics that underwent a switch to oral regimens. The IVOS intervention, as one of the AMS interventions, was observed in 171 out of 640 patients (26.7%) within the study population. Amoxicillin/clavulanic acid emerged as the most frequently switched antibiotic (90 out of 171), followed by clarithromycin (27 out of 171). In contrast, piperacillin/tazobactam and levofloxacin showed only 22 and 20 switches, respectively.

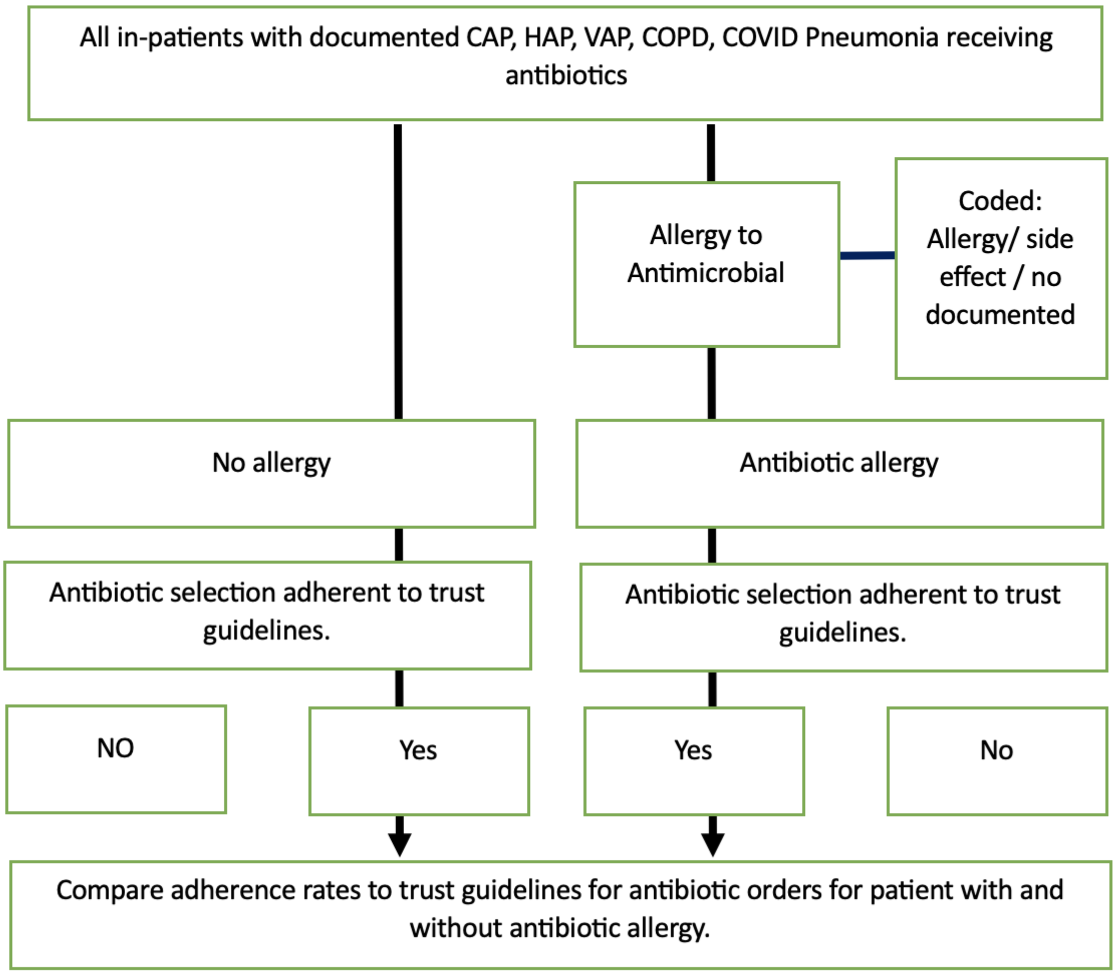
**Figure 4.8.** The number of IV antibiotics that have been switched to oral antibiotics (Total = 171).




### 4.3.7.4. Antibiotic allergy

Figure 4.9. shows the flow diagram of patient-prescribed antibiotics for various RTIs, including CAP, HAP, VAP, COPD, bronchiectasis, and viral pneumonia. The diagram also illustrates the extraction of antibiotic allergy data from the medical records of these patients and the selection of appropriate antibiotics based on adherence rates to trust antibiotic guidelines for patients with and without antibiotic allergies.

**Figure 4.9.** Flow diagram for antibiotic allergy data extraction from the medical records of patients with RTIs.




CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia; and COPD, chronic obstructive pulmonary disease.

Table 4.10. classifies antibiotic safety into three categories: antibiotic allergy, side effects, and undocumented cases for patients prescribed antibiotics following local guidelines (Phillips *et al*., 2019). In both 2019 and 2020, there were 74 reported antibiotic reactions that adhered to local guidelines. Unspecified penicillin was the most common, with 12 cases (16.2%), followed by co-trimoxazole at 4 cases (5.4%).

In terms of side effects or adverse drug events, unspecified penicillin was again the most frequent, with 4 cases (5.4%). Amoxicillin, clarithromycin, and co-trimoxazole each had an equal prevalence of 2 cases (2.7%) (Table 4.10).

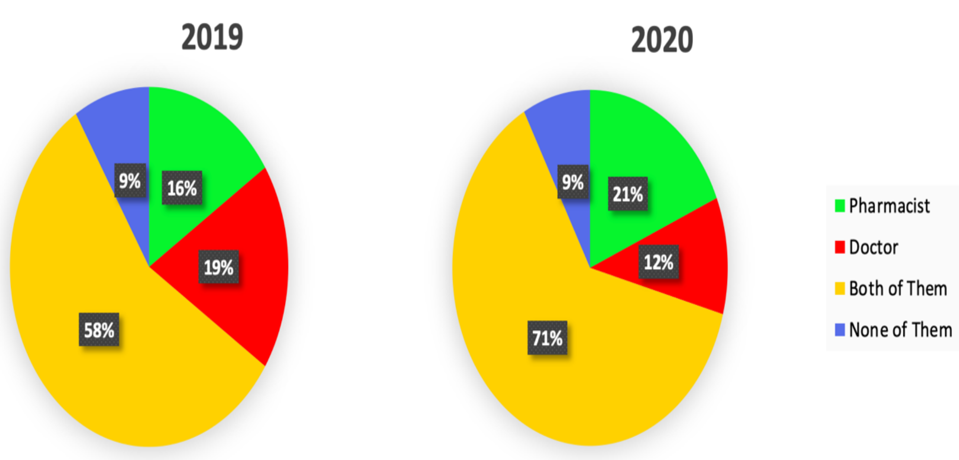
**Table 4.10.** Antibiotic safety classification: allergic reactions, adverse effects, and non-documented.

| **Reported Antibiotic Allergy n= 74 2019 & 2020** | **Allergy** | **Side Effect (Adverse Effect)** | **Not Documented** |
|---|---|---|---|
| Amoxicillin/ Benzylpenicillin | 1 (1.3) | 2 (2.7) | 1 (1.3) |
| Ciprofloxacin/ Levofloxacin | 1 (1.3) | 1 (1.3) | 1 (1.3) |
| Clarithromycin | 5 (6.7) | 2 (2.7) | 1 (1.3) |
| Co-Amoxiclav (Amoxicillin and Clavulanic acid) | 3 (4.05) | 1 (1.3) | 5 (6.7) |
| Co-Trimoxazole (Sulphonamide & Trimethoprim) | 4 (5.4) | 2 (2.7) | 3 (4.05) |
| Erythromycin | 2 (2.7) | 1 (1.3) | 1 (1.3) |
| Flucloxacillin | 1 (1.3) | 1 (1.3) | 6 (8.1) |
| Metronidazole | 1 (1.3) | 1 (1.3) | 1 (1.3) |
| Nitrofurantoin | 1 (1.3) | 1 (1.3) | 6 (8.1) |
| Penicillin (unspecified) | 12 (16.2) | 4 (5.4) | 21 (28.3) |
| Phenoxymethylpenicillin | 1 (1.3) | 1 (1.3) | 2 (2.7) |
| Tazobactam (piperacillin)/ Meropenem | 1 (1.3) | 1 (1.3) | 1 (1.3) |
| Tetracycline & Oxytetracycline | 1 (1.3) | 1 (1.3) | 1 (1.3) |

### 4.3.8. Antimicrobial Stewardship Champion

Figure 4.10 offers a comparison of the involvement of AMS champions in the antibiotic review process, examining the roles of pharmacists, doctors, and instances where neither were involved. The percentages refer to the proportion of cases out of the total number of reviews conducted prior to pandemic (n=320) and during the pandemic (n=320), in 2019 and 2020. Pharmacist involvement rose modestly from 19% to 21%, while doctor involvement decreased from 19% to 12%. However, combined efforts increased from 58% to 71%, indicating potential benefits from multidisciplinary collaboration.

**Figure 4.10.** The role of AMS champions (pharmacists and doctors) in reviewing antibiotics in antimicrobial stewardship implementation (n=320 pre-pandemic and n=320 during the pandemic).



## 4.4. Discussion

This retrospective study analysed the clinical and demographic characteristics of patients admitted to Bedfordshire Hospitals NHS Foundation Trust with RTIs during pre-pandemic and during-pandemic periods. The study aimed to evaluate the implementation of AMS as a crucial element of the UK's Five-Year AMR strategy, designed to enhance patient care and combat antimicrobial resistance (ESPAUR, 2023). The SSTF AMS toolkit was used to improve antibiotic prescribing (UKHSA, 2023). The results indicated that most clinical and demographic characteristics were not significantly different between the two periods, except for admission speciality and sex. The COVID-19 pandemic significantly influenced the number of patients admitted with RTIs, with an increase in admissions in December 2019 due to the rapid spread of COVID-19 and its impact on respiratory health (ESPAUR, 2023). Antibiotics were prescribed either empirically at admission or after a 48-72 hour period post-admission. Patients with CAP had the highest percentage of antibiotic prescriptions, around 40% pre-pandemic in 2019 and 43% during-pandemic in 2020. This aligns with a study in Denmark, where penicillin with beta-lactamase inhibitor was commonly prescribed for CAP. Only 31.3% of CAP cases were treated according to regional guidelines, with most patients receiving IV antibiotics within 4 hours and switching to oral antibiotics by day 5 (PHE, 2018).

The elderly demographic, particularly those aged 66-85 years, constituted the majority of the study population, emphasising the need for safe AMS interventions in this age group. This finding aligns with a 2023 study from the Netherlands, which demonstrated that a multifaceted antibiotic stewardship intervention effectively reduced antibiotic prescribing in older adults (Hartman et al., 2023). The study also outlined the methodology for extracting antibiotic allergy data from patients' medical records and selecting appropriate antibiotics per trust antibiotic guidelines for individuals with or without antibiotic allergies. A 2019 UK study categorised antibiotic safety into three classifications: antibiotic allergy, side effects, and undocumented cases concerning patients who received antibiotics following local guidelines (Phillips et al., 2019). The study found a high proportion of patients with penicillin allergies, impacting patient safety. In both 2019 and 2020, 74 antibiotic reactions were reported, all adhering to local guidelines, with unspecified penicillin being the most prevalent.

A clear and specific diagnosis is critical for selecting the right antibiotic, yet data on severity risk assessments like the CURB-65 score for CAP were limited (NICE, 2016). Laboratory tests such as WBCs, PCR, serum creatinine, and chest X-rays played a crucial role in these decisions. In 2020, the prevalence of positive chest X-ray findings indicating pneumonia was higher compared to 2019, with an odds ratio of 1.75 (p-Value = 0.037). The absence of a clear and specific diagnosis at the time of patient admission can significantly influence antibiotic selection (Flaws et al., 2009). Key factors for effective antibiotic selection include understanding the causative organism, infection severity, local resistance trends, and patient-specific considerations, aligning with RPS and NICE guidelines for AMS (RPS, 2021; NICE, 2016). Adherence to local guidelines indicated that 50% of patients received appropriate empirical antibiotics upon admission, with no significant difference between the pre-pandemic and during-pandemic periods. However, non-adherence to guidelines increased during the pandemic in 2020, with inappropriate antibiotic prescribing rising from 36% pre-pandemic to 64% during-pandemic. This emphasised the necessity of sustaining AMS during pandemics. This trend aligns with international research, such as a study in Sweden showing that 60% of inpatients were prescribed antimicrobials, with significant changes in treatments by day five (Molstad et al., 2022). A study in England assessed the risks and appropriateness of antibiotic prescribing in primary care during the pandemic, finding high and variable levels of repeat antibiotic prescribing and highlighting the need for updated treatment guidelines (Zhong et al., 2023). This study examined empirical antibiotics ('Start Smart') and repeat antibiotic prescribing during ongoing clinical management ('Then Focus'), finding higher appropriateness rates in 'Then Focus' criteria, with a slight decrease from 63% in 2019 to 59% in 2020.

Comparing comorbidities pre-pandemic and during-pandemic revealed significant differences in chronic conditions, including increased cardiovascular diseases, hypercholesterolemia, kidney diseases, liver diseases, asthma, and COPD during the pandemic. A 2020 study in Wales found that sputum purulence was the most precise predictor of bacterial pathogens in COPD exacerbations, while elevated CRP levels did not enhance predictive value (Francis et al., 2020). A 2020 study in Mexico found that chronic conditions, such as cardiovascular diseases and chronic kidney disease, increased the risk of pneumonia and mortality in COVID-19 patients (Hernández-Vásquez et al., 2020). A 2021 study from Manchester showed that short and long antibiotic courses are equally effective for treating acute infections, indicating that shorter courses may help reduce antimicrobial resistance without increasing complications (Palin et al., 2021). This study found no significant difference in the effectiveness of different antibiotic course lengths, with similar proportions of short and long courses in 2019 and 2020.

Antimicrobial stewardship is crucial in secondary care settings, and the Start Smart-Then Focus approach is recommended for all antibiotic prescriptions. This study examined AMS implementation in all seasons pre-pandemic and during-pandemic, finding that 'De-escalation' AMS intervention showed an increasing trend at the start of the COVID-19 pandemic, while 'Escalation' intervention had the most significant increase in 2020. The 'Stop Antibiotics' intervention experienced a decline in usage during 2020, suggesting the need for updated approaches in antimicrobial stewardship (Abdelsalam Elshenawy et al., 2023). The IVOS was another vital component of AMS interventions, with 26.7% of patients undergoing 'IVOS' intervention. Amoxicillin/clavulanic acid and clarithromycin were the most commonly switched antibiotics, indicating their suitability for conversion to oral regimens (Abdelsalam Elshenawy et al., 2023).

A 2022 Lancet study showed that the antibiotic review kit intervention reduced antibiotic use among adult acute general medical inpatients, suggesting hospitals adopt the kit to curb antibiotic overuse (Budgell et al., 2022). This study also investigates factors impacting AMS implementation, finding no significant difference in antibiotic review days between 2019 and 2020. The classification of antibiotic review into three categories highlights the importance of regular review at different treatment stages. The 48-72 hours review category, including 'Escalation' and 'IV-to-Oral Switch', was the most commonly employed AMS intervention, suggesting the significance of early intervention (Abdelsalam Elshenawy et al., 2023). The 'Five Rights of Antibiotic Safety' are essential for ensuring proper antibiotic use in hospitals before and during the COVID-19 pandemic (ISMP, 2017). These rights encompass the right patient, drug, dose, time, and duration, reducing antibiotic resistance, minimising adverse drug events, and optimising patient outcomes (UKHSA, 2021). The decrease in inappropriate duration from 2019 to 2020 suggests progress in this aspect of prescribing, but continued efforts are necessary (Abdelsalam Elshenawy et al., 2023).

This study examined antibiotic prescribing patterns at an English NHS Foundation Trust using the AWaRe classification system for antibiotics. The AWaRe classification effectively tracks antibiotic usage, establishes goals, and observes stewardship initiatives' impact (WHO, 2021). Amoxicillin/clavulanic acid, in the 'Access group,' was the most frequently prescribed antibiotic in both pre-pandemic and during-pandemic periods. Its total prescriptions decreased slightly in 2020, but its relative percentage among all antibiotics increased. The study observed a significant increase in azithromycin, categorised in the 'Watch' group, reflecting a broader shift in prescription practices during the pandemic. International studies corroborate this trend, indicating a growing preference for azithromycin across diverse geographical and clinical settings (Mudenda et al., 2023; Mohamad et al., 2022; Kalungia et al., 2022; Prakash et al., 2021). This increase could be due to rising RTIs, including suspected COVID-19, and early inclusion of antibiotics like azithromycin in treatment protocols (Mugada et al., 2021).

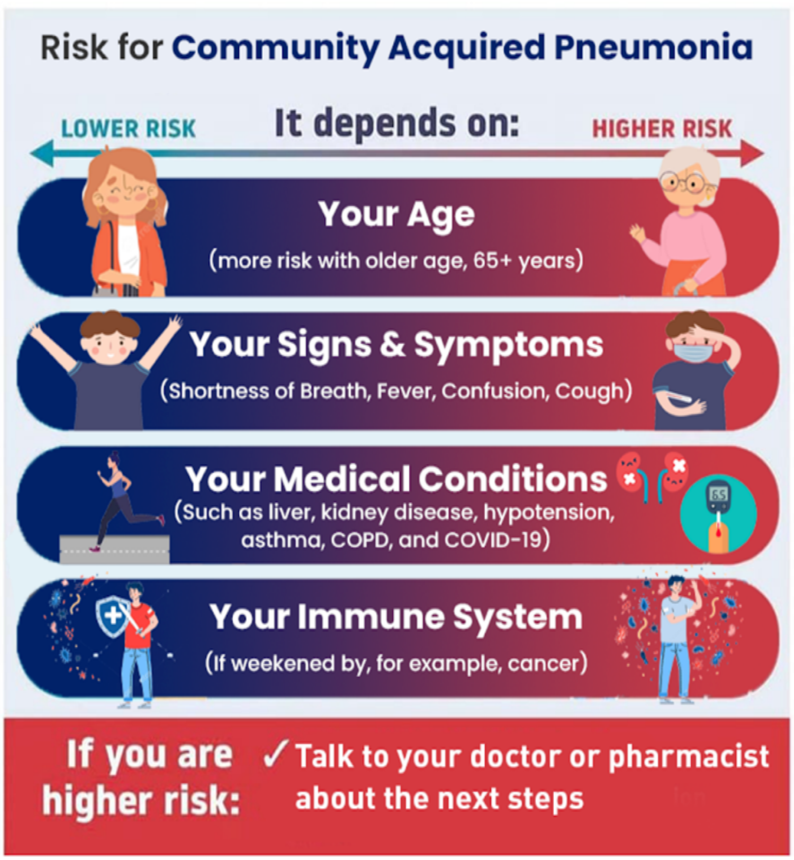
The pharmacist's contribution increased during-pandemic, reaching 21% compared to 19% in 2019. The doctor's involvement declined from 19% in 2019 to 12% in 2020. Combined efforts of pharmacists and doctors significantly increased, rising from 58% pre-pandemic to 71% during-pandemic, underscoring the potential synergistic impact of a collaborative approach (RPS, 2019). Pharmacist access to patient health records, including diagnostic results and up-to-date local formulary information, enables more informed clinical decisions regarding antibiotics (RPS, 2022). This study emphasises the pivotal roles of pharmacists and doctors as AMS champions during the pandemic.

The presence of AMS dashboard including items beyond antibacterial items, DDD, multidrug-resistant organisms and HCAIs would be beneficial, considering factors such as comorbidities, laboratory results, main diagnoses, days of antibiotic review, AMS interventions, top antibiotics, AMR, antibiotic decisions, infections, and wards with high antibiotic consumption (WHO, 2019). Such a comprehensive visual tool would significantly enhance AMS implementation, identify gaps in antibiotic prescribing, and offer practical solutions to improve prescribing and mitigate AMR (Global AMR R&D, 2023). An AMS educational programme or roadmap is essential for continuously educating and training healthcare professionals in AMS practices, highlighting ongoing learning's significance (Future Learn, 2023).

Incorporating quality improvement projects and case-based discussions within this programme is critical, especially during emergencies or crises. Case-based learning tailored to common cases during the COVID-19 pandemic can optimise antibiotic use (CQC, 2023). A quality improvement programme ensures sustainable AMS practices, offering solutions to problems identified by dynamic dashboards (Global AMR R&D, 2023). This is vital during emergencies, such as the COVID-19 pandemic, to maintain effective AMS implementation and mitigate AMR (UKHSA, 2023).

Public and Patient Involvement was integral, involving protocol review and feedback from the Citizens Senate, aligning with NIHR's briefing notes stressing public involvement's significance (NIHR, 2021). This study developed a CAP awareness poster based on logistic regression findings, aiming to educate health professionals and the public about CAP risks and symptoms, highlighting public and patient engagement's critical role in raising CAP awareness (RightCare CAP Toolkit, 2020) (Figure 4.10).

**Figure 4.11**. Comparative risk analysis: higher vs. lower risk of community-acquired pneumonia in patients admitted with RTIs.




CAP, community-acquired pneumonia ; and COPD, chronic obstructive pulmonary disease.

## 4.5. Limitations

The study, while insightful, has certain limitations. It is conducted in an acute care setting within a secondary care hospital. Furthermore, the exclusion of individuals under 25 years old and challenges in calculating patient days could affect the evaluation of antibiotic usage. This limitation narrows its demographic reach. Additionally, its concentration on RTIs restricts its applicability to other types of infections. The analysis, based on 640 records, only covers the first and second courses of antibiotics, potentially missing important data, particularly in light of the reduction in hospital stays observed from 2019 to 2020. The study's systematic sampling approach may not have captured the full spectrum of antibiotic prescribing practices. Being retrospective and cross-sectional, the study might not accurately assess the diverse health conditions of patients and the compliance with prescribing guidelines. These limitations indicate that the study may not provide a complete understanding of the impact of antibiotic prescribing on patient outcomes, emphasising the necessity for additional research in this field.

## 4.6. Conclusion

In this retrospective study, the impact of the COVID-19 pandemic on antibiotic prescribing and AMS practices was evaluated, highlighting the pivotal role of AMS in healthcare, particularly in combating AMR. It highlighted the importance of monitoring antibiotic use in accordance with local guidelines. It emphasised the need for accurate diagnoses, such as in cases of community-acquired pneumonia, to select the appropriate antibiotics and mitigate AMR. Results of this study indicated an increased use of amoxicillin/clavulanate from the 'Access' drug category and antibiotics from the 'Watch' category, such as azithromycin and ciprofloxacin, during the pandemic. The study reinforced the crucial role of pharmacist-led AMS in addressing AMR and stressed the importance of implementing sustainable AMS interventions, particularly 'De-escalation,' during emergencies or crises. Additionally, it underscored the significance of considering chronic conditions in antibiotic decision-making for COVID-19 patients. It advocated for ongoing AMS efforts and the implementation of effective and comprehensive AMS programmes during the post-pandemic era. The focus was on integrating immediate patient care with long-term strategies for fighting AMR in sustainable public health.

**Summary of this chapter**

This chapter has discussed the overall findings of the retrospective medical records review study conducted in this research project. The next chapter will present the findings from the subsequent prospective survey study, also derived from this research.

# Chapter 5

# Prospective Survey Study

# Chapter 5: Study 3 - Exploring Healthcare Professionals' Knowledge, Attitudes, and Perceptions Towards Antibiotic Prescribing and Antimicrobial Stewardship During the COVID-19 Pandemic: A Prospective Survey Study in a Secondary Care Setting.

The previous chapter presented an evaluation of antibiotic prescribing and AMS implementation prior to and during the pandemic in 2019 and 2020. This chapter explores the knowledge, attitudes, and perceptions of healthcare professionals towards antibiotic prescribing and AMS practices during the COVID-19 pandemic. The aim is to provide an in-depth understanding of AMS implementation and the prescribing behaviors of healthcare professionals during the pandemic (Chapter 5).

## 5.1. Introduction

Antimicrobial stewardship is an organisational approach that requires collaboration among healthcare professionals across the hospital to ensure the safe use of antibiotics, appropriate antibiotic prescribing, and effective AMS implementation. Collaborative approaches have demonstrated effectiveness in reducing antibiotic overuse (Lee et al., 2017; WHO, 2019). Understanding antibiotic prescribing behaviours and their pivotal role in addressing the pressing global health issue of AMR is crucial (UK.GOV, 2016). The COVID-19 pandemic has potentially exacerbated AMR. Globally, as of December 2023, approximately 774 million individuals had been diagnosed with COVID-19, resulting in nearly 7 million deaths (WHO, 2023). This crisis significantly impacted the healthcare system and prompted a closer examination of healthcare professionals' prescribing behaviour and its implications on AMS. The pandemic has potentially worsened the issue of AMR (WHO, 2019). Emerging evidence suggests that the increased use of antimicrobial therapy during the pandemic may have contributed to a rise in resistant infections (Ghosh *et al*., 2021).

In 2022, ECDC reported a 15% surge in AMR-related hospital deaths for the preceding year, attributing this rise to the pandemic (ECDC, 2022). The widespread misuse and excessive use of antimicrobials during the pandemic in healthcare facilities and the broader community have further magnified this problem (Gulumbe *et al*., 2023). Such imprudent use has deepened the AMR crisis, yielding detrimental global effects (Knight et al., 2021). AMS focuses on ensuring the right antimicrobial prescriptions and the best antibiotic usage practices, aiming to diminish AMR through specific policies and guidelines (NICE, 2023). For this reason, it is essential to explore healthcare professionals' perspectives during the COVID-19 pandemic for effectively tackling AMR (Wojcik et al., 2021).

Knowledge, attitude, and practice (KAP) towards AMR and AMS among HCPs are essential areas of exploration, given their role in prescribing antibiotics in acute care settings (Nader Nemr *et al.,* 2023). A

2020 study assessing the KAP of doctors regarding AMS found that approximately 56% recognised the term AMS. However, the study also reported that over 50% of the HCPs were unfamiliar with AMS (Hadi Al Sulayyim *et al*., 2023). A robust understanding of bacterial resistance to antimicrobials is pivotal in preventing AMR since deficient knowledge, attitudes, and perceptions can lead to improper usage. The KAP concerning AMR among HCPs is especially vital, considering their influence on appropriate antibiotic prescriptions to patients. However, research examining HCPs' KAP during the COVID-19 pandemic is scarce, with only one study centred on nursing students (Balliram *et al*., 2021).

Prior studies have yielded varied outcomes; some suggest a limited awareness of AMR among HCPs, while others report satisfactory knowledge levels (Pinto Jimenez *et al*., 2023). Given the unprecedented challenges introduced by the pandemic, it's conceivable that the understanding of AMR among HCPs might have waned during this time. Addressing these uncertainties, this study seeks to explore the KAP of HCPs towards antibiotic prescribing, AMR, and AMS during the COVID-19 pandemic and identify the factors affecting AMS practices during the pandemic (Nader Nemr *et al*., 2023).

## 5.2. Methods

### 5.2.1. Research questions

A quantitative, survey-based approach was employed, utilising a 12-item questionnaire derived from a literature review of behaviour change, antibiotic prescribing, and AMS practices in UK healthcare settings, as well as behavioural analysis from Public Health England (PHE, 2015; Ashiru-Oredope *et al.,* 2021). The principal research questions guiding this study were: (1) What was the knowledge of HCPs regarding antibiotic prescribing during the COVID-19 pandemic? (2) What were the attitudes and perceptions of HCPs towards antibiotic prescribing during the COVID-19 pandemic? And (3) What factors influenced HCPs' attitudes towards AMS practices during the COVID-19 pandemic?

### 5.2.2. Study design and setting

This study utilised a cross-sectional design, employing a survey to explore HCPs' knowledge, attitudes, and perceptions about antibiotic prescribing PP and DP. The research was executed through an online survey targeting doctors, nurses, and pharmacists within Bedfordshire Hospitals NHS Foundation Trust. Data collection was facilitated using the secure and UH-trusted platform Qualtrics XM (Qualtrics, 2015). The survey commenced on June 12, 2023, and completed on September 13, 2023.

### 5.2.3. Study population (inclusion/exclusion criteria)

The inclusion criteria were as follows: (i) Participants must be HCPs, specifically doctors, nurses, and pharmacists; (ii) Participants must be adults, with a minimum age of 25; and (iii) Participants must be registered with their respective professional regulatory organisations: doctors with the General Medical Council (GMC), pharmacists with the General Pharmaceutical Council (GPhC), and nurses with the Nursing and Midwifery Council (NMC). Doctors, nurses, or pharmacists were ineligible to participate if they were not working within the Trust between 2019 and 2020.

### 5.2.4. Patient and public involvement

For public and patient involvement, the study protocol and participant information sheet (PIS) were submitted to representatives of the East of England Citizens' Senate. They conducted a thorough review and provided valuable feedback. The feedback from the East of England Citizens' Senate focused on improving the study protocol, as mentioned in the previous Chapter. Regarding the PIS, their comments suggested the need for more details about data security measures, the inclusion of patient-centred summaries, and the incorporation of patient-centred outcome measures using simple, plain language and visually appealing colours. The student researcher created a poster for patients and the public, presented in simple and plain language, as displayed in Appendix 47. Furthermore, the student researcher included additional details about confidentiality and anonymisation procedures in the PIS.

### 5.2.5. Public benefits

The pandemic exacerbated the AMR situation, amplifying the threat it posed. This research, which centred on the implementation of AMS in acute care settings both before and during the COVID-19 pandemic, offers pivotal insights for public health. It emphasises the importance of optimising antibiotic use to combat antibiotic resistance and ensure the sustained effectiveness of treatments. These insights not only advance better patient outcomes but also protect essential antibiotics for future generations and highlight lessons learned from the COVID-19 pandemic. The findings of this study will assist policymakers in their decision-making, guide healthcare professionals in responsible antibiotic prescribing, and enhance public awareness about AMR. Appropriate antibiotic use is pivotal in tackling the AMR challenge and safeguarding lives.

### 5.2.6. Registration

This study has been registered in the ISRCTN registry, a primary registry recognised by WHO and ICMJE that accepts all clinical research studies (ISRCTN, 2021). Additionally, it was registered in Octopus, the global primary research record (Octopus, 2021).

### 5.2.7. Data collection tools and approach

A structured questionnaire (Appendix 52) was developed using closed and open-ended 12 questions, based on the literature review on behaviour change and antibiotic prescribing in UK healthcare settings and behavioural analysis (PHE, 2015). The questionnaire consisted of four sections: ‘Demographics Information’ of the participants, ‘Knowledge’, ‘Attitudes & Perceptions’, and regarding antibiotic prescribing and ‘Antimicrobial Stewardship Practices’ during the COVID-19 pandemic (Table 5.1). Before commencing the primary fieldwork, the questionnaire was piloted with 20% of the sample (50 out of 240 respondents), who were not included in the main survey. This pilot work evaluated the questionnaire's capability to address the research questions, ensuring validity and reliability.

Furthermore, it assisted in estimating the time needed to complete the questionnaire, which was projected to be approximately 10 minutes. The questionnaire undertook amendments based on the pilot work outcomes. The pilot test, involving 50 respondents, evaluated the questionnaire's suitability, validity, and estimated completion time (approximately 10 minutes). Subsequent adjustments were implemented based on the pilot test feedback to optimise questionnaire effectiveness for the main survey.

The survey consisted of 12 questions, categorised into four distinct categories. It was designed to collect demographic details and to explore the KAP of HCPs towards antibiotic prescribing and AMS practices during the COVID-19 pandemic. It consisted of four categories: the first category, 'Demographic Information,' gathered fundamental personal data such as age, gender, and the highest educational qualification achieved. This section also inquired about the respondents' job roles, areas of specialisation, and lengths of professional experience. The second category, 'Knowledge,' assessed the respondents' understanding of AMR and antibiotic stewardship. The third category, 'Attitudes & Perceptions,' delved into the respondents' viewpoints and opinions regarding antibiotic prescribing and AMS during the pandemic. The fourth category, 'Antimicrobial Stewardship Practices,' explored the impact of the COVID-19 pandemic on AMS activities within the Foundation Trust. Collectively, these categories aimed to provide a comprehensive overview of the approaches to and experiences with AMS during this challenging period, as depicted in Figure 5.1. For more details about the survey questionnaire, please refer to Appendix 52.

**Figure 5.1.** An overview of the survey structure with four categories.

## Demographic Information:

**Q1 of 12. What is your age?**
- 25-31 years old
- 32-41 years old
- 42-51 years old
- 52-61 years old
- 62-75 years
- More than 75 years

**Q2 of 12: What is your Gender?**
- Female
- Male
- Non-binary
- Prefer not to say

**Q3 of 12: What is the highest educational degree you have completed?**
- Undergraduate degree
- Postgraduate degree (master/doctoral)
- Other ... (Please specify)

**Q4 of 12. What is your professional background?**
- Nurse
- Pharmacist
- Doctor
- Other ... (specify)

**Q5 of 12: What is your job banding?**
- Band 4 - Band 5 - Band 6 - Band 7 - Band 8a - Band 8b - Band 8c - Band 9

**Q6 of 12: What is your specialty? Please type your answer in the box below.**

**Q7 of 12: How many years of professional experience do you have?**
- Less than five years
- Six to 20 years
- More than 20 years.

## Knowledge

**Q8 of 12. This question entails 10 statements. Please indicate the level of agreement with the following statements:**

| Item | Strongly disagree | Disagree | Neutral | Agree | Strongly agree |
|---|---|---|---|---|---|
| Empty antibiotics pipeline results in an unlikely solution to AMR to be found soon. | ☐ | ☐ | ☐ | ☐ | ☐ |
| AMR is a public health problem that affects clinical practice. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Actions in combating AMR within the trust will affect society and future generations. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Implementing Antimicrobial Stewardship promotes the judicious use of antibiotics. | ☐ | ☐ | ☐ | ☐ | ☐ |
| The implementation of Antimicrobial Stewardship enhances patient outcomes within the Trust. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Intravenous antibiotic therapy proved more effective than oral options during the COVID-19 pandemic. | ☐ | ☐ | ☐ | ☐ | ☐ |
| According to hospital antimicrobial guidelines, a shorter antibiotic treatment duration is preferable over a longer one. | ☐ | ☐ | ☐ | ☐ | ☐ |
| A blood culture test should be requested upon patient admission prior to initiating any antibiotic therapy. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Delayed antibiotic prescribing strategy contributes to effective Antimicrobial Stewardship. | ☐ | ☐ | ☐ | ☐ | ☐ |

## Perceptions & Attitudes

**Q9 of 12. Please indicate the level of agreement with the following statements:**

| Item | Strongly disagree | Disagree | Neutral | Agree | Strongly agree |
|---|---|---|---|---|---|
| During the pandemic, the antibiotic guidelines in my trust were updated. | ☐ | ☐ | ☐ | ☐ | ☐ |
| The changing clinical conditions of Covid patients influenced antibiotic prescribing during the COVID-19 pandemic. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Time pressure challenges affected antibiotic decision-making during the COVID-19 pandemic | ☐ | ☐ | ☐ | ☐ | ☐ |
| During the COVID-19 pandemic, clinical judgment was prioritised over antimicrobial guidelines. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Prescribing broad-spectrum antibiotics is often viewed as more effective when dealing with resistant pathogens. | ☐ | ☐ | ☐ | ☐ | ☐ |
| During the COVID-19 pandemic, patients should continue antibiotics even with negative culture. | ☐ | ☐ | ☐ | ☐ | ☐ |
| During the pandemic, communication with microbiologists and AMS team supported more informed decisions about antibiotic use. | ☐ | ☐ | ☐ | ☐ | ☐ |

**Q10 of 12. Which of these AMS strategies has an impact on antibiotic prescribing during the COVID-19 pandemic?**

| Item | Negative | Positive | No impact |
|---|---|---|---|
| AMS ward rounds | ☐ | ☐ | ☐ |
| Antibiotic Review | ☐ | ☐ | ☐ |
| Prospective audit and feedback | ☐ | ☐ | ☐ |
| Regular antimicrobial use surveillance | ☐ | ☐ | ☐ |
| AMS education and training | ☐ | ☐ | ☐ |
| Intravenous-to-oral antibiotic switch | ☐ | ☐ | ☐ |
| Multidisciplinary team meetings (MDTMs) | ☐ | ☐ | ☐ |

## Antimicrobial Stewardship Practices

**Q11 of 12: Please indicate how much you agree with following regarding AMS during COVID.**

| Item | Strongly disagree | Disagree | Neutral | Agree | Strongly agree |
|---|---|---|---|---|---|
| Antibiotic prescribing was complied with local antimicrobial guidelines. | ☐ | ☐ | ☐ | ☐ | ☐ |
| I was informed of the resistance pattern in my Trust. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Overuse/misuse of antimicrobials during Covid could impact Antimicrobial Resistance (AMR). | ☐ | ☐ | ☐ | ☐ | ☐ |
| Review the use of IV antibiotics post- receipt of culture results. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use of technology platforms like Zoom, Teams, or Skype for multidisciplinary meetings. | ☐ | ☐ | ☐ | ☐ | ☐ |

**Q12 of 12: Are there any key messages you have learnt during the Covid that you would like to share, e.g. Antimicrobial Stewardship?**

AMS, antimicrobial stewardship; AMR, antimicrobial resistance; and MDR: multidisciplinary team meetings.

### 5.2.8. Sample size

To ensure the feasibility and accuracy of the calculated sample size, figures were obtained from NHS digitals indicating the total number of employed registered pharmacists as 206, registered nurses as 2,140, and registered doctors as 5,636. Additionally, the total number of health professionals (headcount) was recorded as 7,982 (NHS digitals, 2022). The sample size for the survey was determined to be 240, with a margin of error of 5%, a confidence interval of 95%, and an anticipated response rate of 20%. A UH statistician supported and verified all sample size calculations for both phases.

The sample size calculation was assessed by an online calculator (Raosoft, 2004) based on the formula below:

x = Z(c/100)2r(100-r)
n = N x/((N-1)E2 + x)
E = Sqrt[(N - n)x/n(N-1)]
[N is the population size, r is the fraction of responses of interest, and Z(c/100) is the critical value for the confidence level c].

The following values were entered: margin of error: 5%, confidence level: 95%, population size: 7,982, and response distribution: 20% (Israel, 1992; Raosoft, 2004).

### 5.2.9. Sampling strategy:

The R&D department within the Trust sent the invitation email electronically to the HCPs' secure email addresses on the 22nd of June 2023. It contained an invitation letter, which included the PIS and the survey link. For more details about the PIS and survey questionnaires, refer to Appendix 49 and Appendix 52. This email was designed to invite HCPs to participate in the survey. Following this, subsequent emails were circulated by both the R&D and the communication team within the Trust to foster engagement and encourage survey responses. For further details, please refer to the information provided in Table 5.1. Completion and submission of responses in the online survey were considered as implied consent for participation. Participants were free to decide on participation for as long as the survey link was active. Once submissions were finalised, all collected data were anonymised. Only the research team had access to this data.

### 5.2.10. Recruitment and survey administration

Upon receiving approval from the East Midlands - Leicester South REC and UH ethics in June 2022, the R&D team at the Bedfordshire Hospitals NHS Foundation Trust provided the C&C document, confirming the Trust's eligibility to undertake the survey study, with details found in Appendix 41. Efforts were made to ensure the survey respondent's confidentiality and to encourage HCPs' participation within the Trust consistently. Participants could withdraw before submitting the survey, but once submitted, their responses were anonymised for analysis.

On behalf of the student researcher, the R&D department, AMS pharmacists, and the microbiology consultant, AMS lead within the Trust, circulated the survey amongst a study population of doctors, pharmacists, and nurses within the Trust, adhering to predetermined inclusion/exclusion criteria. An inviting email was prepared, containing a 'Call to Participate in the Survey', along with the PIS, the survey link, an attractive poster, and a QR code to enhance accessibility and encourage responses. Additionally, this invitation was disseminated digitally via newsletters and group emails, as noted in Table 5.1. The survey was designed to be completed within an approximate time of 10 minutes.

Innovative dissemination methods were employed within the Trust to encourage participation among HCPs. Various distribution channels were utilised in collaboration with the R&D team, AMS pharmacists, and the microbiology consultant. In addition to the traditional approach of sending the survey invitation email to the HCPs within the Trust, selecting optimal times for survey distribution—either early morning, during lunchtime, or post-duty—was another critical strategy aimed at achieving higher response rates. The R&D recommended that the research student use innovative ways to encourage survey dissemination; this was achieved by placing survey posters in several strategic locations, such as the Trust, MDT rooms, nurse stations, notice boards, medicine rooms, and pharmacy departments. For the comprehensive poster on novel distribution strategies, please refer to Appendix 42 and Appendix 43. The HCPs posters, detailed in Appendix 44 and 45, were adapted in different sizes to suit each location's specific requirements.

The Communication Team within the Trust also played a pivotal role in the survey distribution. They managed to send the weekly newsletter, 'The Week's News', to all HCPs within the Trust, which also played a crucial role in circulating the survey link and invitation package to HCPs within the Trust (Appendix 47). Before the survey closed, a reminder email was sent by the Communication Team within the Trust, including 'A Vital Call to Action' in the weekly newsletter to encourage more survey responses. Outreach was also made to the AMS pharmacists and microbiology consultant to distribute the survey link through WhatsApp groups, group emails, and other channels to disseminate the survey among HCPs.

The survey was completed on September 13, 2023. The data collection process was conducted through an online-based distribution method. The survey was disseminated via an invitation email that provided two means of access: a direct link and a unique barcode. A chronological record of the survey distribution at Bedfordshire Hospitals NHS Foundation Trust (encompassing both L&D and Bedford hospitals) is detailed in Table 5.1.

**Table 5.1.** Chronological order of the survey distribution among HCPs at the Trust.

| Date | Survey Activity |
|---|---|
| **The 12th of June 2023** | • A visit was made to the L&D hospital to ensure the distribution of the invitation package by the R&D and AMS pharmacist, who sent an invitation email to the HCPs to invite them to participate in the survey initially.<br>• The researcher had a meeting with the R&D department to discuss the survey distribution, poster design, and suitable printing sizes.<br>• The R&D recommended printing two sizes: an A4-sized poster to be displayed in the wards and an A5 poster to be displayed on medicine trolleys.<br>• Additionally, they recommended using laminated posters to avoid contamination within the wards.<br>• Finally, they suggested designing another size for the poster to be used as a header in the invitation emails. They also recommended that the researcher distribute the survey and discuss the purpose of the survey with the staff in the wards to encourage responses. |
| **The 19th of June** | • To promote survey responses, the researcher printed 50 A4-sized survey posters and requested that ward managers and the head of department distribute them in L&D hospital.<br>• The researcher attended the AMS round, discussing ways to distribute the survey within the Trust successfully with the AMS lead, microbiology consultant, and AMS pharmacists.<br>• Doctors, nurses, and pharmacists were approached by researchers, who explained the survey's purpose and target population as a strategy to increase recruitment and distribution. A week later, an increase in the responses was recorded.<br>• Survey posters were placed and displayed in several strategic locations in L&D hospital, such as nurses' stations, staff rooms, main halls, notice boards, and medicine trolleys in the bays.<br>• One ward manager proposed placing the survey poster on the computer desk in the nurses' station.<br>• Another sister in charge shared the poster within the nurses' WhatsApp group. A different ward manager forwarded the survey link to doctors and nurses using group emails.<br>• The pharmacy cooperated by displaying the survey on the AMS Clinical Board, the main notice board, and the digital pharmacy screen and by sending it to all pharmacists via email. |
| **The 22nd of June** | • The AMS pharmacist at Bedford Hospital sent the in-survey invitation package to the pharmacists, while the R&D sent the invitation package to the doctors and nurses using group emails.<br>• The researchers printed 50 copies of A4 and A5 posters and requested that the ward managers and head of department distribute them in the hospital.<br>• The survey posters were placed and displayed in various strategic locations, such as MDT rooms, staff rooms, treatment rooms, doctor rooms, main halls, notice boards, nurses' stations, medicine trolleys in ward bays, and clean rooms at Bedford Hospital.<br>• One ward manager suggested placing the survey poster as a mouse pad for the main desktop computers in the wards.<br>• Another sister in charge placed the poster in front of the desktop computer and on the counter. |
| **The 7th of July** | • The communication team within the Trust sent the survey invitation package in the weekly newsletter, 'The Week,' to all HCPs within both hospitals. |
| **The 21st of July** | • After two weeks, the communication team within the Trust re-sent the survey invitation package in the weekly newsletter 'The Week' to all HCPs within both hospitals. |

| | |
|---|---|
| **The 29th of July** | • The R&D department resent the survey invitation package to the doctors, pharmacists, and nurses using the group emails. |
| **16th of August** | • There was no increase in responses, possibly due to the summer holidays.<br>• The researcher met with the supervisors to discuss methods to encourage survey responses.<br>• They recommended waiting until September, when people return from summer holidays, and then resending the survey link. |
| **6th of September** | • The researcher sent an email to the R&D and AMS pharmacists at both hospitals, as well as the AMS lead, requesting the re-circulation of the survey packages and suggesting the addition of a sense of urgency to the invitation email.<br>• The researcher drafted a message with an urgent tone to be used for survey dissemination.<br>• The researcher sent an email to the communication team, requesting the inclusion of the survey links in the weekly newsletter 'The Week' and using an attractive title: 'A Vital Call to Action'. |
| **13th of September** | • As the number of responses decreased, the researcher communicated with the AMS pharmacist and the AMS lead in the Trust, suggesting they circulate the survey via the Trust's WhatsApp groups for pharmacists, doctors, and nurses. |
| **15th of September** | • The end of the data collection period. |

L&D, Luton and Dunstable Hospital; R&D, Research and Development; AMS, antimicrobial stewardship; HCPs, healthcare professionals; and MDT, multidisciplinary team.

### 5.2.11. Statistical analysis

The research student collected, extracted and analysed the results. The responses from the participants were provided to the researcher as a completely anonymised set for analysis. The survey results were analysed using descriptive statistics and IBM SPSS Statistics version 27.0 for Windows (IBM, 2020).

### 5.2.12. Survey Pilot

To ensure the survey's validity, a pilot test was conducted with a representative sample of 20% (50 out of 240 participants), comprising pharmacists, nurses, and doctors. Responses from this pilot test were carefully analysed using both Excel and SPSS programs. To maintain the validity of the survey, and to ascertain the extent to which the survey instrument measures what it is intended to measure, both face and content validity were conducted (Cobern *et al*., 2020). For face validity, liaison was undertaken with AMS experts within the Trust, including the microbiology consultant and AMS pharmacists at both hospitals of the Trust. The survey was sent to them with a request to review the questions and statements, and to evaluate their appropriateness to answer the research question and fulfil the objectives of the survey. They provided their feedback to the research students, which was subsequently discussed with the supervisors and incorporated into the final version of the survey. This process contributed to enhancing the face validity of the survey, ensuring it was suitably tailored for the targeted audience. It also ensured the relevance and clarity of the questions, confirming that the survey would accurately assess the study's intended objectives.

Additionally, the supervisors reviewed the survey to ensure further clarity and validity. For content validity and to ensure the survey measured its intended focus, the research student shared it, along with the protocol, with the AMS expert team at RPS for review. This step involved input from professionals skilled in the relevant field (RPS, 2023). These AMS research experts assessed the survey to determine whether the survey effectively answer the research questions. The RPS team meticulously reviewed the survey to confirm its consistency with the research aims and provided detailed feedback. This feedback was thoroughly discussed with the supervisory team and, where possible, integrated into the final version of the survey to ensure the overall validity of the study.

The survey's reliability was assessed by importing the pilot test results into the SPSS software (Tourangeau, 2020; Online SPSS, 2023). This step helped to evaluate the consistency and accuracy of the survey instrument. Through these rigorous methods, the aim was to ensure the survey's reliability. To assess internal consistency, Cronbach's Alpha was applied to a pilot sample of anonymous responses. The results showed excellent reliability for the ‘Knowledge’ category (Cronbach's alpha = 0.832) and the ‘AMS Practices’ category (Cronbach's alpha = 0.890). The ‘Attitude & Perceptions’ category demonstrated good reliability (Cronbach's alpha = 0.791), while the different ‘AMS Strategies' Impact on antibiotic prescribing category indicated moderate reliability (Cronbach's alpha = 0.727). With an average reliability score of 0.80 across all sections, there was a clear indication of a high degree of internal consistency, further affirming the questionnaire's reliability (Tourangeau *et al*., 2020).

## 5.3. Results

A total of 240 HCPs responded to the survey, with results recorded online and subsequently analysed. Data was exported to an Excel sheet from the secure online platform, ‘Qualtrics’ (Qualtrics.com, 2023). The researcher organised and cleaned the data, providing codes for the 5-point Likert scale responses as follows: 0 for Strongly Disagree; 1 for Disagree; 2 for Neutral; 3 for Agree; and 4 for Strongly Agree.

The response rate was determined by comparing the number of received responses with the total number of surveys distributed over a specified period. Within a three-month period, the objective of attaining the required sample size of 240 participants was successfully met. Out of 7,982 health professionals, 240 responded, resulting in a response rate of approximately 3%.

### 5.3.1. Healthcare professionals' demographic characteristics

Most survey respondents were pharmacists (n=125, 52%). The total number of doctors and nurses that responded were as follows: pharmacists (n=125, 52%), doctors (n=72, 30%), and nurses (n=43, 18%). Table 5.2 illustrates the breakdown of participants' age characteristics: most respondents (n=96, 40.0%) were between 32 and 41 years old. In regard to education, most participants held a postgraduate master's degree (n=163, 68.0%) or a postgraduate PhD degree (n=43, 18.0%), while only a small percentage had an undergraduate degree (n=24, 10%). Regarding years of experience, those with 6-20 years were most represented among respondents (n=132, 55%). Table 5.2 provides a detailed breakdown of the HCPs' demographic characteristics. Most respondents were female (56%), and the predominant qualification was a pharmacist (52%). Concerning educational achievements, the majority of respondents held a postgraduate master's degree (68%). Regarding job banding, the majority were in band 7 (27%).

The survey responses were mainly from pharmacists and nurses, totaling 197 out of 240 responses. Doctors provided only 72 responses. The Agenda for Change (AFC) job banding did not significantly affect their choices. For more representation of the demographic characteristics among the respondents, please refer to Appendix 55.

**Table 5.2:** Demographics characteristics of the survey respondents.

| | | *n* | % |
|---|---|---|---|
| **Age** | 25-31 years old | 58 | 24.0% |
| | 32-41 years old | 96 | 40.0% |
| | 42-51 years old | 36 | 15.0% |
| | 52-61 years old | 38 | 16.0% |
| | 62-75 years old | 12 | 5.0% |
| **Educational achievement** | Undergraduate degree | 24 | 10.0% |
| | Postgraduate degree (Diploma) | 10 | 4.0% |
| | Postgraduate degree (Master Degree) | 163 | 68.0% |
| | Postgraduate degree (PhD Degree) | 43 | 18.0% |
| **Gender** | Female | 134 | 54.0% |
| | Male | 89 | 35.9% |
| | Non-binary | 5 | 2.0% |
| | Prefer not to say | 12 | 4.8% |
| **Professional background** | Pharmacist | 125 | 52.0% |
| | Doctor | 72 | 30.0% |

| | | | |
|---|---|---|---|
| | Nurse | 43 | 18.0% |
| **Job banding** | Band 5 | 43 | 18.0% |
| | Band 6 | 58 | 24.0% |
| | Band 7 | 65 | 27.0% |
| | Band 8a | 22 | 9.0% |
| | Band 8b | 24 | 10.0% |
| | Band 8c | 10 | 4.0% |
| | Band 9 and more | 18 | 8.0% |
| **Years of experience** | ≤5 years | 48 | 20.0% |
| | ≥20 years | 60 | 25.0% |
| | 6-20 years | 132 | 55.0% |

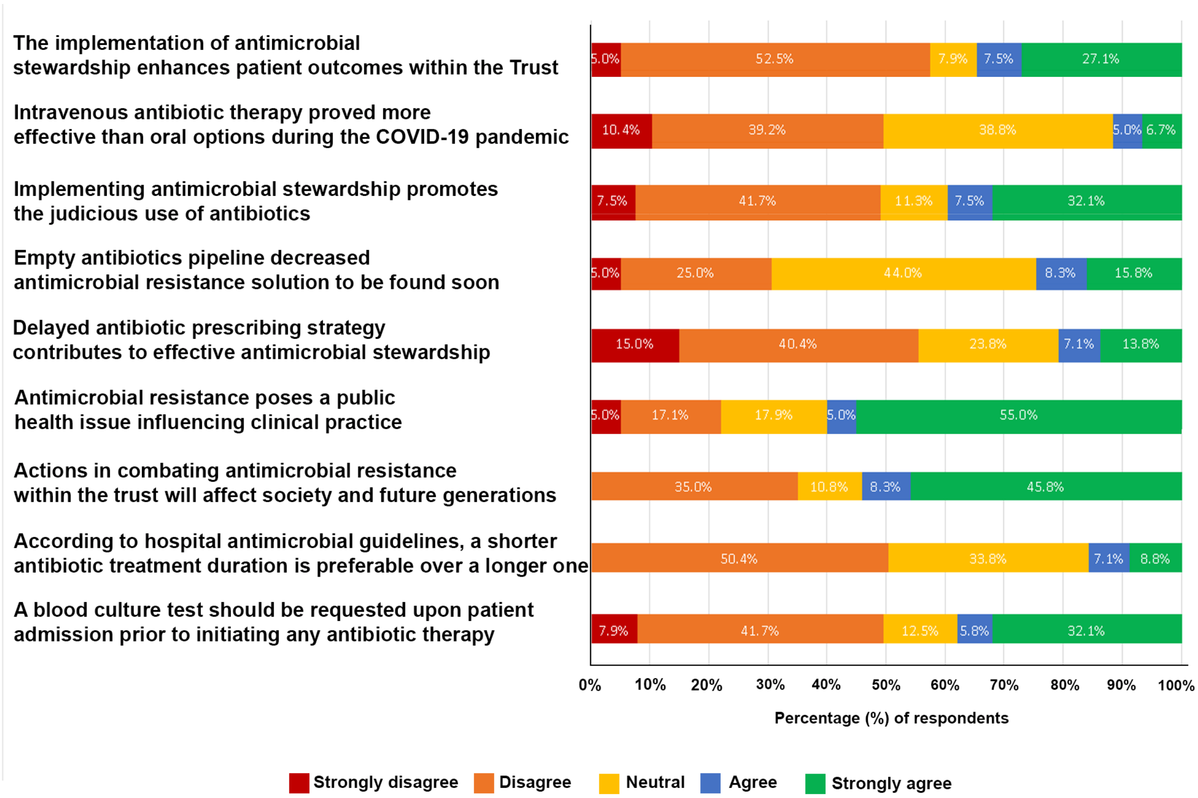
### 5.3.2. Knowledge of healthcare professionals towards antibiotic prescribing and antimicrobial stewardship during the COVID-19 pandemic.

The median knowledge score of the study group was 50.13%. Regarding Knowledge, most of the respondents reported that they strongly agree that antimicrobial resistance poses a public health issue influencing clinical practice (n=132, 55.0%). Additionally, most strongly agreed that Actions in combating antimicrobial resistance within the trust will affect society and future generations (n=110, 45.8%).

Among participants, respondents expressed strong and equal agreement with the statements that implementing antimicrobial stewardship promotes the judicious use of antibiotics and that a blood culture test should be requested upon patient admission prior to initiating any antibiotic therapy (n=77, 32.1%). However, there was insufficient knowledge regarding the statement that 'the implementation of antimicrobial stewardship enhances patient outcomes within the Trust' (n=126, 52.5%). This agreement suggests that participants recognise the importance and benefits of AMS. It does not necessarily indicate a lack of knowledge or confidence in staff implementation of AMS. Instead, it highlights their understanding and support for AMS implementation during the pandemic.

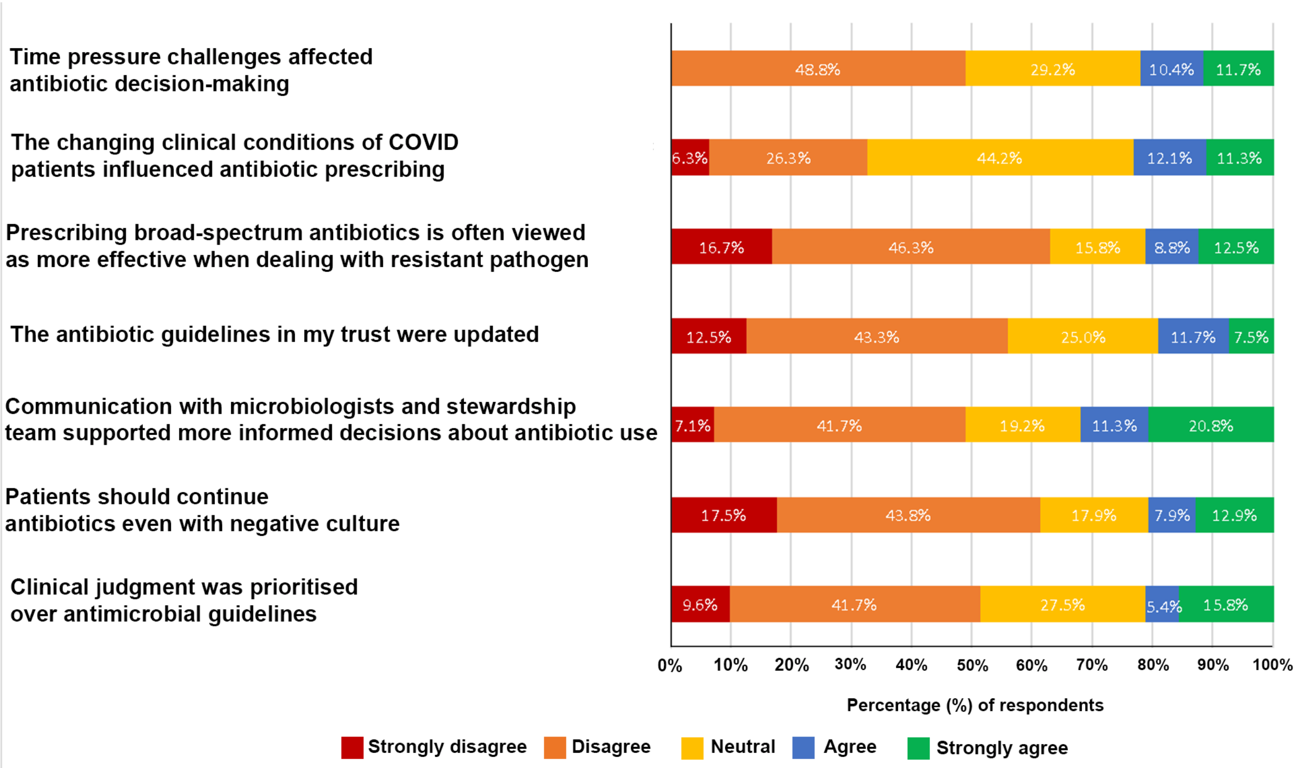
Respondents disagreed with the statement, "According to hospital antimicrobial guidelines, a shorter antibiotic treatment duration is preferable over a longer one" (n=121, 50.4%) (Figure 5.2). This statement aimed to reflect local guidelines, such as the five to seven days recommended duration for CAP antibiotics, and to explore whether health professionals prefer shorter or longer antibiotic durations according to these guidelines and patient conditions.

**Figure 5.2.** Stacked bar chart for knowledge of healthcare professionals towards antibiotic prescribing and antimicrobial stewardship during the COVID-19 pandemic.



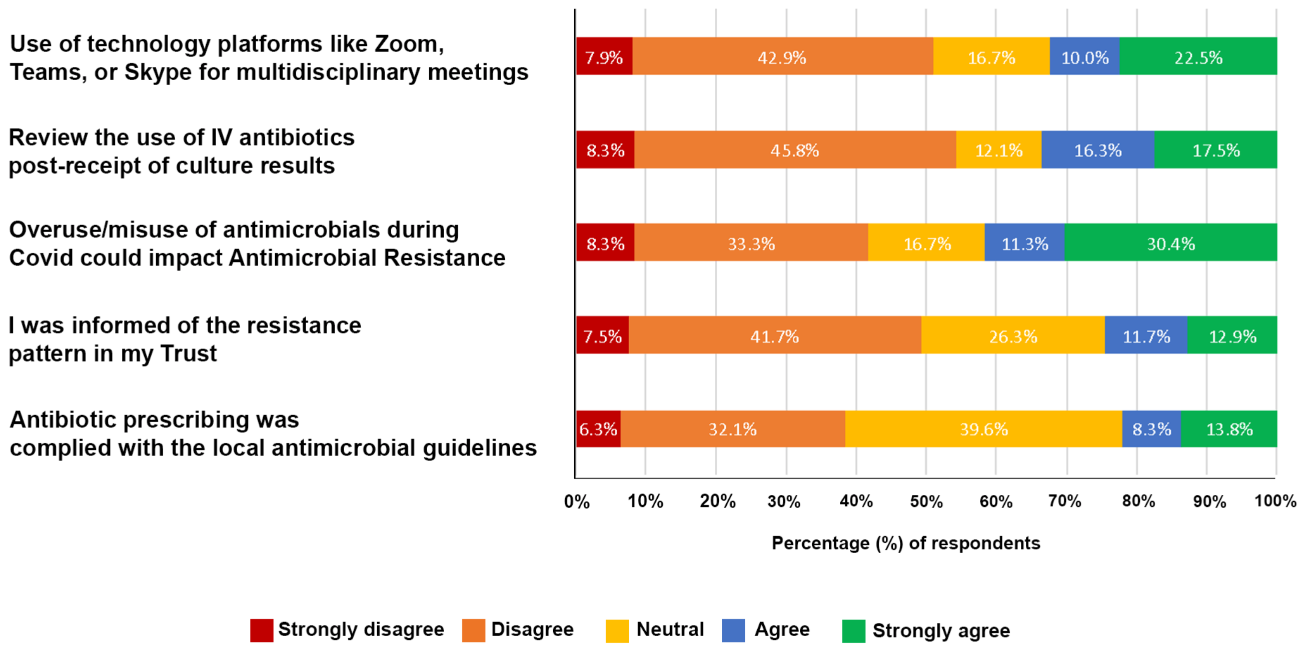
In terms of the participants' attitudes and perceptions, the median attitude score was 44.03%. Approximately 21% strongly agreed that communication with microbiologists and the stewardship team supported more informed decisions about antibiotic use, and 16% strongly agreed that clinical judgment was prioritised over antimicrobial guidelines. However, approximately 49% (n=117) disagreed with the statement, 'Time pressure challenges affected antibiotic decision-making,' and about 46% (n=111) disagreed with the statement, 'Prescribing broad-spectrum antibiotics is often viewed as more effective when dealing with a resistant pathogen' (Figure 5.3).

**Figure 5.3.** Stacked bar chart for attitude and perception of healthcare professionals regarding antibiotic prescribing during the COVID-19 pandemic.



For practice, the median practice score was 45%. Approximately 42% of respondents strongly agreed, and agreed with the statement, 'Overuse/misuse of antimicrobials during COVID could impact antimicrobial resistance' (n=100). Regarding the statement 'Review the use of IV antibiotics post-receipt of culture results,' it showed (n=81, 33.8%), and concerning 'Use of technology platforms, such as Zoom, Teams, or Skype for multidisciplinary meetings,' it showed (n=78, 32.5%). However, some respondents disagreed with the statement, 'Antibiotic prescribing was in compliance with the local antimicrobial guidelines' (n=77, 32.1%) (Figure 5.4).

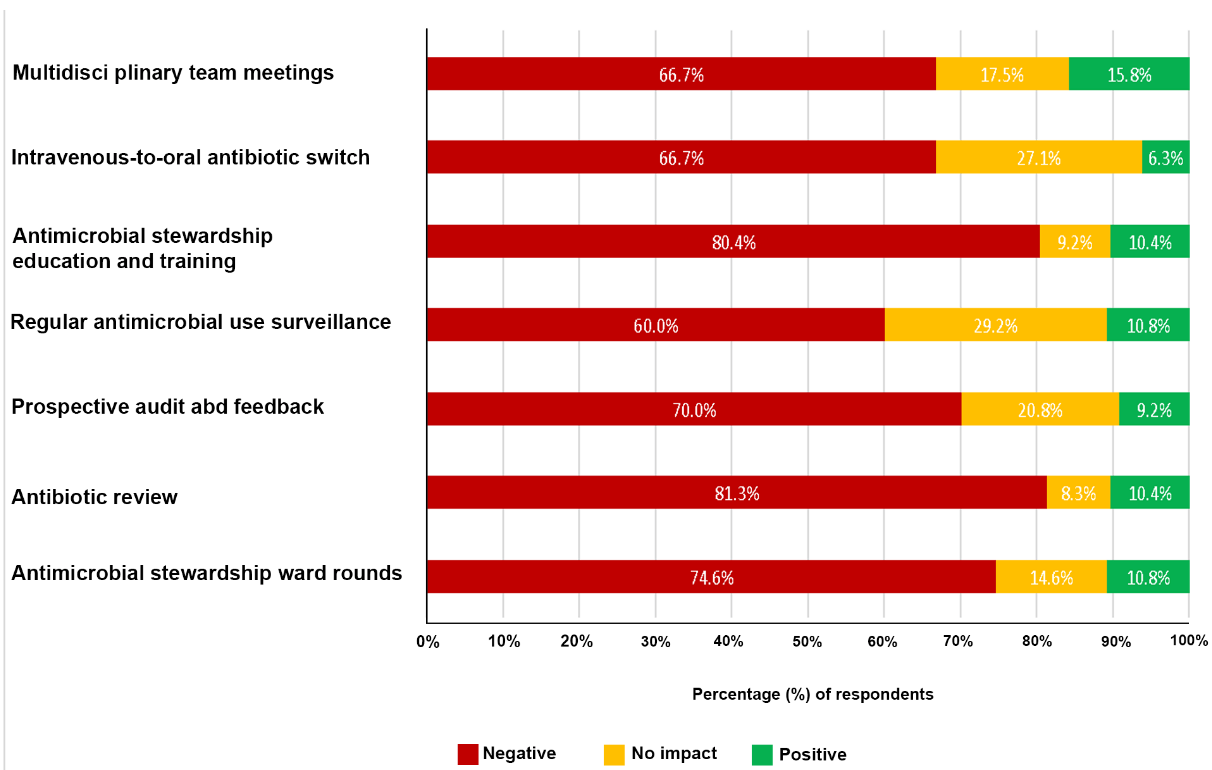
**Figure 5.4.** Stacked bar chart for the practice of healthcare professionals towards antibiotic prescribing during the COVID-19 pandemic.



### 5.3.3. Impact of COVID-19 on antimicrobial stewardship activities/strategies

Most of the AMS activities, as listed in Figure 5.5., were considered to be negatively affected by the COVID-19 pandemic. Respondents were asked, 'Which of these AMS strategies have impacted antibiotic prescribing during the COVID-19 pandemic', regarding the impact of COVID-19 on their routine AMS activities. The greatest negative impact was observed in antibiotic review, at 80.4% (193/240). Additionally, 81.3% (195/240) of respondents believed COVID-19 adversely affected antimicrobial stewardship education and training, and 74.6% (179/240) felt it negatively influenced antimicrobial stewardship ward rounds. Furthermore, 70.0% of respondents (168/240) expressed concern about the detrimental impact of the pandemic on the prospective audit and feedback. However, 70/140 (29.2%) participants felt that COVID-19 had no impact on regular antimicrobial surveillance. On the other hand, only 15.8% (38/240) felt that the impact of COVID-19 on multidisciplinary team meetings was positive.

**Figure 5.5.** Impact of COVID-19 on antimicrobial stewardship activities/strategies (n = 240 survey respondents).



Univariate logistic regression analysis for factors associated with good knowledge, a positive attitude, and good practice is presented in Table 5.3. Factors significantly associated with good knowledge included being in the age category of 32-41 years old, being of female gender, having an educational achievement of a postgraduate doctoral degree, and having a professional background in the pharmacist category. No factors were statistically significantly associated with a positive attitude. Factors significantly associated with good practice included being in the age category of 32-41 years old, being of male gender, and having a professional background in both pharmacist and doctor categories.

**Table 5.3.** Univariate analysis for factors associated with (good knowledge, positive attitude and good practice).

| Factor | | Knowledge | | | Attitude and Perceptions | | | Practice | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | AOR | (95% CI) | P-value | AOR | (95% CI) | P-value | AOR | (95% CI) | P-value |
| Age | 25-31 years old | 0. 89 | (1.07-2.15) | 0.45 | 0. 89 | (1.09-2.03) | 0.46 | 3.81 | (1.08-4.03) | 0.36 |
| | 32-41 years old | 5.00 | (2.17-6.25) | 0.01* | 2.04 | (0.98-1.03) | 0.36 | 2.07 | (1.04-3.10) | 0.001* |
| | 42-51 years old | 1.11 | (1.14-2.05) | 0.78 | 1.09 | (1.14-2.05) | 0.78 | 1.21 | (1.33-2.69) | 0.36 |
| | ≥ 52 years old | 1 | 1 | 1 | 1 | 1 | 1 | | 1 | |
| Gender | Female | 0.69 | (0.21-2.29) | 0.05* | 1.06 | (0.27-4.14) | 0.93 | 2.19 | (0.67-7.19) | 0.19 |
| | Male | 1.00 | (0.29-3.40) | 0.95 | 1.10 | (0.29-4.43) | 0.88 | 1.96 | (0.58-6.62) | 0.27* |
| | Others* | Ref. | 1 | | 1 | 1 | 1 | 1 | 1 | 1 |
| Educational achievement | Postgraduate degree (Doctoral Degree) | 1.63 | (0.18-1.51) | 0.04* | 1.03 | (0.18-1.51) | 0.92 | 1.41 | (0.11-1.49) | 0.17 |
| | Postgraduate degree (master's degree) | 0.75 | (0.31-1.79) | 0.51 | 3.64 | (0.58-3.63) | 0.34 | 2.11 | (0.45-2.74) | 0.82 |
| | Postgraduate degree (Diploma Degree) | 1 | 1 | | 1 | 1 | | 1 | 1 | |
| Professional background | Doctor | 3.67 | (0.74-7.17) | 0.19 | 3.12 | (1.13-5.25) | 0.39 | 3.46 | (1.85-6.44) | 0.03* |
| | Pharmacist | 4.68 | (2.26-6.79) | 0.03* | 1.06 | (0.47-2.39) | 0.88 | 1.28 | (0.53-3.06) | 0.001* |
| | Nurse | 1.57 | (0.87-2.83) | 0.13 | 1.64 | (0.05-2.85) | 0.07 | 1.57 | (0.87-2.83) | 0.13 |
| | Others* | Ref. | 1 | | 1 | 1 | | 1 | 1 | |
| Job banding | Band 5 | 0.40 | (0.12-1.31) | 0.13 | 2.01 | (0.49-8.21) | 0.33 | 1.82 | (0.53-6.21) | 0.33 |
| | Band 6 | 3.9 | (2.95-6.13) | 0.99 | 3.12 | (0.79-12.31) | 0.10 | 0.53 | (0.17-1.64) | 0.27 |
| | Band 7 | 5.8 | (3.83-8.13) | 0.01 | 1.00 | (0.24-4.12) | 1.00 | 0.60 | (0.20-1.76) | 0.35 |
| | Band 8 | 0.08 | (0.24-3.96) | 0.99 | 15.7 | (0.65-1.52) | 1.10 | 1.92 | (0.29-3.95) | 0.69 |
| | Others | Ref. | 1 | | 1 | 1 | | 1 | 1 | |
| Years of experience | ≤5 years | 1.16 | (0.59-2.27) | 0.66 | 0.89 | (0.41-1.89) | 0.76 | 0.95 | (0.48-1.88) | 0.88 |
| | 6-20 years | 0.58 | (0.31-1.07) | 0.08 | 0.81 | (0.39-1.65) | 0.56 | 1.87 | (0.93-3.76) | 0.07 |
| | ≥20 years | 1 | 1 | | 1 | 1 | | 1 | 1 | |

AOR, Adjusted Odds Ratio; CI, Confidence Interval; and P-value: Probability value.

Multivariate analysis for factors associated with good knowledge, a positive attitude, and good practice is presented in Table 5.4. Factors significantly associated with good knowledge include an age category of 32-41 years old, a professional background in the pharmacist category, and 6-20 years of experience. The age category of 32-41 years old and job banding of band 5 were significantly associated with a positive attitude. Additionally, the age category of 32-41 years old, professional background in the doctor category, and ≤5 years of experience were significantly associated with good practice.

The age category of 32-41 years old was four times more likely to have good knowledge compared to the other age groups (AOR=4.006, CI=1.160-5.25, *p*-Value =0.01). Compared with other specialities or Professional backgrounds, pharmacists were nine times more likely to have good knowledge (AOR=9.54, CI=1.26-5.78, *p*-Value=0.03. Participants who had Job banding of band 5 were 14 times more likely to have a positive attitude (AOR=14.14, CI=1.44-8.74, *p*-Value =0.02). The age category of 32-41 years old was twice as likely to have a positive attitude compared to 25-31 years old age groups (AOR=2.05, CI=1.01-3.08, *p*-Value =0.004).

**Table 5.4.** Multivariate analysis for factors associated with overall scores (good knowledge, positive attitude and good practice).

| Factor | | Knowledge | | | Attitude and Perceptions | | | Practice | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | AOR | (95% CI) | P-value | AOR | (95% CI) | P-value | AOR | (95% CI) | P-value |
| Age | 25-31 years old | 0.49 | (0.07-3.15) | 0.34 | 0.49 | (0.07-2.15) | 0.34 | 2.01 | (0.98-1.03) | 0.367 |
| | 32-41 years old | 4.006 | (1.16-5.25) | 0.01* | 2.05 | (1.01-3.08) | 0.004* | 1.08 | (1.02-1.9) | 0.004* |
| | 42-51 years old | 1.178 | (0.65-2.12) | 0.58 | 1.29 | (0.67-2.19) | 0.58 | 0.04 | (0.29-7.37) | 0.20 |
| | ≥ 52 years old | 1 | 1 | | 1 | 1 | | 1 | 1 | |
| Gender | Female | 7.93 | (0.36-2.69) | 0.18 | 0.22 | (0.01-4.86) | 0.34 | 1.78 | (0.13-3.63) | 0.65 |
| | Male | 9.84 | (0.53-9.69) | 0.12 | 0.26 | (0.02-3.18) | 0.31 | 1.79 | (0.15-1.22) | 0.64 |
| | Others* | Ref. | 1 | | 1 | 1 | | 1 | 1 | |
| Educational achievement | Postgraduate degree (Doctoral Degree) | 1.08 | (0.08-4.28) | 0.93 | 3.08 | (0.08-3.28) | 0.78 | 0.22 | (0.01-2.85) | 0.25 |
| | Postgraduate degree (Master Degree) | 0.50 | (0.16-1.57) | 0.23 | 2.24 | (0.52-2.63) | 0.27 | 1.18 | (0.37-3.76) | 0.77 |
| | Postgraduate degree (Diploma Degree) | 1 | 1 | | 1 | 1 | | 1 | 1 | |
| Professional background | Doctor | 2.30 | (0.74-7.13) | 0.14 | 2.12 | (0.93-4.35) | 0.26 | 1.90 | (1.01-5.17) | 0.04* |
| | Pharmacist | 9.54 | (1.26-5.78) | 0.03* | 1.04 | (0.45-2.42) | 0.91 | 1.55 | (0.60-3.98) | 0.35 |
| | Nurse | 1.64 | (0.41-1.42) | 0.12 | 1.361 | (0.71-2.59) | 0.34 | 1.64 | (0.79-3.41) | 0.17 |
| | Others* | Ref. | 1 | | 1 | 1 | | 1 | 1 | |
| Job banding | Band 5 | 0.41 | (0.05-3.31) | 0.40 | 14.14 | (1.44-8.74) | 0.02* | 0.23 | (0.03-1.67) | 0.14 |
| | Band 6 | 3.40 | (2.13-5.13) | 0.97 | 4.96 | (0.35-9.16) | 0.23 | 0.27 | (0.04-1.84) | 0.18 |
| | Band 7 | 4.61 | (3.13-7.13) | 0.01 | 0.89 | (0.84-1.12) | 0.60 | 2.06 | (0.03-2.48) | 0.23 |
| | Band 8 | 0.75 | (0.06-3.24) | 0.82 | 15.74 | (0.65-1.52) | 0.09 | 1.72 | (0.12-2.05) | 0.69 |
| | Others | Ref. | 1 | | 1 | 1 | | 1 | 1 | |
| Years of experience | ≤5 years | 1.02 | (0.35-2.97) | 0.96 | 0.55 | (0.17-1.75) | 0.31 | 4.15 | (1.27-5.48) | 0.01* |
| | 6-20 years | 0.25 | (0.07-0.90) | 0.03* | 0.68 | (0.18-2.53) | 0.56 | 2.68 | (0.75-9.49) | 0.12 |
| | ≥20 years | 1 | 1 | | 1 | 1 | | 1 | 1 | |

AOR, Adjusted Odds Ratio; and CI, Confidence Interval.

As age increased by ten years, the odds of showing good practice decreased by 1% from (AOR=2.07, CI=1.04-3.10, *P*=0.001) in the 32-41 years old age category, to (AOR=1.21, CI=1.33-2.69, *p*-Value=0.36). Being a doctor-led participant is three times more likely to demonstrate good practice compared to participants from other specialities (AOR=3.46, CI=1.85-6.44, *p*-Value=0.03). Compared to participants with a diploma, staff with a PhD or a master's degree were 1.4 and 2.1 times more likely to demonstrate good practice, respectively (PhD: AOR=1.41, CI=0.11-1.49, *p*-Value=0.17; Master's: AOR=2.11, CI=0.45-2.74, *p*-Value=0.82).

**5.3.4. Antimicrobial stewardship lessons from COVID-19: healthcare insights.**

Upon asking the HCPs about the 'Key lessons on AMS during the COVID-19 pandemic, ' 23 out of 240 respondents provided their insights. Among them, 12 were pharmacists, nine were doctors, and only two were nurses. Pharmacists raised several issues, as described in the following quotes:

> *"The AMS practice should be standard in hospitals, as there is considerable inappropriate use of antibiotics occurring without any clinical justification"; "HCAIs and broad-spectrum use have increased"; "Technology platforms negatively impacted the overall review of patients and AMS"; During the pandemic, most considerations for AMR were overlooked, with antibiotics routinely prescribed to treat viral illnesses"; and "Antibiotics need to be reviewed after 72 hours of treatment."*

On the other hand, doctors highlighted the importance of updating and disseminating reliable information, especially during a pandemic, as reflected in the following quotes:

> *"Easy access to non-curated information, such as social media, had more impact than evidence-based medicine (EBM) guidelines in intranet and email chains"; "Antibiotics were liberally used to reduce inflammation and to cover bacterial infections due to the urgency of the situation"; "Doctors should receive updates, especially during an emergency"; and "Antibiotic review is crucial."*

For the nurses, only two responses from nurses, their perspectives quotes are described as follows:

> *"During the pandemic, much of the AMR thinking was discarded, and antibiotics were routinely prescribed for viral illnesses"; and "Mental fatigue affects decision-making, and unclear frameworks and guidelines can also lead to anxiety and panic when deciding on antibiotic use."*

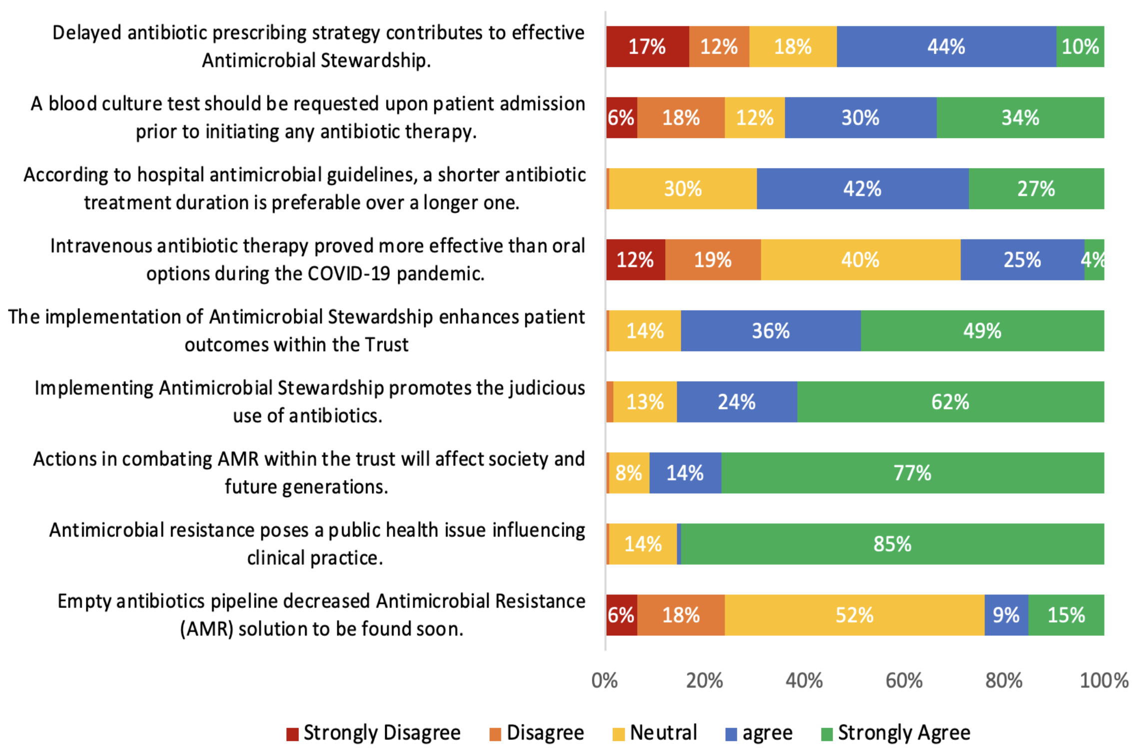
These responses shed light on the multifaceted challenges of maintaining AMS and appropriate antibiotic prescribing during a public health crisis and the urgent need for clear guidelines and communication to support healthcare staff in their decision-making.

### 5.3.5. The pharmacist's knowledge towards antimicrobial stewardship during the pandemic.

When focusing solely on responses from pharmacists in this survey, there were 125 responses from this profession, as shown in Figure 5.4. A sub-analysis was then conducted on these pharmacists' KAP towards antibiotic prescribing and antimicrobial stewardship practices during the pandemic. Interestingly, pharmacists demonstrated strong knowledge, attitudes, perceptions, and practices regarding antibiotic prescribing, antimicrobial resistance, and AMS. More than 80% of the pharmacists agreed with statements about AMS and AMR, reflecting their depth of knowledge (Figure 5.6.). In terms of attitudes and perceptions, over 70% agreed that time pressure during the pandemic affected decision-making in antibiotic prescribing, and that changing clinical conditions of COVID-19 patients influenced antibiotic prescribing practices (Appendix 56).

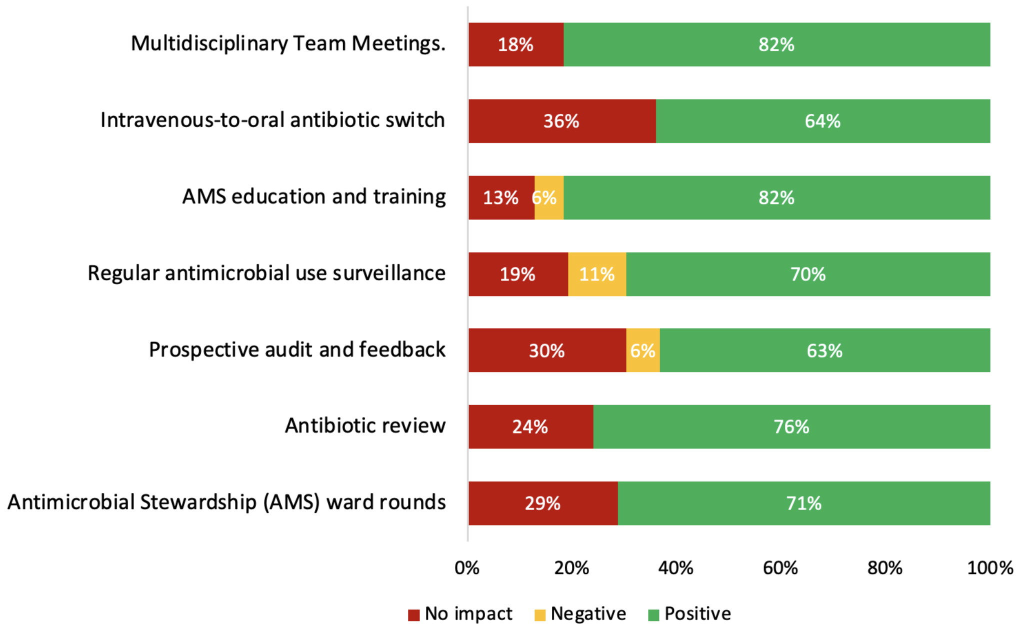
Regarding AMS perceptions, more than 80% of pharmacists concurred with statements such as 'Overuse/misuse of antimicrobials during COVID-19 could impact AMR' and 'It is essential to review the use of IV antibiotics following the receipt of culture results (Appendix 56).

**Figure 5.6.** Stacked bar chart for knowledge of pharmacists towards antimicrobial stewardship during the COVID-19 pandemic (n = 125 survey respondents).



Another interesting finding from this sub-analysis is the pharmacists' KAP towards AMS activities during the pandemic. It was observed that over 60% of pharmacists reported a positive impact of the COVID-19 pandemic on most AMS activities. These activities included AMS ward rounds, antibiotic reviews, prospective audits and feedback, regular surveillance of antimicrobial use, ‘AMS education and training’, ‘Intravenous-to-oral antibiotic switching’, and ‘Multidisciplinary AMS team meetings’ (Figure 5.7.).

**Figure 5.7.** Impact of COVID-19 on antimicrobial stewardship activities/strategies (*n*= 125 survey respondents).




## 5.4. Discussion

This survey questionnaire was developed based on behaviour change and antibiotic prescribing in healthcare settings. Literature review and behavioural analysis from PHE (PHE, 2019). It was conducted in one English NHS Foundation Trust and focuses on assessing HCPs’ KAP towards antibiotic prescribing, AMR, and AMS during the COVID-19 pandemic. The study participants demonstrated good knowledge and practice; however, their attitude requires further improvement. Such findings highlight a deficiency in efficacious AMS educational and training programmes.

Furthermore, this study identified certain HCPs who need to improve their knowledge and practice towards antibiotic prescribing, especially during the pandemic. This includes health professionals such as doctors, pharmacists, and nurses. HCPs who hold advanced educational achievements (PhD and Masters), and HCPs with less than five years and from 6-20 years of experience. The study provides vital insights into HCPs’ knowledge and perceptions concerning antibiotic prescribing, AMR, and AMS during the COVID-19 pandemic, with a median knowledge score of 50.13%. Recently, a study in Saudi Arabia reported a median (IQR) knowledge score among primary healthcare workers about antibiotic use of 72.73% (27.27%–81.82%) (Hadi Al Sulayyim et al., 2023). In Pakistan, doctors' knowledge of AMS and AMR was relatively poor (Althagafi *et al*., 2022).

In the current study, participants exhibited good knowledge on only two questions related to knowledge, with >50% accuracy. Approximately 55% agreed that AMR poses a public health issue influencing clinical practice, which is congruent with a study conducted in Switzerland (Lomazzi *et al*., 2019). Additionally, about 46% agreed that actions to combat AMR within the trust will affect society and future generations, which aligns with the United Nations (UN) report (UN, 2019).

However, critical knowledge gaps were identified in this study, particularly regarding specific antimicrobial stewardship strategies, emphasising a need for targeted educational interventions. This is similar to the study of ECDC national focal points for antimicrobial resistance and national focal points for communication from all EU countries, two EEA countries (Iceland and Norway), and selected European health professional organisations or groups. The findings of the survey highlighted the need to continue to raise awareness about the prudent use of antibiotics and antibiotic resistance, and also to enhance healthcare workers' engagement in addressing these issues (Ashiru-Oredope *et al*., 2021). The ECDC survey also emphasised the need to design interventions based on education, resources, and guidelines, which focus specifically on promoting behaviour that leads to prudent prescription, dispensing, and administration of antibiotics (Ashiru-Oredope *et al*., 2021).

The attitude of the HCPs in the current study exhibited the highest positivity regarding the promotion of communication among HCPs in AMS implementation, which is considered a gap and barrier in the implementation and functioning of AMS (Lazure *et al*., 2022). A small percentage of participants in the current study strongly agreed and agreed with the statement, 'Time pressure challenges affected antibiotic decision-making.' Additionally, 'Prescribing broad-spectrum antibiotics is often viewed as more effective, aligning with findings from other studies (Allen *et al*., 2022; Om *et al*., 2016). This suggests the importance of using varied approaches in addressing AMS barriers among HCPs.

Interestingly, for practice, about 42% strongly agreed with the statement, 'Overuse/misuse of antimicrobials during COVID could impact Antimicrobial Resistance.' A study published in 2022 indicated prevalent unnecessary antibiotic prescriptions during COVID-19, raising concerns about accelerating AMR and potential future pandemics (Malik *et al*., 2022). Additionally, 34% of participants agreed with the statement, 'Review the use of IV antibiotics post-receipt of culture results.' A 2021 study highlighted the importance of antibiotic review. The AMS intervention enhanced early antibiotic review and stop rates but necessitated further optimisation, particularly in decision-tool utilisation (Roy-Bentley *et al*., 2022).

Regarding the statement "Use of technology platforms like Zoom, Teams, or Skype for multidisciplinary meetings," 33% of participants agreed, aligning with a UK study during the pandemic that acknowledged technology as a crucial facilitator for stewardship, e.g., virtual meetings and ward rounds (Ashiru-Oredope *et al*., 2021). The pandemic dissolved barriers, enhancing collaboration and necessitating innovative approaches, such as adapting AMS implementation for antibiotic review. The virtual use of technology is proposed as vital for managing future emergencies and AMR (Ashiru-Oredope *et al*., 2021). In this study, approximately 22% of respondents concurred that "Antibiotic prescribing was in compliance with the local antimicrobial guidelines." While COVID-19 has influenced clinical judgment and antibiotic selection, adherence to the AMS toolkit from the PHE, "Start Smart, Then Focus," is pivotal, especially during crises, to uphold judicious antibiotic use as far as possible (GOV.UK, 2023). Furthermore, elevating awareness of antimicrobial guidelines is anticipated to positively influence AMS and resistance in the long term. Regarding the impact of COVID-19 on AMS activities, this study found that most AMS strategies were negatively affected by the pandemic. The COVID-19 pandemic has negatively affected the AMS activities. Notably, 80.4% and 81.3% of participants reported the negative impact of antibiotic review and AMS education, respectively. Despite 29.2% observing no change in routine antimicrobial surveillance, the decline in AMS ward rounds (74.6%) and concerns in audits (70%) underline the pressing need to adapt AMS strategies during health crises, guarding against potential AMR. These results were congruent with a UK study in 2021 (Ashiru-Oredope *et al*., 2021). In that UK study, 65% felt COVID-19 negatively impacted AMS activities since its 2019 emergence. Of these respondents, 31% reported a negative impact, 34% indicated some negative effects, 7% observed positive outcomes, 25% had mixed feelings, and 2% saw no change. There were significant disruptions in the audit and education processes. Concerns about the increased use of broad-spectrum antibiotics were validated by PHE Fingertips data, which showed an uptick in prescriptions since 2017 (Ashiru-Oredope *et al*., 2021).

**5.4.1. Factors associated with good knowledge, positive attitude, and good practice.**

The current study identified factors significantly associated with good knowledge, including the age category of 32-41 years, being female, possessing a postgraduate doctoral degree, and having a pharmacist professional background as associated factors with HCPs' knowledge about COVID-19. A study conducted during COVID-19 in 2020 found that professional and educational levels were associated with factors affecting HCPs' knowledge about COVID-19 (Al Sulayyim *et al*., 2020). Conversely, another study in 2022 reported that higher knowledge among health professionals was associated with more working experience and fewer working hours (Simegn *et al*., 2022). In the 2023 study conducted in Malaysia, participants with a PhD degree were 13.5 times more likely to possess good knowledge compared to those with a diploma (Hadi Al Sulayyim *et al*., 2023). Furthermore, the current study identified factors associated with a positive attitude, including the age category of 32-41 years and job banding of band 5, which were significantly associated with a positive disposition. The survey responses, primarily from nurses and pharmacists under AfC job banding, totaled 197 out of 240. Only 72 responses were from doctors, who had specific sections relevant to their medical specialities roles and grades.

In contrast, a study conducted during COVID-19 did not reveal an association between nursing students' attitudes towards AMR and demographic characteristics (Mohd Jainlabdin *et al*., 2021). Regarding the factors associated with good practice, the current study identified the age category of 32-41 years, male gender, and having a professional background in both pharmacist and doctor categories as pertinent. In contrast, a previous study discussed the practice score of nursing students regarding AMR and antibiotic use but did not find an association with other variables, such as gender and experience (Mohd Jainlabdin *et al*., 2021). Although it is challenging for pharmacists to balance the demands of daily clinical duties with maintaining oversight of the rapidly emerging evidence base, there has also been a positive increase in multidisciplinary working. Pharmacists' contributions have been welcomed in an ever-changing, evidence-based environment, and they have felt valued for their input (Ashiru-Oredope *et al*., 2021).

### 5.4.2. Enhancing healthcare professionals' KAP towards antibiotic prescribing and AMS

The combination of traditional and technological methods for survey dissemination had a significant effect on the response rate and sharing among HCPs in the Trust. For instance, using a QR code for the survey, prominently displayed, was a pivotal contributor to the research project's success, yielding impressive outcomes (Appendix 42 and Appendix 45). The concept of a QR code could be employed to communicate crucial AMS policy updates, providing instant, easy access to antimicrobial guidelines (J A Jenkins *et al*., 2022). This can offer HCPs practical tools to maintain effective AMS implementation within their busy schedules (Tonkin-Crine *et al*., 2023). Additionally, strategically placing posters within the Trust, inclusive of the survey's QR code, serves as a reminder for HCPs to participate in the survey. (Appendix 46). This method could also be used to disseminate the AMS policy, antimicrobial guidelines, or an updated AMS package—adaptable to changes in antibiogram results, AMS educational activities, or guidelines (Ina Gajic *et al*., 2022). The strategic positioning of posters in Wards, such as an antibiotic board beside computers or even as mouse pads, could innovatively share updates on AMS guidelines, enhancing visibility and access for HCPs in daily practice (Appendix 45).

Therefore, preparing AMS educational resources and training programs could enhance awareness about AMS and facilitate its implementation during crises, promote the judicious use of antibiotics, reduce AMR, and protect patient lives (Majumder *et al*., 2020). A deficiency in robust AMS educational and training programs exacerbates the AMR challenge (Majumder *et al*., 2020). Thus, establishing a practical, comprehensive AMS training program is essential (WHO, 2019). This program, using active learning techniques like project-based learning and case-based discussions, could enhance AMS implementation (ACCP, 2023). Additionally, training for AMS leads is necessary to co-lead AMS implementation, conducting gap analyses, action plans, AMS metrics, and dashboard visualisation (WHO, 2019). This strategic planning for AMS implementation in the healthcare system may differ depending on the situation, MDROs, pandemics, or crises (UKHSA, 2023). It may also visualise AMS implementation across hospital wards, identifying high-risk areas like Accident & Emergency (A&E) or Intensive Therapy Units (ITUs), and take steps to improve antibiotic prescribing (José-Artur *et al*., 2020).

The impact of the COVID-19 pandemic on AMS practices in the healthcare sector has been profound and multifaceted. A survey of HCPs revealed that 23 out of 240 respondents, including pharmacists, doctors, and nurses, provided valuable insights into AMS during this challenging period. Pharmacists highlighted the necessity for standardising AMS practices in hospitals due to the significant misuse of antibiotics. Additionally, an observed increase in HCAIs and the use of broad-spectrum antibiotics is partly attributed to the pandemic's pressures.

A major concern was the negative impact of technology platforms on patient review and AMS activities. There was a tendency to overlook antimicrobial resistance considerations, with antibiotics often inappropriately prescribed for viral illnesses. Doctors stressed the importance of reliable information dissemination, especially during emergencies. Their responses indicated a reliance on empirical antibiotic use, raised by the urgency of the situation and the influence of non-curated information, such as social media, over trusted EBM guidelines. Nurses, albeit fewer in number, echoed the sentiment that the pandemic led to a disregard for AMR thinking, with antibiotics frequently prescribed for viral infections. They also highlighted the mental strain on HCPs, leading to decision-making challenges and anxiety.

In 2021, a UK study assessed the impact of COVID-19 on antimicrobial stewardship activities/programs found a significant reduction in AMS activities. It reported that 64% of respondents observed a negative impact on routine AMS practices, such as audits, quality improvement initiatives, education, and multidisciplinary work (Ashiru-Oredope *et al*., 2021). The COVID-19 pandemic also opened avenues for innovation and collaboration, presenting opportunities to strengthen AMS in the post-pandemic era. The long-term implications of reduced AMS activities on AMR incidence remain to be seen, but the potential for development and improvement in AMS practices is evident. Further qualitative research is required to investigate the comprehensive HCPs' perspective during the pandemic and provide a more in-depth understanding of this issue.

## 5.5. Limitation

The current study has several strengths. First, this study focused on the assessment of KAP of HCPs towards antibiotic prescribing, AMS and AMR, particularly during the COVID-19 pandemic. Second, the study represents the KAP of HCPs during COVID-19 who worked in acute care settings and who were first approached in any upcoming emergency crisis. Third, the impact of COVID-19 on AMS activities. Finally, univariate and multivariate analyses identified factors associated with the KAP of HCPs.

However, the study has a few limitations. First, the ability to generalise the findings to all HCPs in the UK is limited because the study encompassed just one NHS Foundation Trust in England. Out of a total of

7980 healthcare professionals within the trust, only 240 participated in the study, which represents approximately 3% of the HCPs. Second, the respondents were HCPs who currently worked in the Trust. Some of them have left the Trust since the pandemic. However, it provided an overview of the situation DP, which could help in providing insights regarding antibiotic prescribing during the crisis, how AMS was affected and actions that could be taken to establish an ongoing advocating AMS programme, which would be beneficial to stand by in any upcoming emergency. Preparing educational and training resources that can help increase awareness regarding AMS and facilitate its implementation in the crisis would help promote the judicious use of antibiotics, decrease the AMR, and protect patients' lives. Additionally, the survey was designed with the understanding that AfC job banding primarily applies to nurses and pharmacists. For doctors, specific sections relevant to their medical specialities were included. Job banding did not significantly affect their choices. This issue, along with the fact that the survey responses were mainly from nurses and pharmacists (197 out of 240 responses), while only 72 responses were from doctors, indicates that the results may not fully represent all professional roles within the Trust.

## 5.6. Conclusion

The current study emphasises the need to elevate awareness among HCPs and foster knowledge, positive attitudes, and effective practices towards antibiotic prescribing. Factors influencing KAP include age, gender, professional background, and years of experience. The absence of robust AMS educational and training programmes intensifies the AMR challenge. Thus, it's essential to establish effective educational initiatives quickly. Moreover, this study identified HCPs who could benefit from targeted intervention programmes. This survey reveals new insights into COVID-19's impact on antibiotic prescribing, AMR, and AMS activities. Significant disruptions were observed in AMS ward rounds, audits, and education. The broader consequences of decreased AMS activities on AMR might become apparent in the coming years, necessitating vigilant monitoring for issues like rising antibiotic-resistant organisms. The pandemic highlighted the importance of innovative tools, educational resources, increased awareness, and collaboration. These elements might fortify AMS in the future, enhancing the roles and support for pharmacists.

### Summary of this chapter

This chapter has discussed the overall findings of the prospective survey study conducted in this research project. The next chapter will present an overall discussion and the proposed practical AMS tools derived from this research.

# Chapter 6

# Discussion and Conclusion

## 6.1 Discussion

This chapter discusses the main findings, including the high prevalence of inappropriate antibiotic prescribing and the impact of COVID-19 on AMS practices. It introduces practical AMS implementation tools and highlights barriers to effective antibiotic prescribing. The strengths and limitations of the research are acknowledged. Reflections on the research process are provided, followed by future research directions and recommendations for policymakers, academia, and healthcare professionals. The chapter concludes by emphasising the importance of sustainable AMS practices and offering quality solutions to improve antibiotic prescribing, advocating for effective and sustainable AMS implementation to combat antimicrobial resistance and save patient lives.

### 6.1.1 Overall discussion of the main findings.

Based on the published literature, the first study investigated AMS implementation in acute care settings prior to and during the COVID-19 pandemic. AMS strategies and measures were explored to understand AMS practices better, revealing the most used AMS interventions during the COVID-19 pandemic in acute care settings (Study 1, Chapter 3).

Inappropriate antibiotic prescribing is one of the crucial reasons for the increase in AMR globally (WHO, 2019). One of the key findings this research has highlighted is the high prevalence of inappropriate antibiotic prescribing in the medical records of adult patients (age 25 and above). As per local guidelines, inappropriate antibiotic prescribing increased from 36% in 2019 to 64% in 2020. Differences were observed in AMS interventions, with an OR of 2.77 (95% CI 1.37-5.70, *p-Value*=0.005) for 'De-escalation'. For this reason, maintaining AMS interventions, particularly 'De-escalation', is vital during antibiotic reviews in order to align with local guidelines and the severity of the infection (Study 2, Chapter 4).

The initial antibiotic prescribing under the ‘Start Smart’ initiative was influenced by factors such as the main diagnosis. Community-acquired pneumonia was the predominant diagnosis in approximately 128 pre-pandemic patients, but the difference in the number of CAP patients before and after the pandemic was statistically insignificant. Unclear diagnoses like URTI, LRTI, and pneumonia affected appropriate antibiotic choice at admission. COVID-19 pneumonia showed a statistically significant difference between 2019 and 2020, with an OR of 20.24 (95% CI 5.82 to 128.19, p-Value<0.001). For comorbid conditions, no notable differences were detected before and during the pandemic, except for hypercholesterolemia (OR 1.90, 95% CI 1.14 to 3.20, p-Value=0.014), heart failure (OR 2.06, 95% CI 1.23 to 3.52, p-Value=0.007), kidney diseases (OR 0.52, 95% CI 0.32 to 0.84, p-Value=0.008), and asthma (OR 0.50, 95% CI 0.25 to 0.95, p-Value=0.038). There were no significant differences in antibiotic therapy duration, whether short-term (≤3 days) or long-term (≥ 6 days), both before and during the pandemic.

The prevalence of inappropriate antibiotic prescribing remained high, with rates of 50% in 2019 and 49% in 2020, despite following local guidelines. The study overviewed factors impacting 'Then Focus' antibiotic prescribing in patients with respiratory tract infections before and during the COVID-19 pandemic. No significant differences were observed in laboratory tests, such as WBC, CRP, and serum creatinine. However, chest X-ray examinations were more notable in diagnosing pneumonia during the pandemic, with an OR of 1.75 (95% CI 1.04 to 2.97, p-Value=0.037). There were no significant changes in the days of antibiotic review. AMS interventions showed meaningful differences in 'Continue Antibiotics' (OR 3.36, 95% CI 1.30-9.25, p=0.015) and 'De-escalation' (OR 2.77, 95% CI 1.37-5.70, p=0.005). The percentage of inappropriate antibiotic prescriptions increased from 36% in 2019 to 64% in 2020. The implementation of AMS is crucial to the UK's five-year (2024-2029) action plan to combat antimicrobial resistance, aiming to optimise antibiotic use and promote the sustainability of AMS implementation (UKHSA, 2023).

It is imperative to consider effective AMS interventions to address the high prevalence of inappropriate antibiotic prescribing, maintain patient care, and mitigate the threat of AMR (Study 2, Chapter 4). Results from Study 1 (Chapter 3) suggest that AMS implementation in acute care settings should involve strategies, guidelines, clinical pathways, and education, with doctors, pharmacists, and multidisciplinary teams playing crucial roles. Advocacy for AMS must continue in the post-pandemic era to ensure patient safety, with lessons learned from COVID-19 informing future practices. Findings from the systematic review in Study 1, Chapter 4, recommend starting AMS programmes with core strategies such as formulary restriction, antibiotic review, and prospective audit with feedback. These core strategies should be established before adding supplemental strategies like de-escalation, dose optimisation, parenteral-to-oral switch, guidelines, and education. Integrating computerised decision support systems and surveillance is necessary to maximise technical support for sustained AMS implementation. Common AMS measures include DDD, DOT, and quality improvement indicators, with a need for standardisation to facilitate outcome comparison and effective AMS implementation (WHO, 2019; BSAC, 2018).

As AMS is an organisational programme, its implementation necessitates the collaboration of healthcare professionals and a multidisciplinary team to uphold its interventions and achieve its goal of preserving the judicious use of antibiotics. Implementing AMS requires a deep understanding of the knowledge, attitudes, and perceptions of healthcare professionals towards antibiotic prescribing, AMR, and AMS. Study 3 (Chapter 5) addressed these issues, emphasising the need to promote knowledge, positive attitudes, and effective practices regarding antibiotic prescribing. Factors influencing knowledge, attitudes, and practices include age, gender, professional background, and years of experience. The survey revealed new insights into COVID-19's impact on antibiotic prescribing, AMR, and AMS activities, highlighting the importance of innovative tools, educational resources, increased awareness, and collaboration (Abdelsalam-Elshenawy et al., 2023). There is also a need for practical tools for AMS implementation to maintain a roadmap for effective AMS implementation at both the patient and organisational levels.

This includes a dashboard for measures and metrics of AMS implementation, a targeted educational programme to promote its practices, and easily accessible antimicrobial guidelines for healthcare professionals. These tools aim to improve antibiotic prescribing and keep healthcare professionals updated. The research students proposed four practical tools to promote effective and sustainable AMS implementation in healthcare systems and among healthcare professionals.

### 6.1.2. Proposed practical tools for AMS implementation.

The proposed antimicrobial stewardship implementation practical tools outlined in Table 6.1 offer a practical toolkit to enhance antibiotic use in healthcare. It encompasses an organisational roadmap for hospital-wide stewardship, a dynamic dashboard for real-time decision-making, a comprehensive training course, and an AMS card for both the healthcare system and individual healthcare workers. The goal is to promote smart antibiotic initiation and focused targeting to improve patient outcomes.

**Table 6.1**. Proposed antimicrobial stewardship practical tools.

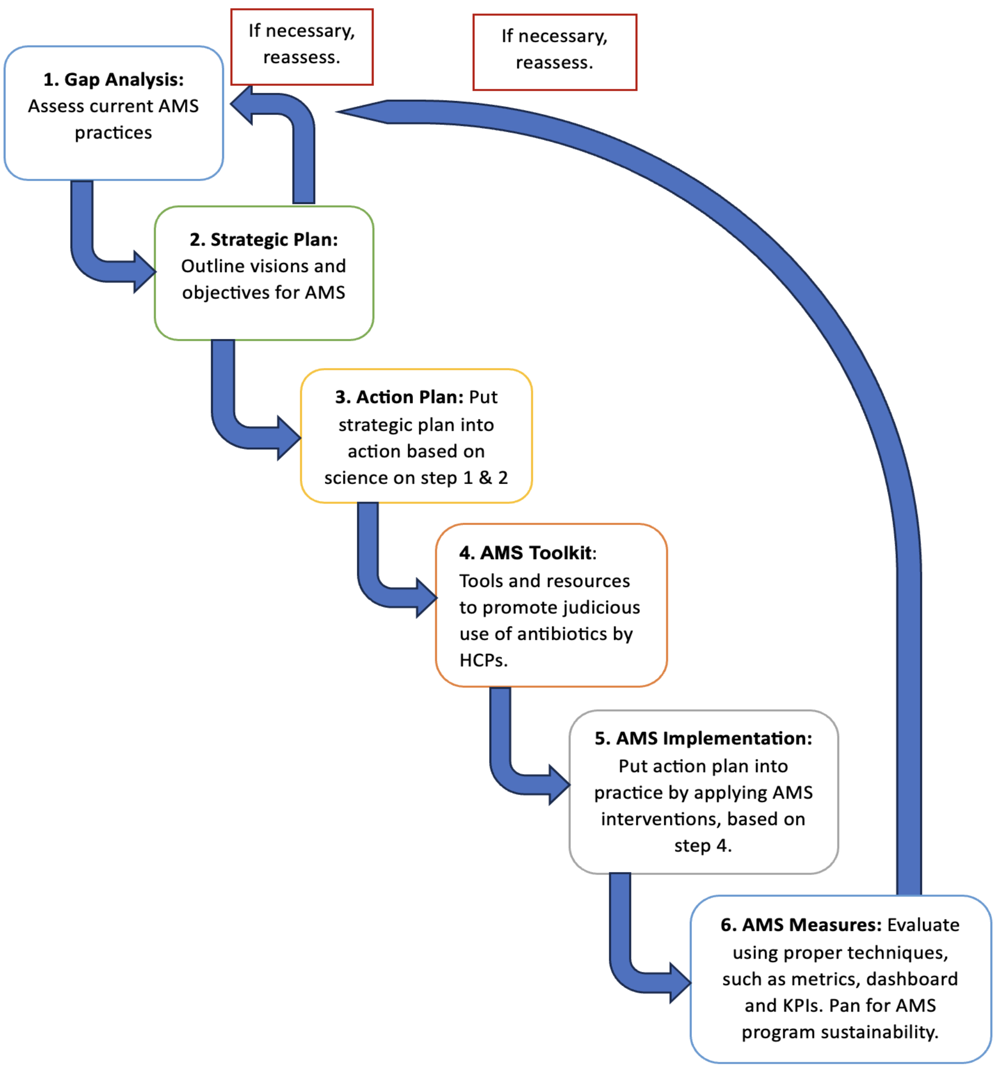
| Antimicrobial Stewardship Practical Tools | | | |
|---|---|---|---|
| Antimicrobial Stewardship Roadmap Framework | Antimicrobial Stewardship Dynamic Dashboard | Antimicrobial Stewardship Comprehensive Training Program | Antimicrobial Stewardship Card |
| • Healthcare system framework: organisational-level antimicrobial stewardship from gap analysis to comprehensive evaluation.<br><br>• Healthcare professional framework: individual-level antimicrobial stewardship: how to apply in a potentially infected patient. | • Antimicrobial stewardship dashboard - "start smart": initial antibiotic course upon admission or empirical antibiotic therapy.<br><br>• Antimicrobial stewardship dashboard - "then focus": pathogen-directed therapy or targeted antibiotic therapy. | • AMS roadmap training program the health system (Organisational-level).<br><br>• AMS roadmap training program for health professionals (Individual-level). | • Antimicrobial stewardship card for healthcare professionals. |

#### 6.1.2.1 Antimicrobial stewardship roadmap.

**Healthcare system framework: organisational-level antimicrobial stewardship from gap analysis to comprehensive evaluation.**

Figure 6.1. presents a sequential and cyclical roadmap for AMS implementation. The process begins with understanding the existing AMS practices and ends with evaluation and potential reassessment. This flowchart provides a systematic and structured approach to implementing AMS practices. Here's a step-by-step breakdown:

**Figure 6.1.** Healthcare system framework: organisational antimicrobial stewardship from analysis to evaluation.




HCPs, healthcare professionals; and KPIs, key performance indicators.

**1- Gap analysis tool:** The first step involves evaluating current AMS practices. This analysis helps identify areas of improvement, understand current strengths, and determine the limitations of the existing program. This tool is the starting point where existing AMS practices are assessed to identify areas of improvement in antibiotic prescribing. Essentially, it helps determine what is lacking or needs to be enhanced in the current AMS implementation. As evident in Chapter 3, Study 1. The gap analysis tool AMS lead/pharmacists/teams use in acute care settings helps assess and guide AMS's step-by-step implementation. Recommendations can be tailored to accommodate hospitals and resources. This AMS health system roadmap toolkit could be used to evaluate any current AMS program activities and identify opportunities for improvement. After completing an initial assessment, the AMS lead can use the tool to routinely review and document progress and plan for new AMS program initiatives and changes concerning clinical situations, such as COVID-19 pandemic. Additionally, understanding the hospital antibiotic prescribing process and the current AMS practices helps establish an effective AMS implementation on an ongoing basis and decreases AMR challenges (AMS Gap Analysis Tool, 2023). As explored in the literature review, the hospitals established AMS based on the AHRQs resources, tools and education, maintaining proper and sustainable AMS implementation (Weston *et al*., 2013).

**2- AMS strategic plan:** A strategic plan should be formulated based on the gap analysis. A strategic plan is crafted based on the insights gained from the gap analysis. This plan outlines the visions and objectives tailored to AMS's specific needs and goals. This plan outlines the overarching vision, objectives, and strategies for effective antimicrobial stewardship implementation.

**3. Action plan:** Once the strategy is in place, it needs to be transformed into actionable steps. This plan is grounded in scientific evidence and is shaped by the findings of the initial two steps. It contains a detailed plan of steps and initiatives to be undertaken, emphasising how to put the strategies from the strategic plan into action.

**4. AMS toolkit:** It is pivotal to have the right tools and resources, in order to facilitate the implementation of the action plan. As evidenced in Study 1, Chapter 3, the AMS toolkit from PHE provided a toolkit that can be part of AMS and, most importantly, ensure optimal patient care and safety by reducing inappropriate antibiotic prescribing. It promotes the judicious use of antibiotics by HCPs and offers them the necessary support to facilitate effective AMS practices (GOV.UK, 2023). Many other AMS tools, resources, and guidelines could be used in AMS awareness and practices. They can be used to assist healthcare professionals in promoting judicious antibiotic use, such as Target AMS tools (RCGP, 2021), and NICE guidance, advice and quality standards (NICE, 2021).

**5. AMS implementation:** Here, the actual deployment takes place. The action plan is put into real-world practice by applying various AMS interventions. This step is directly informed by the AMS Toolkit, ensuring that all interventions align with the comprehensive strategy. This action plan is the execution phase, where the action plan is put into practice, incorporating the tools from the AMS toolkit.

**6. AMS measures:** Once implemented, it's pivotal to evaluate the effectiveness of the program. These measures could be conducted using appropriate evaluation techniques, such as AMS dashboards, metrics, and KPIs. The antibiotic dashboards provide a mechanism to track, monitor, and visualise the progress and outcomes of AMS efforts. This dashboard might include metrics, such as antibiotic consumption rates, top prescribed antibiotics, duration of antibiotics, compliance with the local guidelines, antibiotic review and decisions, day of antibiotic review, and measure the AMS interventions, such as 'IV-to-oral Switch', 'De-escalation', 'Discontinuation' and 'Escalation'. These measures or metrics provide insights into the program's sustainability and impact. Additionally, they offer an integrated AMS program that can be sustainable and withstand any emergency or crisis, such as the COVID-19 pandemic.

The cyclical nature of the roadmap, highlighted by the reassessment loops, emphasises continuous improvement. If discrepancies or results are not as expected at any stage, there's always an opportunity to reassess and recalibrate the approach, ensuring the AMS program's ongoing relevance and effectiveness. It is essential to reevaluate the AMS implementation on an annual basis and provide a feedback report that should be shared with all HCPs, non-clinical staff and top management. Then, any additional required modifications as part of AMS practices according to the current situation in acute care settings will be included.

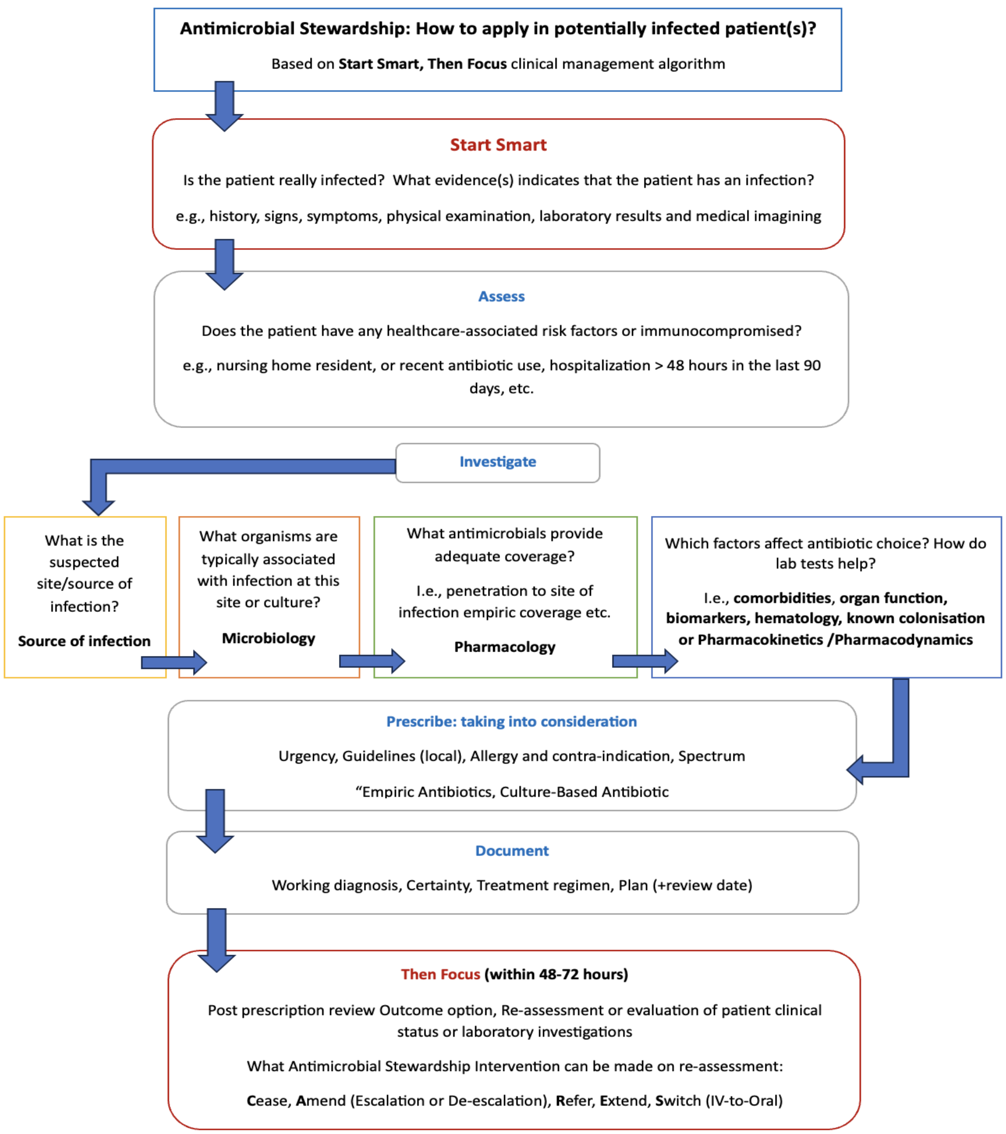
As evidenced in Study 1, Chapter 3, the AMS program should be updated with the hospital's local antimicrobial guidelines based on any change in the situation, such as COVID, or with regards to the results of the antibiogram, histogram and surveillance. The hospitals that updated AMS based on antibiograms have effective AMS outcomes (Surat et al., 2021). It is essential to mention the role of AMS training and education among HCPs. Based on the systematic literature review in Study 1, Chapter 3, AMS education was one of the most integrated AMS strategies PP and DP. In Study 3, Chapter 5, HCPs mentioned that AMS education was the second most negatively affected AMS intervention DP.

Finally, the key takeaways from the annual AMS report should be re-written in lay language to be shared with the public, either as posters in the patient waiting areas or on the hospital's public website. This flowchart AMS roadmap is a structured, systematic process: identifying gaps, strategising, planning, implementing, and continually monitoring and educating. It showcases a holistic approach to antimicrobial stewardship, ensuring it's effectively integrated into healthcare practices. As evidenced by Study 1 (Chapter 3), Study 2 (Chapter 4) and Study 3 (Chapter 5), the following AMS Roadmap educational program is proposed as a comprehensive AMS Training Program. This program represents an additional step to educate and train healthcare professionals in AMS practices continually. It emphasises the importance of ongoing learning in this field.

**Healthcare professional AMS framework: individual-level antimicrobial stewardship: how do you apply it to a potentially infected patient(s).**

The proposed AMS framework, ‘antimicrobial stewardship: how to apply in potentially infected patients’ aims to provide a systematic and structured roadmap for applying the SSTF toolkit when prescribing antibiotics. This framework ensures that antibiotics are used judiciously. The provided flowchart outlines the process for implementing Antimicrobial Stewardship in potentially infected patients using the "Start Smart, Then Focus" clinical management algorithm (Figure 6.2.). Here's a step-by-step breakdown:

**Figure 6.2.** Healthcare professional guide: individual antimicrobial stewardship for potentially infected patients.



### Start Smart:

The first step is determining if the patient is genuinely infected. This step is assessed by considering various evidence, such as history, signs, symptoms, physical examination results, laboratory test outcomes, and medical imaging. It's essential to correctly identify whether an infection is present before prescribing antibiotics to avoid misuse and potential antimicrobial resistance.

**Assess:**

- Check if the patient has any healthcare-related risk factors or if they are immunocompromised.
- Consider factors like if the patient resides in a nursing home, recent antibiotic usage, or hospitalisation for more than 48 hours in the past 90 days.

**Investigate:**

- Microbiology: Determine the suspected site or source of the infection. Identify organisms typically linked with the course of infection or from cultures. Microbiology evaluation is pivotal in narrowing down the choice of antibiotics.
- Pharmacology: Determine which antimicrobial agents provide adequate coverage for the identified organism. The understanding of the pharmacology of antibiotics should be based on factors like how well the antibiotic penetrates the infection site and its empirical coverage.
- Other factors that might influence the choice of an antibiotic: For instance, how do lab tests, other patient comorbidities, organ function, biomarkers, haematology, known colonisation, and pharmacokinetics or pharmacodynamics of the drug influence the decision?

**Prescribe:**

- Before prescribing, consider the urgency of the situation, local guidelines, potential allergies, contraindications, and the spectrum of the antibiotic.
- Two types of antibiotics can be prescribed: Empiric (based on clinical judgment before laboratory confirmation and local guidelines) and Culture-Based (based on microbial culture results).

**Document:**

- Maintain a record of the working diagnosis, the level of certainty of this diagnosis, the chosen treatment regimen, and a plan which includes when to review the case next.

### Then Focus (within 48-72 hours):

The ‘Then Focus’ principle is essential in the re-evaluation phase. After the initial prescription, review the patient's clinical status or lab results. Decide on the necessary antimicrobial stewardship intervention based on this re-assessment. Options include ceasing the treatment, amending it (either escalating or de-escalating the therapy), referring the patient elsewhere, or switching the treatment mode (e.g., from intravenous to oral). This flowchart emphasises the importance of a systematic, evidence-based approach to antibiotic prescription, reducing the risk of AMR and ensuring effective patient care.

This proposed AMS healthcare professional framework, designed for stewardship at the individual level in potentially infected patients, emphasises a thorough and systematic approach that includes initial assessments and continuous re-evaluations. This differs from the Computerised Decision Support Systems (CDSS), which seek to automate AMS interventions (Catho *et al*., 2021). Both are aimed at optimising antimicrobial usage, but the AMS framework offers a more interactive guide for clinicians, in contrast to the automated, guideline-adherent nature of CDSS (Catho *et al*., 2021).

Additionally, in the COMPuterised Antibiotic Stewardship Study (COMPASS), two CDSSs for antimicrobial prescriptions were developed and implemented into the electronic health records of two public hospitals in Switzerland, showcasing an applied model of CDSS (Catho *et al*., 2018). When comparing the proposed AMS Framework to COMPASS, the former provides a detailed, step-by-step approach that may be more suited to healthcare settings where individualised care is paramount. In contrast, COMPASS and similar CDSS are recommended for use in environments where integration with existing digital healthcare systems can enhance AMS through automation and standardisation, which can be particularly beneficial in managing large patient populations and streamlining workflow. The choice between the two systems may depend on the specific needs of the healthcare setting, the scale of operations, and the desired balance between personalised care and efficiency (Catho *et al.*, 2021).

The 'Start Smart, Then Focus' AMS toolkit provides a structured approach for HCPs to implement AMS. SSTF is an evidence-based guide for secondary care clinicians and leaders, crafted to mitigate the risk of AMR while upholding the quality of patient care for those with infections (UKHSA, 2023). Its application is confined to inpatient care settings, encompassing acute, community, and mental health trusts, where a relatively high intensity of antimicrobial use is observed, and patients' conditions can be monitored over time. This facilitates the review and adjustment of initial diagnoses and treatment plans. The proposed AMS roadmap framework, founded on the principles of SSTF, is devised to apply AMS based on SSTF practically. It provides a practical way and step-by-step method to ensure effective AMS implementation and optimised antibiotic prescribing within healthcare settings (Figure 6.2).

#### 6.1.2.2. Antimicrobial stewardship dynamic dashboard

As highlighted in the systematic literature review (Study 1, Chapter 3), measuring prescribing performance is pivotal to assessing the impact of AMS implementation and its demonstrable benefits for patients (Abdelsalam Elshenawy *et al*., 2023). Enhancing antimicrobial use necessitates the identification of measurable elements or metrics that evaluate the outcomes of AMS. These metrics or measures can serve various purposes, including KPIs, quality assurance, quality improvement, and benchmarking, both intra-hospital and Inter-hospital. Determining what to measure is vital to sustain AMS interventions (WHO, 2019). Every hospital should select appropriate measures or metrics that ensure the effective implementation of AMS (Abdelsalam Elshenawy *et al*., 2023).

As detailed in Study 2, Chapter 4, utilising a tangible tool, such as the 'Data Extraction Tool, was pivotal for data collection from 640 patients across eight-time points. A measurable dashboard facilitates consistent assessment of antibiotic prescribing, monitoring of AMS implementation, and identifying areas needing improvement in the health system. It aids in recognising educational needs, monitoring the increase in broad-spectrum antibiotics, and identifying prevalent diagnoses, such as CAP. Encouraging educational activities on local antibiotic guidelines, especially for CAP, can ensure appropriate antibiotic use, conserve broad-spectrum antibiotics, and thereby reduce the incidence of HAIs, such as CD and MRSA (Study 2, Chapter 4).

In Study 3, Chapter 5, the impact of the COVID-19 pandemic on AMS was examined. Many respondents acknowledged the significant public health issue of AMR affecting clinical practices. When HCPs were questioned about the AMS strategies that influenced antibiotic prescribing during the pandemic, a majority felt that the pandemic negatively impacted AMS education and training. There was also heightened concern over the pandemic's detrimental effect on prospective audit and feedback. Observations of potential negative outcomes, such as increased usage of broad-spectrum antibiotics, increase in multidrug-resistant organisms, extended hospital stays, and antibiotic misuse, emphasised the importance of maintaining AMS, especially during future pandemics (Ashiru-Oredope *et al.,* 2021).

The AMS Dashboard depicted in Figure 6.3 represents a critical instrument for tackling the challenges associated with antibiotic prescribing and the broader scope of antimicrobial stewardship, as well as reducing AMR risk. It facilitates real-time visualisation, allowing immediate actions to ensure sustainable AMS implementation and combat the rise of AMR. This dashboard ensures continuity in AMS practices in emergencies or crises, such as COVID-19 pandemic. It also provides an informative tool for department heads, leaders, and chief executives, empowering them to make informed decisions. This visual aid is critical for tracking antimicrobial stewardship and effectively using AMS strategies to curb antimicrobial resistance, while prioritising patient safety.

It is a pivotal tool in the fight against antimicrobial resistance. This dashboard is essential for healthcare providers to monitor, analyse, and optimise the use of antimicrobial agents. It advocates for the prudent use of antimicrobials, ensuring treatments 'Start Smart' with broad-spectrum agents when necessary and are then refined under the 'Then Focus' criteria based on clinical evidence, culture results, and investigations. This AMS dashboard offers a systematic approach that aids in reducing unnecessary antibiotic prescribing, lowering the risk of AMR, and ensuring patient safety. In the meantime, when antibiotic resistance poses a growing challenge, the AMS dashboard serves as an example for informed therapeutic decisions (Global AMR R&D, 2023). During the COVID-19 pandemic, a significant new public health threat emerged, exerting immense pressure on healthcare professionals. However, the persistent global crisis of AMR cannot be overlooked. Given these challenges, urgent actions and measures are necessary to sustain AMS practices during the pandemic. Specifically, there's a need to rely on existing AMS principles across the hospital sector. Advocacy for AMS must persist throughout the pandemic and post-pandemic era (Khor *et al*., 2020).

Figure 6.3 displays an ‘Antimicrobial Stewardship Dashboard’ or ‘AMS Dashboard’, which focuses on the theme of ‘Start Smart: Initial Empirical Antibiotic Therapy.’ This AMS dashboard is based on the "Start Smart Then Focus" toolkit from PHE and the results of the previous three studies (GOV.UK, 2023).

The dashboard provides various data visualisations about antimicrobial therapy in acute care settings. A breakdown of the contents is presented as follows:

- **Selection filters:** A selection filter is an interactive control or mechanism allowing users to display specific data subsets from a larger dataset selectively. These filters help users to focus on specific data to derive insights, view patterns, or make decisions. Using selection filters in dashboards offers several advantages (Patsidis et al., 2023). Firstly, they enhance interactivity, allowing users to engage with the data and explore specific subsets without compromising the integrity of the original dataset. This direct interaction facilitates improved decision-making, as users can concentrate on particular data segments to derive more informed conclusions.
- Furthermore, the filters are designed with ease of use in mind, ensuring that even non-technical users can effortlessly filter and analyse data without delving into complex formulas or functions.
- Additionally, incorporating these filters contributes to a more visually appealing and user-friendly dashboard presentation. The Filters in Figure 6.3 below provide a user-friendly way to filter data interactively. It can filter the data by the following:
    - Month: Options include March, June, September, and December.
    - Main Diagnosis: Options shown are bronchiectasis, CAP, COPD infective exacerbation, HAP, and VAP.
    - Wards: Options include Ward 10, Ward 11, ITU 1, and ITU 2.

- **Admission to the hospital of age groups**: A bar graph showing the number of admissions by age group. The age groups displayed are 26-35, 66-75, and 46-55.
- **Main diagnosis of the admitted patients:** A bar graph showcasing the primary health issues of the admitted patients. The diagnoses include CAP, VAP, HAP, COPD infective exacerbation, and bronchiectasis.
- **Secondary diagnosis or co-morbidities among admitted patients:** A bar graph representing secondary health issues or co-morbidities. The conditions shown are COVID-19, COPD, kidney disease, and dyslipidemia.
- **Top antibiotic allergy:** A bar graph detailing the top antibiotic allergies. The antibiotics listed are penicillin, clarithromycin, metronidazole, co-trimoxazole, and doxycycline.
- **Top five prescribed antibiotics:** A pie chart showcasing the most prescribed antibiotics. The antibiotics shown are co-amoxiclav IV 1.2gm, piperacillin-tazobactam iv 4.5gm (tazocin), meropenem IV, ciprofloxacin 250 mg tablets, and amoxicillin IV 500mg.
- **Antimicrobial stewardship interventions:** A bar graph indicating various interventions. These interventions are ‘Continue Antibiotics’, ‘No Intervention’, ‘IV-to-Oral Switch’, ‘De-Escalation’, and ‘Escalation’.
- **Antibiotic review:** A pie chart illustrating the frequency of antibiotic reviews, with the durations being 3-5 Days (41%), 48-72 Hours (47%), and 7 Days (12%).
- **AMS champion:** A pie chart detailing the professionals who review the antibiotics. The roles mentioned are AMS team (13%), microbiology (37%), pharmacist (19%), and doctor (31%).

The dashboard offers a detailed overview of the hospital's antimicrobial prescribing practices and AMS. This dashboard could include patient demographics, primary and secondary health conditions, prevalent antibiotic allergies, the most frequently prescribed antibiotics, intervention strategies, and the roles involved in the antibiotic review process (Figure 6.3). The data presented below in Figure 6.3 is not actual; it is only for illustrating the AMS dashboard based on the data extraction tool described in Study 2, Chapter 4.

The technology required to implement the AMS Dashboard, as discussed in Study 1, Chapter 3, involves data visualisation software that can process and display complex datasets interactively. This would include software licenses for programs capable of handling large amounts of patient data across various time points, such as the 'Data Extraction Tool' used for collecting data from 640 patients in Study 2, Chapter 4. The cost for such implementation would vary based on the software chosen but typically involves purchasing licenses, potential server costs for hosting the data, and possibly hiring IT specialists to maintain and update the system (BSAC, 2018). The investment in this technology is critical for real-time visualisation and monitoring of antibiotic prescribing, enabling immediate action and informed decision-making to maintain effective AMS practices (IBM, 2019).

**Building AMS dashboards: insight, integration, and application**

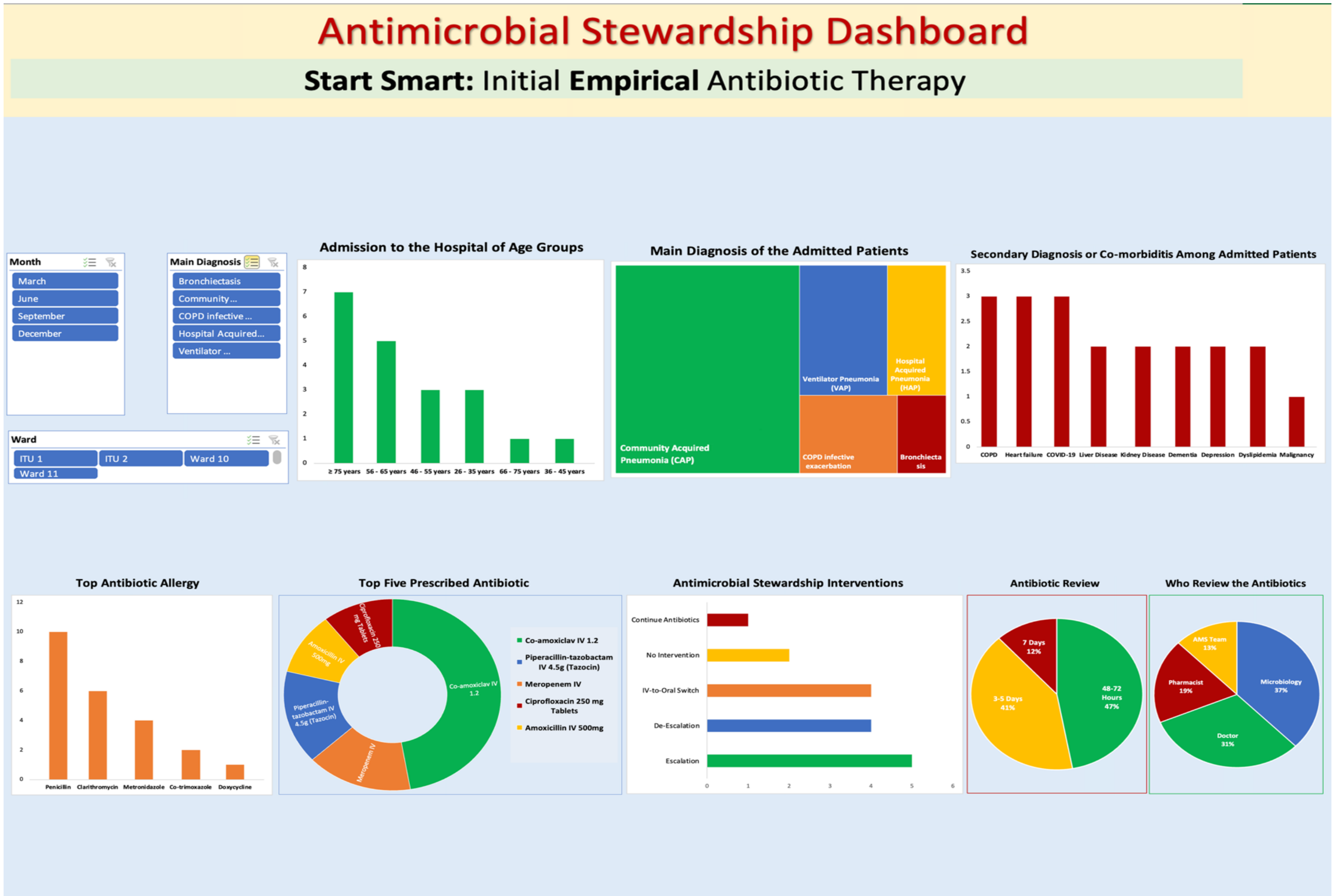
In order to develop this AMS dashboard, the research student communicated with the AMS lead for the East of England NHS England and inquired about the AMS dashboards used among NHS Trusts in the UK. They were directed to the Future NHS website, as discussed in the literature review in Study 1, Chapter 3 (Future NHS, 2023). The research student reviewed all available AMS dashboards (Future NHS, 2023; NHS England, 2021). Most focused on antibiotic consumption by items, trusts, and over months/years, providing a clear understanding of antibiotic use trends and patterns over time. Additionally, some dashboards utilised DDD and metrics for microorganisms and MDROs (Future NHS, 2023; WHO, 2023). However, none offered a comprehensive view of antibiotic prescribing by wards within hospitals or for the SSTF AMS toolkit, such as in the proposed AMS dashboard (Figure 6.3).

Subsequently, the research student examined the metrics and reports of ESPAUR from 2017 to 2023, as well as the ECDC and WHO dashboards (UKHSA, 2023; EDED, 2023). None focused on dynamic antibiotic prescribing, AMS interventions, antibiotic review, or the 'CARES' decision-making process, including all the steps of the SSTF stewardship toolkit (UKHSA, 2023). The research student drew upon all their expertise and the Global AMR R&D dashboard guide (Global AMR R&D, 2023). Additionally, the research student attended basic and advanced Excel Researcher Development Programme (RDP) sessions at UH and utilised online tutorials from Microsoft Excel and IBM on data visualisation, employing Pivot Tables, graphs, and charts (Microsoft, 2023; IBM, 2023). This was complemented by the 'Data Extraction Tool' developed from Study 2, Chapter 4, which offered numerous insights into AMS and factors affecting its implementation. Please see the 'Data Extraction Tool' of Study 2 in Appendix 35.

After investing over 100 hours in creating a dynamic, interactive AMS dashboard based on real clinical practice data for patients admitted with infections, the research student realised it provided a visual aid only for initial empirical antibiotic prescribing or 'Start Smart' (UKHSA, 2023). The next step was to create a 'Then Focus' AMS dashboard using the same Excel tools to give a comprehensive view of pathogen-directed antibiotic prescribing following laboratory investigations. Both dashboards are adaptable to any hospital system. They can be used in daily practice, utilising the filter tool to identify problems in a timely manner and offer practical solutions to improve antibiotic prescribing, sustain effective AMS implementation, and reduce AMR risk. The proposed AMS dashboards can also compare antibiotic prescribing and AMS over time, within and between hospitals, serving as benchmarks. They can be integrated according to hospital needs and stakeholder plans. Furthermore, the AMS dashboard could be tried in primary care settings but requires further research.

Finally, the dashboard could be integrated with Artificial Intelligence (AI) technology to offer easy-to-read outcomes and enhanced visibility into antibiotic prescribing and AMS, providing more frequent data to improve antibiotic prescribing and effective AMS. To access the demonstration of the AMS dynamic dashboard, please see Appendix 57.

**Figure 6.3.** Antimicrobial stewardship dashboard - "start smart": initial empirical antibiotic therapy.




CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia; COPD: chronic obstructive pulmonary disease; and ITU, intensive therapy unit.

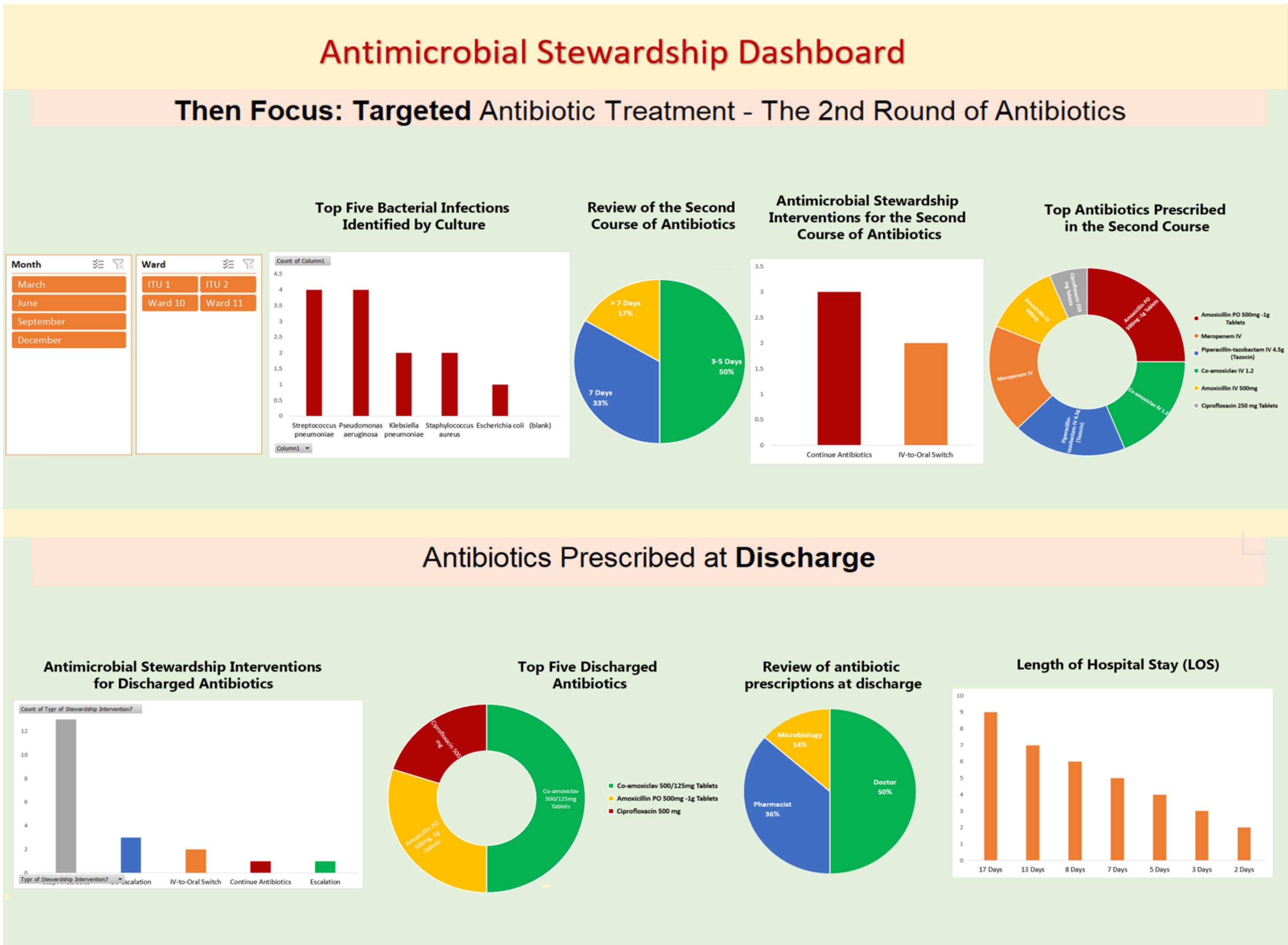
Figure 6.4 provides a streamlined explanation of AMS implementation throughout a patient's hospital stay, focusing on 'Then Focus' antibiotic prescribing or pathogen-directed therapy, which includes the administration of a second course of antibiotics. This dashboard displays various data visualisations related to antimicrobial therapy and AMS implementation during a patient's hospital stay (Abdelsalam Elshenawy *et al*., 2024). Below is an overview of its components:

- **Selection filters:** A selection filter is an interactive control or mechanism allowing users to display specific data subsets from a larger dataset selectively. These filters enable users to focus on particular data to derive insights, view patterns, or make decisions. The Filters in Figure 6.4. below provides a user-friendly way to filter data interactively. It can filter the data by the following:
    - **Month:** Options include March, June, September, and December.
    - **Ward**: Options include ITU 1, ITU 2, Ward 10, and Ward 11.

- **Top five bacterial infections per culture**: A bar graph indicating the top bacterial infections identified from cultures. The infections listed are Streptococcus pneumoniae, Pseudomonas aeruginosa, Klebsiella pneumoniae, Staphylococcus aureus, and Escherichia coli category.
- **Antibiotic review in the second antibiotic course**: During the second course of the antibiotic review, a pie chart provides a visual representation of the duration of antibiotic assessments. The chart indicates that 50% of the reviews take place within a span of 3 to 5 days, 33% are conducted over 7 days, while the remaining 17% extend beyond 7 days.
- **Antimicrobial stewardship interventions in the second antibiotic course**: A bar graph showcasing interventions, including ‘Continue Antibiotics’ and ‘IV-to-Oral Switch’.
- **Top five discharged antibiotics**: A pie chart representing the most commonly prescribed antibiotics upon patient discharge. The antibiotics mentioned are co-amoxiclav 500/125mg tablets, amoxicillin PO 500mg-1g tablets, and ciprofloxacin 500 mg.
- **Antibiotic review in discharged antibiotics**: A pie chart provides insight into the professionals responsible for the assessments. The chart reveals that doctors undertake 50% of these reviews, while pharmacists account for 36%. The microbiology team is responsible for 14% of the evaluations.
- **Antimicrobial stewardship interventions in discharged antibiotics**: A bar graph demonstrating various interventions upon discharge. These interventions include ‘Stop Antibiotics’, ‘De-Escalation’, ‘IV-to-Oral Switch’, ‘Continue Antibiotics’, and ‘Escalation’.
- **Length of stay**: A bar graph depicting the number of days patients stayed in the hospital. Durations represented are 17 Days, 13 Days, 8 Days, 7 Days, 5 Days, 3 Days, and 2 Days.

This targeted antibiotic dashboard provides detailed insights into antibiotic prescribing and AMS practices related to the second round of antibiotic treatments in an acute care setting. The data covers the prevalent bacterial infections, interventions, antibiotics prescribed at discharge, and patient stay length.

**Figure 6.4.** Antimicrobial stewardship dashboard - "then focus": targeted antibiotic therapy.




LOS, length of stay.

#### 6.1.2.3. Antimicrobial stewardship roadmap: comprehensive training course

In response to the urgent need for action to tackle the effects of antimicrobial resistance on the healthcare system, this training program aims to support health professionals, pharmacists, doctors, and nurses to drive the antimicrobial stewardship agenda in their workplaces.

As highlighted in the systematic literature review (Study 1, Chapter 3), education is a supplementary strategy vital for AMS implementation (Abdelsalam Elshenawy *et al*., 2023). Before the pandemic, AMS education using active learning activities showed promising outcomes. For instance, a study conducted across hospitals in the USA employed educational activities and webinars. These initiatives encouraged collaboration with the clinical microbiology laboratory and integrated nurses into stewardship activities, addressing antibiotic allergies.

This AMS educational programme, titled ‘Building Stewardship: A Team Approach Enhancing Antibiotic Stewardship in Acute Care Hospitals’ and provided by AHRQ safety programme, proved particularly effective. It stressed the importance of antimicrobial stewardship programmes and strategies for their implementation and addressed operational challenges, such as understanding pharmacodynamics, business models, and electronic surveillance (Weston *et al*., 2013). The AHRQ educational tools were also used in another study in an innovative manner, such as 1-page documents with accompanying user guides on infectious disease syndromes. These documents were versatile, serving as (1) informational display posters, (2) discussion points during clinical rounds, and (3) templates for drafting local guidelines (Tamma *et al*., 2021).

However, during the pandemic, only one study highlighted AMS education, emphasising its crucial impact. Structured AMS education was deemed essential to manage emergencies or crises effectively (Ashiru-Oredope *et al*., 2021). An educational programme within the health system designed for AMS leaders and top management significantly aids in the implementation of AMS. This program's effectiveness is further enhanced when accompanied by a supplementary AMS educational initiative for healthcare professionals. Such a comprehensive approach not only promotes hospital-wide AMS practices but also addresses the threat of AMR. It also equips the system to respond effectively to any future emergencies or pandemics. Therefore, AMS education was pivotal for the successful implementation of AMS (Elshenawy *et al*., 2023).

As outlined in Study 2, Chapter 4, the rise in inappropriate dosing in 2020 (13%) deserves attention. as it may indicate a need for more adherence to established guidelines or insufficient knowledge among prescribers. It's essential that healthcare professionals are provided access to the most recent evidence-based guidelines, and targeted educational interventions might help address this discrepancy. However, it remains crucial to continue refining prescribing practices to maintain and improve this progress. Additionally, encouraging educational activities on local antibiotic guidelines, especially for CAP, can ensure appropriate antibiotic use, conserve broad-spectrum antibiotics, and thereby reduce the incidence of hospital-acquired infections (Study 2, Chapter 4).

In Study 3, Chapter 5, the influence of the COVID-19 pandemic on AMS was explored. Many participants felt that the pandemic negatively impacted AMS education and training. The study participants demonstrated good AMR knowledge but insufficient AMS knowledge; however, their attitude and practice require further improvement. This emphasised a potential shortage in effective AMS educational and training initiatives. Additionally, key knowledge deficiencies, especially about antimicrobial stewardship strategies, were evident. The presence of targeted and comprehensive AMS educational interventions was essential during the pandemic. This aligns with a study conducted by the ECDC involving national focal points for antimicrobial resistance and national focal points for communication from all EU countries (ECDC, 2022). Additionally, the findings from Study 3, Chapter 5 emphasised the importance of maintaining healthcare professionals' engagement in tackling these challenges. Results from this study also highlighted the importance of developing educational activities in AMS interventions and guidelines.

Another study emphasised the need to design educational activities on AMS interventions, resources, and guidelines, which focus specifically on promoting behaviour that leads to prudent prescription, dispensing, and administration of antibiotics (Al-Taani *et al*., 2022). Upon asking HCPs about the AMS strategies that influenced antibiotic prescribing during the pandemic, most believed that the pandemic had a negative effect on AMS education and training. Observations of potentially adverse outcomes, including increased usage of broad-spectrum antibiotics, a rise in multidrug-resistant organisms, prolonged hospital stays, and antibiotic misuse, underscored the importance of maintaining consistent AMS education, especially during subsequent pandemics or spikes in COVID-19 (Ashiru-Oredope *et al*., 2021).

Therefore, preparing AMS educational resources and training programs could enhance awareness regarding AMS and facilitate its implementation during a crisis, promote the judicious use of antibiotics, reduce AMR, and protect patient lives. The lack of robust AMS educational and training programs exacerbates the AMR challenge (Majumder *et al*., 2020). Hence, it is essential to establish a practical, comprehensive AMS training program. This survey offers fresh insights into the impact of COVID-19 on antibiotic prescribing, AMR, and AMS activities. Notable disruptions were observed in AMS ward rounds, audits, and education. The pandemic underscored the significance of innovative tools, educational resources, heightened awareness, and collaboration. These elements could strengthen AMS in the future, amplifying the role of education in enhancing antibiotic prescribing practices and mitigating the AMR challenge (Study 3, Chapter 5).

The presence of a robust educational program for the AMS roadmap framework is paramount for combating AMR and maintaining effective AMS implementation. It's imperative for AMS leads, champions, and top management to have a thorough understanding of this roadmap to ensure the successful implementation of AMS. Through comprehensive education on the roadmap, stakeholders can seamlessly navigate from gap analysis to comprehensive evaluation, enabling them to identify challenges and strategies and implement AMS initiatives efficiently. As AMR continues to pose a significant threat to global health, empowering HCPs with the knowledge and tools provided by the AMS roadmap becomes essential to ensure patient safety, optimise antibiotic use, and address this global challenge effectively.

Addressing the critical demand to mitigate AMR's impact on healthcare, this training initiative is designed to empower health professionals, pharmacists, doctors, and nurses to champion AMS within their respective work environments. This AMS roadmap training program aligns with the key measures outlined in the UK AMR 5-year action plan (2019-2024) (GOV.UK, 2019). It incorporates findings from the three studies alongside the "Start Smart, Then Focus" Antimicrobial Stewardship Toolkit, which aims to refine antimicrobial prescriptions in healthcare domains (UKHSA, 2023).

The proposed AMS roadmap training program is designed to equip health professionals, AMS leads, and stakeholders with the tools and knowledge necessary to integrate AMS into the healthcare system effectively. By promoting a continuous commitment to AMS learning, professionals can further improve their AMS practices using the roadmap frameworks outlined in Chapter 7. This approach aims to foster sustainable improvements in antibiotic prescribing. The proposed HCP’s AMS Framework provides a step-by-step guide for treating potentially infected patients, focusing on individual judgment and tailored care. This contrasts with the CDSS used in the COMPASS study, which automates the AMS process by integrating decision support into the EHR. While the AMS Framework may require more hands-on application, CDSS leverages technology to ensure adherence to guidelines. However, the AMS Framework, with its emphasis on individual assessment and follow-up, could be more adaptable in scenarios that deviate from standard procedures, unlike the CDSS, which might be more rigid but efficient for standardised care across larger scales (Catho *et al*., 2021). Especially with the AMS Dashboard

Additionally, promoting lifelong learning among HCPs is of paramount importance. Lifelong learning in AMS could be achieved through continuous professional development. Throughout their careers in the health system, HCPs should immerse themselves in this commitment to lifelong learning by participating in training programs, attending annual conferences, staying updated with recent antimicrobial guidelines, and engaging in webinars. Such dedication to continual learning enhances clinical practice and mitigates AMR challenges, especially during emergencies and crises.

This training aims to help learners develop AMS knowledge and skills that are applicable across health systems, support learners to become confident in leading AMS interventions and promote a systematic thinking approach in any potentially infected patients and provide an opportunity for learners to develop and demonstrate advanced AMS implementation and measures (Table 6.1).

**Proposed outcomes:**

By the end of the training, learners will be able to:

- Outline how AMS strategies can be used to mitigate the risk of AMR in general and in their workplace.
- Assess AMS practices against the principles of antimicrobial management and make recommendations to improve practice and maintain the rational use of antibiotics.
- Describe the usual clinical case presentations and identify appropriate management strategies for common infectious conditions based on local and national antimicrobial guidelines.
- Analyse problems and effectively use AMS interventions and the AMS dashboard to provide metrics for AMS implementation and benchmarking.
- Lead a quality improvement project to maintain AMS intervention in their workplace using project-based learning.

**Proposed learning topics**

- 20 'Essential' topics need to be covered by the end of training, as outlined in Table 6.1 below.
- Learners can also individualise their development plan by using health professional training. However, the AMS lead should take both health professionals and health system training programs in order to be able to lead AMS implementation effectively.

**Who could be involved?**

The proposed AMS roadmap comprehensive training program could receive accreditation from CPD, allowing learners to actively engage with their workplaces to find opportunities to apply learning into practice as part of the CPD activities embedded in the training. The suggested project-based learning proposed in this training program will enable learners to engage peers and other stakeholders in their workplace to complete their training activities. This may include consulting and involving stakeholders in the design and delivery of their improvement project. Collaboration is the key to success with improvement initiatives. This suggested training program could be maintained using a variety of supporters, such as face-to-face training, self-directed learning, group learning, learner support, case-based discussion and presentation, and project-based learning (Table 6.2).

**Table 6.2.** Key areas of learning of the AMS roadmap training program for both health professionals and the health system.

| | **Patient-Level AMS Implementation Programme Outline** | **Organisational-Level AMS Implementation Programme Outline** |
|---|---|---|
| **Week 1** | Training Introduction: Understanding antimicrobial resistance (AMR), antimicrobial stewardship (AMS) Toolkit, and creating urgency to change. | How to conduct ‘gap analysis’. Assess current AMS practices. |
| **Week 2** | How to implement antimicrobial stewardship in patients who may have infections. | |
| **Week 3** | Types of bacteria, microbiology, epidemiology, pharmacotherapy. | Create a ‘strategic plan’ and outline the visions and objectives for AMS. |
| **Week 4** | Antimicrobial medicines classifications, mechanism of actions, mechanism of resistance, spectrum of activity, adverse effects, and drug interactions. | |
| **Week 5** | Infections and special populations, pharmacokinetics (PK) /pharmacoepidemiology (PD)* | Create an ‘Action Plan’ and put a strategic plan into action based on weeks 2 and 3. |
| **Week 5** | Factors affecting the antibiotic prescribing process and principles of infection management. | |
| **Week 6** | AMS case presentation, case-based discussion. | Antimicrobial stewardship implementation, putting an action plan into practice by applying AMS interventions. |
| **Week 7- 10** | Management of infectious syndromes and national antimicrobial guidelines, such as sepsis, respiratory tract infections, skin and soft tissue infections, urinary tract infections, Clostridioides Difficile Infection (CDI) and antibiotic prophylaxis. | |
| **Week 11- 12** | Antifungal stewardship, including anti-fungal pharmacology, PK, PD, and management of fungal infections using a systematic thinking approach. | AMS measures/dashboards and Communication, leadership and management. |
| **Week 13** | AMS case presentation, case-based discussion. | |
| **Week 14** | AMS interventions. | How to prepare AMS Dashboard |
| **Week 15** | AMS measures/dashboards. | |
| **Week 16** | Infection Prevention and Control | |
| **Week 17** | Antibiogram role in AMS | |
| **Week 18- 20** | AMS final project, such as quality improvement project, key performance indicator (KPIs), including project presentation, discussion, and feedback.<br><br>End of training assessment: it can be a 1-to-1 discussion with an expert and an assessment of the training portfolio. | AMS final project, such as AMS action plan.<br><br>End of training assessment: it can be a 1-to-1 discussion with an expert and an assessment of the training portfolio. |
| Certificate of completion. | | |

PK, pharmacokinetics; PD, pharmacodynamics; CDI, clostridioides difficile infection; and KPI, key performance indicator.

**Patient-level and organisational-level AMS implementation programme outline.**

The proposed patient-level AMS implementation training programme for healthcare professionals aims to provide a comprehensive understanding of antimicrobial resistance and antimicrobial stewardship. It begins with an introduction to the significance of AMR and the AMS toolkit, then progresses to practical aspects of managing infections and various antimicrobial medicines. The programme integrates case studies to maintain a practical approach and culminates in a final AMS project. Participants are encouraged to engage in discussions, present AMS measures, and undergo an assessment to gauge their understanding and application of the training (Table 6.1).

The proposed organisational-level AMS implementation training programme focuses on equipping leadership and strategic roles within the health system with the knowledge and skills necessary for effective AMS implementation. It covers understanding current AMS practices, identifying gaps, and developing strategic visions and actionable plans. The programme includes a final AMS project and a thorough assessment to ensure readiness for practical application (Table 6.1).

Both proposed AMS programmes aim not only to convey knowledge but also to introduce a sense of urgency, collaboration, and lifelong continuous AMS learning. At the end of the training, participants could be awarded a certificate of completion, indicating their preparedness in AMS implementation. This AMS programme can be submitted to relevant providers for accreditation through continuing professional development (CPD), ensuring it becomes part of ongoing professional development (CPD, 2023). Platforms such as the ‘WHO Open Course’ website and ‘Future Learn’ online courses offer global and nationally accessible training (Open WHO, 2023; Future Learn, 2023).

The ‘Future NHS’ website, after discussions with the Antimicrobial Stewardship lead for the East of England NHSE (Future NHS, 2023), emerged as a potential host for the programme, given its resources and networking for NHS professionals. This AMS training programme could also be featured on RPS website (RPS, 2023). This opportunity allows transforming sessions from the AMS training programme into a practical and educational article. The AMS programme could be targeted for pharmacy practice postgraduate diplomas, as well as postgraduate training programmes in public health and clinical healthcare. It could be tailored to various curriculum modules, such as medicine optimisation, patient safety, quality improvement, and infection management.

The potential for international expansion is significant, with plans to translate the training into Arabic and adapt it for use in Middle Eastern and Arabic nations, such as the United Arab Emirates, Saudi Arabia, and Egypt. This expansion would broaden the programme's influence on AMS practices and help mitigate the AMR challenge.

#### 6.1.2.4. Antimicrobial stewardship card

The systematic literature review (Study 1, Chapter 3) identified guidelines and clinical pathways as essential strategies for AMS implementation, particularly during the COVID-19 pandemic. Providing accessible and regularly updated guidelines was crucial for improving antibiotic prescribing and mitigating AMR (Elshenawy et al., 2023; Velazquez-Meza et al., 2022). Study 2, Chapter 4, noted that during the pandemic, local antimicrobial guidelines for the trust were updated (Bedfordshire, 2019) and integrated into the MicroGuide Antibiotic Prescribing Guidelines App, available on Apple and Google Play (MicroGuide, 2019). The MicroGuide App supports AMS goals by providing updated, concise information at the point of care, aiding in safe and effective prescribing. However, it has limitations, such as the need for frequent updates and the effort required for integration, along with time constraints and potential distractions that can make accessing the guidelines challenging (Brown et al., 2022).

One of the significant limitations of the MicroGuide App is its reliance on a stable internet connection for updates, a significant obstacle in settings with limited or unreliable Wi-Fi or data connectivity. Busy healthcare professionals might miss critical updates if they do not regularly refresh the app. The variable access of healthcare workers also hinders the app's usability on smartphones or tablets during working hours. The learning curve associated with the app might pose a barrier in time-sensitive clinical environments. Moreover, being a digital tool, the MicroGuide App is prone to software glitches and technical problems, which can disrupt its functionality (Kieran *et al*., 2021).

In Study 3, Chapter 5, it was found that prominently displaying a QR code for the survey questionnaire significantly contributed to the research project's success, yielding impressive results. The study revealed that a majority of healthcare professionals (55%) strongly agreed that antimicrobial resistance (AMR) is a public health issue impacting clinical practice. Additionally, 45.8% concurred that actions to combat AMR within the trust would have societal implications and affect future generations. However, there was a notable knowledge gap, with only 52.5% of participants sufficiently aware that antimicrobial stewardship enhances patient outcomes within the Trust. Continuous awareness, education, and frequent updates about changing AMS policies are essential for HCPs. Changes can be influenced by seasonal variations, antibiogram updates, shifts in AMR patterns, or healthcare-associated infections (HAIs). Easily accessible information and educational resources, particularly through AMS pharmacists, significantly enhance this process. AMS pharmacists are well-positioned to co-lead AMS implementation and provide timely updates based on dynamic dashboard metrics, antibiogram results, audits, and AMS rounds, which are crucial for maintaining AMS practices (UKHSA, 2023). Given the limitations of the MicroGuide App, the proposed AMS Card could serve as a complementary or alternative tool, offering instant, offline access to essential guidelines. The AMS Card is straightforward, user-friendly, and reliable as a quick-reference tool in various clinical situations. Unlike digital tools, the physical presence of the card ensures constant visibility and accessibility, free from technical malfunctions or limited battery life issues, enhancing the overall efficacy of AMS initiatives (PHE, 2023).

The integration of a QR code that links to the latest AMS policy and AMR guidelines, especially when connected to the updated hospital intranet, can significantly ease HCPs' access to these essential resources. Such streamlined access is expected to foster more appropriate antibiotic prescribing practices. Therefore, having an AMS card that is easily accessible, perhaps even designed to be illuminated and attached to the ID lanyards of doctors, pharmacists, and nurses, would provide a convenient and visible means to access these guidelines and their updates. Moreover, positioning this QR code in strategic locations such as wards, boards, and nurse stations would further enhance its accessibility and ensure that the most current information is always within reach. Despite the availability of mobile tools, internet resources, and hospital systems, the high workload and numerous distractions in healthcare settings necessitate a more readily accessible solution. An AMS card presents a practical option in this context. Such a card could significantly improve antibiotic prescribing practices and facilitate the streamlined implementation of AMS.

Here are some essential tips that should be considered while designing the AMS Card:

1. The AMS Card should be designed in a simple and attractive manner.
2. The QR link on this card should be a constantly updated link, such as to a 'Google Drive Folder', the Hospital System AMS Folder, or a MicroGuide updated link. Technically, this link will remain the same, but the content it leads to will be frequently updated according to AMS changes.
3. The AMS lead, such as an AMS pharmacist or microbiologist, will be responsible for updating this link and providing the necessary notes for the HCPs regarding any updates in antibiotic prescribing following the hospital's antibiogram results.
4. The card size should be small, potentially the same size as the hospital ID card, to ensure easy handling by HCPs during their daily clinical practice.
5. From an infection control perspective, the AMS Card should be designed to be illuminated, making it suitable for use in ITU and sterile areas within the Trust.
6. The AMS Card could be printed in various sizes, depending on what is most suitable for placement in hospital wards, to ensure easy accessibility.
7. Any updates to the AMS Card should be communicated by the 'Communication Team' or through 'Group Emails' to keep HCPs informed about any changes to the card.

These tips provide an efficient method for accessing AMS guidelines, improving antibiotic prescribing practices. Easily accessible antimicrobial guidelines will help mitigate AMR challenges, save patient lives, and maintain effective AMS implementation. Figure 6.5 shows a preliminary AMS Card design adaptable for various Trusts. This card includes a QR code linking to a secure Google Drive folder, regularly updated to reflect healthcare changes. The card is simple and easily replaceable if lost, with proposed employee details to enhance adherence. The QR code could also link to the hospital's intranet AMS folder or mobile app guidelines, like Microguide. The AMS Card benefits hospitals in middle and low-income countries with limited resources, offering consistent AMS guidance, even in emergencies. The QR code provides access to online AMS resources and educational activities, standardising AMS implementation in acute care settings and promoting effective practices. It can also present the latest antibiogram results, keeping healthcare professionals informed about antimicrobial resistance patterns, HAIs prevalence, sepsis, CDIs, and other infections. Additionally, specific criteria like the CURB-65 score for respiratory infections can be integrated into the QR code, reminding healthcare professionals of these criteria when prescribing antibiotics.

**Figure 6.5.** Draft of AMS card featuring QR code access to AMS resources.


The AMS Card, designed for offline use, requires significant development investment but is especially beneficial in settings with weak network infrastructure, such as low-income countries. It offers a cost-effective solution to digital resource challenges, providing healthcare professionals with immediate access to the latest AMS guidelines. The AMS Card's customisation allows it to fit specific needs and protocols, extending its potential for international use. It serves as a key AMS resource, accessible online and printable for use in resource-limited hospitals, making it both practical and economical. Implementing AMS should start with the AMS roadmap for healthcare professionals and settings, providing a framework for AMS implementation. A dynamic AMS dashboard can help visualise antibiotic prescribing patterns and changes over time. AMS education is crucial for raising awareness and facilitating implementation and sustainability. These initiatives can be integrated into various healthcare systems and tailored to each hospital's needs, promoting effective and robust AMS implementation capable of withstanding crises like the COVID-19 pandemic.

**Development and implementation of proposed antimicrobial stewardship practical tools with AI integration.**

The proposed antimicrobial stewardship tools were meticulously developed through a comprehensive analysis of previous findings, integrating best practices and existing initiatives such as the Start Smart Then Focus toolkit (UKHSA, 2023). Derived from earlier chapters' findings and incorporating elements from platforms like Future NHS, WHO, and the UN, the AMS Dashboard offers a thorough overview of AMS implementation from admission to discharge, identifying incidents and proposing solutions. Unlike existing dashboards, it provides a holistic view of AMS practices (Future NHS, 2023; WHO, 2020; UN, 2019). The AMS Roadmap Framework and Training Programme address both organisational and individual levels, offering practical guidance for healthcare professionals. The AMS Card with a QR Code enhances access to guidelines, providing offline availability and quick reference in clinical situations, supplementing digital tools like the MicroGuide Application (MicroGuide, 2023). These tools ensure effective AMS implementation, addressing diverse needs while integrating dynamic updates and accessible resources.

The AMS roadmap framework involves establishing clear protocols, ensuring institutional commitment, and regularly updating practices based on the latest research. The AMS dynamic interactive dashboard visualises and manages antibiotic prescribing in real time, offering insights into patterns and trends to aid decision-making. The AMS pocket guide, featuring QR codes, ensures easy access to up-to-date guidelines. The AMS educational programmes utilise case studies, simulations, and evidence-based guidelines to train healthcare professionals in AMS application and implementation. Implementation and monitoring involve securing leadership commitment, defining roles, continuously improving strategies based on data, and fostering collaboration among stakeholders.

These tools offer a comprehensive approach, combining advanced tools, accessible guidelines, and targeted education to combat antimicrobial resistance and improve patient outcomes, thereby enhancing stewardship efforts globally. These proposed AMS tools ensure the sustainability of AMS implementation, aligning with the UN Sustainable Development Goals (SDGs), particularly SDG 3, which demands urgent measures to ensure worldwide health and well-being (UN, 2023). Additionally, they are aligned with the research theme of the upcoming UK National Action Plan to confront antimicrobial resistance (2024-2029), aiming to optimise antibiotic prescribing and sustain antimicrobial stewardship implementation (UKHSA, 2023). By integrating these components, the tools not only improve patient care and save lives but also contribute to public health and global efforts to mitigate antimicrobial resistance, ensuring high-quality healthcare standards.

Integrating Artificial Intelligence (AI) into the proposed AMS practical tools can significantly enhance their capabilities and effectiveness. AI can optimise antimicrobial stewardship efforts across various components of the model. Predictive analytics can analyse historical data and predict trends in antimicrobial resistance, aiding the development of more effective protocols and guidelines. AI-driven decision support systems can provide recommendations based on real-time data and evidence-based guidelines. The dynamic interactive dashboard can use algorithms to process and analyse large volumes of data in real time, providing immediate insights into antibiotic prescribing patterns. AI can also detect unusual patterns or anomalies in prescribing practices, indicating inappropriate use or emerging resistance trends, and utilise natural language processing (NLP) to extract and analyse relevant information from electronic health records (EHRs) and clinical notes.

For the antimicrobial stewardship pocket guide, AI-driven chatbots accessible via QR codes can answer questions and provide guidance on antimicrobial use in real time, while AI can offer personalised antimicrobial guidelines based on specific patient data and local resistance patterns. In educational programmes for healthcare professionals, AI-driven adaptive learning platforms can tailor educational content to individual learning paces and needs, and virtual simulations created by AI can provide hands-on practice in a controlled, risk-free environment. Implementation and monitoring can be enhanced by using AI to continuously monitor the performance of AMS programmes, providing real-time feedback and identifying areas for improvement. AI can also predict patient outcomes based on antimicrobial use, helping to refine stewardship strategies and improve patient care.

Practical steps for AI integration include ensuring robust data collection systems to gather high-quality data from various sources, collaborating with AI experts to develop tailored predictive models and decision support algorithms, and ensuring seamless integration of AI tools with existing hospital information systems and EHRs. Comprehensive training for healthcare professionals on using AI tools effectively within the AMS framework, along with ongoing support, is crucial. Continuous improvement should be pursued by regularly updating AI models based on new data and emerging evidence, and refining AI tools based on feedback from healthcare professionals and performance data. By integrating AI into the proposed AMS practical tools, healthcare institutions can significantly enhance their antimicrobial stewardship efforts, leading to better patient outcomes, reduced antimicrobial resistance, and more efficient use of resources.

### 6.1.3. Barriers towards appropriate antibiotic prescribing and AMS implementation.

#### 6.1.3.1. Organisational barriers to effective antimicrobial stewardship implementation.

Firstly, barriers related to the healthcare system significantly impact AMS implementation and antibiotic prescribing. Study 2 (Chapter 4) identified issues such as inappropriate diagnoses at admission, often due to the absence of specific criteria like CURB-65 for CAP. Misdiagnosis, especially during the pandemic, can lead to confusion between viral and bacterial infections, affecting antibiotic prescribing. Raising awareness and education about local antibiotic guidelines and incorporating diagnostic criteria into medical notes or hospital information systems can help mitigate these issues.

Reviewing antibiotics 48-72 hours post-admission is crucial for re-evaluating initially prescribed antibiotics based on investigation results. Study 1 (Chapter 3) and Study 3 (Chapter 5) emphasised the importance of reviewing clinical information, including medical history, medication reconciliation, lab results, and diagnostic tests. Conducting AMS rounds to reassess prescribed antibiotics and implementing necessary interventions are vital for maintaining AMS effectiveness. Inconsistencies between medical history and medication lists in electronic records present another barrier. Regular AMS rounds, preferably weekly, are essential for re-evaluating antibiotic use. Study 3 (Chapter 5) highlighted that limited knowledge of AMS strategies among HCPs could result in irrational antibiotic use. Standardising electronic records to match paper-based files and disseminating outcomes from AMS rounds through antibiotic dashboards can enhance AMS initiatives.

Lack of communication among HCPs, particularly during emergencies or pandemics, significantly hinders appropriate antibiotic prescribing and AMS. Designating an AMS champion, such as an AMS pharmacist or lead, and organising regular MDT meetings can advance AMS implementation and foster collaboration among HCPs, non-clinical staff, and hospital leadership. MDT meetings, as identified in Study 1 (Chapter 3), are instrumental in initiating necessary AMS actions during emergencies.

Technology integration is pivotal for appropriate antibiotic prescribing and AMS. However, technical issues with hospital information systems and online platforms like Zoom and Teams can impact the prescribing process. A robust IT department equipped to handle technical problems is essential. While some HCPs prefer in-person AMS ward rounds, a hybrid approach combining digital and in-person methods might be beneficial during emergencies. Enhanced training and awareness about the significance of technology in AMS practices are needed.

Transitioning between hospital prescribing systems or medicine information systems, such as moving from JAC to the Nerve Centre, requires support from a robust IT team. Educational training sessions familiarising staff with new systems before implementation are crucial. The use of multiple systems within HIS, such as JAC for medicine management, ICE for patient admission, lab tests, and radiological investigations, and Viber for patient discharge, complicates information aggregation. Introducing a unified hospital system could streamline AMS monitoring and practices, making data extraction more efficient.

The optimal period for antibiotic review, identified as 48-72 hours post-admission, underscores the importance of continuous monitoring for sustained AMS implementation. Addressing barriers such as streamlining hospital systems, appointing AMS champions, regular MDT meetings, dedicated AMS ward rounds, and reliable IT support is fundamental for consistent AMS application. Limited time and increased workload during emergencies pose significant challenges. Top management must recognise the expertise of clinical pharmacists and doctors, enabling job delegation. Empowering clinical pharmacists to review antibiotics and monitor patients during AMS rounds can alleviate the burden on doctors, enhance patient healthcare outcomes, and promote the prudent use of antibiotics, thereby mitigating antimicrobial resistance.

#### 6.1.3.2. Healthcare professionals' barriers to appropriate antibiotic prescribing and AMS.

Barriers faced by healthcare professionals towards appropriate antibiotic prescribing include limited knowledge about AMS implementation, as highlighted in Study 3, Chapter 5. This encompasses specific knowledge gaps about the IV-to-oral switch and de-escalation. Additionally, HCPs indicated insufficient knowledge related to "AMS implementation," which impacts their ability to request blood cultures at admission or delay administering inappropriate antibiotics, as evidenced in Study 3, Chapter 5.

The pandemic negatively affected AMS education and training, AMS ward rounds, and antibiotic review (Study 3, Chapter 5). Limited education and training on AMS during COVID-19 correlated with inadequate knowledge, attitudes, and practices regarding AMS. Advanced AMS courses have proven effective and can facilitate AMS implementation, as documented in Study 1, Chapter 3. Active learning activities in AMS education were promising before the pandemic (ACCP, 2018). For instance, educational activities and webinars in the US promoted multidisciplinary collaboration in stewardship activities, and addressed antibiotic allergies (Weston et al., 2013). The AHRQ safety programme's educational components, like 'Building Stewardship: A Team Approach Enhancing Antibiotic Stewardship in Acute Care Hospitals,' effectively emphasised ASPs and their deployment strategies, operational challenges, pharmacodynamics, business models, and electronic surveillance (Weston et al., 2013).

During the pandemic, pharmacists played a crucial role in ASPs, often training as stewardship leaders. Their involvement was essential in improving antibiotic use, demonstrating their capability to co-lead AMS teams effectively (Tamma et al., 2021). Pharmacists' roles in AMS extended beyond traditional duties, including conducting AMS audits, reviewing antibiotics, and updating antimicrobial guidelines to prevent resistance (Ashiru-Oredope et al., 2021).

Evidence from Study 2 (Chapter 4) can guide HCPs in identifying predictors of inappropriate antibiotic prescribing, such as allergies, side effects, comorbidities, and investigations (x-rays and lab tests). Adhering to the PHE ‘Start Smart, Then Focus AMS toolkit’ ensures appropriate antibiotic prescribing, especially for patients with predictors like hypotension, heart failure, dyslipidemia, kidney diseases, liver diseases, and asthma. For example, selecting the most appropriate antibiotic and dosage, considering renal dose adjustments or potential allergies, is crucial. During the pandemic, pharmacists addressed these issues by reviewing antibiotics based on creatinine clearance and recommending appropriate dosages (Study 2, Chapter 4).

An important finding from Study 2, Chapter 4, was that if a patient is allergic to a first-line antibiotic, healthcare professionals should select a suitable second-line antibiotic according to local guidelines. For instance, patients with CAP and a CURB-65 score of 1 allergic to amoxicillin should be given clarithromycin (Bedfordshire, 2020). For HAP, local guidelines recommended administering intravenous co-amoxiclav for early onset if the patient had not received prior antimicrobial treatment and had been admitted for less than five days (Bedfordshire, 2020). Uncertain diagnoses, especially at admission, can significantly affect antibiotic choice, leading to inappropriate prescribing and challenging AMS programme implementation (BSAC, 2018). Study 2 highlighted that unclear diagnoses, particularly for LRTIs, URTIs, and pneumonia, were linked to 72% of inappropriate antibiotic prescribing decisions. The analysis of antibiotic use trends during the COVID-19 pandemic revealed insights into prescribing practices and emphasised the need for adherence to the 'Five Rights of Antibiotic Safety' (IHI, 2019).

Healthcare professionals recognise antimicrobial resistance (AMR) as a significant public health concern and advocate for antibiotic prescribing to follow local guidelines. However, during the pandemic, discrepancies in updating guidelines and reviewing antibiotics led to prolonged durations of antibiotic use and misalignment with the latest recommendations (Study 3, Chapter 5). It is crucial to raise awareness among healthcare professionals that antibiotics should not be prescribed for viral infections. Study 3 (Chapter 5) also noted the importance of effective use of technology, combined with educational training, can improve antibiotic prescribing practices. Raising awareness and training on the significance of technology for both meetings and hospital systems is crucial. The pandemic highlighted the positive impact of technology on AMS implementation, with virtual meetings and innovative technological solutions proving effective (Elshenawy et al., 2023).

### 6.1.4. Strengths and limitations

In this research project, the implementation and measures of antimicrobial stewardship implementation were explored based on literature from the past 20 years. Although it is recognised that the COVID-19 pandemic had a significant effect on AMS activities, evidence of its actual effects is scarce. There is an urgent need for further studies to investigate the AMS implementation PP and DP in acute care settings. It is paramount to obtain empirical data to evaluate the effect of a pandemic on AMS. This will help to draw a plan to prevent and mitigate the effect of a crisis or pandemic on AMS and its impact on AMR. This investigation evaluated AMS implementation in acute care settings both prior to and during the COVID-19 pandemic. It provided an understanding of AMS implementation, including monitoring antibiotic usage and bacterial resistance in conditions such as URTIs and pneumonia during 2019 and 2020.

Given that AMS is a comprehensive hospital programme necessitating collaboration amongst health professionals, its efficacious implementation is essential. Furthermore, this research explored healthcare professionals' knowledge, attitudes, and perceptions related to AMR, antibiotic prescribing, and AMS, thereby offering a comprehensive understanding of AMS practices during the COVID-19 pandemic, as they have never been explored before. Methodological considerations to ensure the integrity of this research and the reliability of the findings were deployed in all studies.

In Study 1 (Chapter 3), the systematic literature review was registered with PROSPERO (CRD42021242388), involving two independent researchers for title and abstract screening, quality assessment, and data extraction. This project was also registered with ISRCTN per WHO criteria (14825813). In Study 2 (Chapter 4), a data extraction tool was developed and validated through consultations with the supervisory team to evaluate AMS implementation using the PHE Toolkit. Both the AMS pharmacist and the research student independently assessed 1% of the sample (five records) for inter-rater reliability, achieving ≥80% agreement, resolving discrepancies through discussion. In Study 3 (Chapter 5), a pilot test involving 20% of the sample (50 out of 240 participants) ensured the survey's validity. Data were analysed using Excel and SPSS software. Consultations with AMS pharmacists ensured face validity, and the survey was reviewed by supervisors for clarity. The expert research team at RPS reviewed the survey for content validity, resulting in revisions. Reliability was assessed using Cronbach's Alpha, revealing scores of 0.832 (Knowledge), 0.890 (AMS Practices), 0.791 (Attitude and Perceptions), and 0.727 (Impact on Antibiotic Prescribing), with an overall reliability score of 0.80, indicating significant internal consistency. Both studies involved consultation with a UH statistician to ensure a representative sample size and accurate statistical analysis.

The results of this research yield an antimicrobial stewardship roadmap, encompassing the Healthcare System Framework: Organisational-Level Antimicrobial Stewardship—from Gap Analysis to Comprehensive Evaluation—and the Healthcare Professional Framework: Individual-Level Antimicrobial Stewardship—Guidance on Application for Potentially Infected Patients. This roadmap offers a structured approach for AMS implementation in acute care environments. Additionally, this research project introduces the antimicrobial stewardship dashboard, comprising two main sections. The first, "Start Smart," is the Initial Empirical Antibiotic Therapy dashboard, providing a comprehensive overview of the hospital's antimicrobial prescribing habits and AMS strategies. This dashboard may encompass patient demographics, primary and secondary health conditions, prevalent antibiotic allergies, the most commonly prescribed antibiotics, intervention methods, and the roles engaged in the antibiotic review process. The second segment, "Then Focus," is the Targeted Antibiotic Therapy dashboard, detailing the targeted antibiotic metrics. This section offers in-depth insights into antibiotic prescribing and AMS strategies related to subsequent rounds of antibiotic treatments in acute care scenarios. The data highlights prevalent bacterial infections, interventions undertaken, antibiotics prescribed upon discharge, and the duration of patient stays.

The proposed AMS Roadmap Training Program is divided into two main outlines: Health Professionals Training and Health System Training. The former is tailored for health professionals and delves deeply into AMR and AMS, covering infection types, microbiology, pharmacology, pharmacokinetics, pharmacodynamics, antimicrobial guidelines, and hands-on AMS implementation and measures. Through case studies and a culminating AMS project, participants' understanding of AMS is assessed. The Health System Training Program emphasises AMS gap analysis, the creation of an action plan, and strategic planning. It underscores the development of actionable AMS practices and the use of AMS dashboards. Both programs, which complement each other, conclude with an AMS project. Their primary goal is to promote HCPs capable of combating AMR and championing AMS. Successful participants are awarded a certificate of completion.

There were several limitations to this study. First, it covered an extended period during which changes in policies and practices could have evolved. For instance, antimicrobial guidelines were amended throughout the COVID-19 pandemic and were continually updated; as a result, AMS practices adapted in line with these changes, both within the study period and subsequently. Additionally, some HCPs, who had been working during the pandemic, had since left the Trust by the time the survey was disseminated. As a result, not all of these HCPs were available to participate in the survey. Second, this research focused on investigating AMS implementation in adults, excluding the paediatric population. Third, the study delved into AMS practices only in acute care settings, other areas, such as primary and community healthcare, were not considered in this research. Lastly, this study centred on antibiotic prescriptions for particular infections, such as upper respiratory tract infections and pneumonia, instead of a broader range of infections. This could have led to different results.

### 6.1.5. Reflection on this research project

The process of reflexivity in research is an ongoing process of reflection by the researcher in relation to the research environment. During a research project, it is critical that the researcher is aware of herself and understands her position within the process and her influence on the research process.

My work experience involved 20 years of experience in pharmacy practice, working in acute care settings. I was a supervisor of the emergency university hospital. I have an American Board of Pharmacy Specialties in Pharmacotherapy with an added qualification in infectious diseases. When I read the UK report of 2016, which projected that 10 million people will be expected to die in 2050 (O'Neill, 2014), and saw patients in critical care infected with bacteria resistant to all antibiotics who subsequently died, my passion for antimicrobials was sparked. I feel responsible about antibiotics. I studied for a two-year certification in antimicrobial stewardship from the SIDP in the US. Additionally, I studied for a two-year Teaching and Learning Certificate from the ACCP. I also completed a four-year study for the American board of healthcare quality & patient safety from the National Association for Healthcare Quality (NAHQ) in the US and a master of clinical pharmacy.

Before the pandemic, I led AMS implementation at the Security Force Hospital, including developing the AMS action plan, guidelines, ward rounds, interprofessional education, diagnostic stewardship, antibiogram, infection prevention and control, and multidisciplinary meetings. Through AMS training and education via the antimicrobial stewardship school, and medicine optimisation which was shared with the CDC AMR Challenge, I gained experience attending ward rounds and a weekly infectious diseases clinic with the AMS lead infectious disease consultant in the hospital's medical department. During this time, I recognised issues related to inappropriate antibiotic prescribing, antimicrobial resistance, AMS implementation, and other related health concerns. It was a unique experience, allowing me to shape my future goals of caring for antimicrobial resistance and pursuing a passion for AMS implementation. From 2016-2021, I had intensive academic experience teaching AMS, clinical research & epidemiology, medicine optimisation, medication therapy management, infection management and pharmacy practice to postgraduate pharmacists, nurses, and doctors.

During the COVID-19 pandemic, I worked in clinical practice pathways at West Hertfordshire Hospitals NHS Trust, at Watford General Hospital. I participated in AMS quality improvement projects to improve antibiotic prescribing using the antibiotic review kit, which was shortlisted for the Antibiotic Guardian Award. I also contributed to a quality improvement project on the role of procalcitonin in antimicrobial prescribing. As director of the Antimicrobial Stewardship School, which was shortlisted for the Antibiotic Guardian Award, I gained additional relevant experience. In comparison, conducting AMS rounds at Watford General Hospital during the pandemic in December 2019. The pandemic significantly disrupted healthcare systems, heightened mortality rates, and affected antibiotic prescribing practices, leading to a pause in numerous AMS activities. Recognising the importance of this issue, I aimed to develop a comprehensive understanding of how COVID-19 has impacted AMS and to enhance preparedness for future emergencies, ultimately safeguarding patients from AMR. I felt responsible for utilising my experience in clinical research and passion for antimicrobial resistance to contribute to AMS knowledge.

To improve my writing, I had intensive sessions with the Academic English Consultation at the UH. They supported me in analysing my writing and learning how to improve it. I had several sessions with Dr Mark Holloway, who taught me how to customise my writing according to the intended audience and publication. For example, writing blog posts for the public or the community should use plain language rather than academic style. I also had sessions with Gloria Richards, who taught me how to write professional emails, and my principal supervisor, Prof. Zoe Aslanpour, who taught me how to structure emails in an organised way to achieve my objectives. This was especially important during the NHS ethics application, where I had to communicate with stakeholders, the Caldicott Guardian in the Trust, the director of R&D, and the REC coordinator.

From Study 1, the systematic literature review, I recognised a significant gap in empirical research on AMS implementation worldwide. The review indicated that although AMS has been a subject of investigation over the past two decades, there is scarce evidence concerning the actual impacts of the COVID-19 pandemic. This highlights an urgent need to examine AMS practices both prior to and during the pandemic. Such recognition motivated me to undertake a prevalence study, estimating the rates of inappropriate antibiotic prescribing PP and DP, in 2019 and 2020 at the Bedfordshire Hospital NHS Foundation Trust. To proceed, I secured ethical approval from the HRA and UH in the UK. This process enlightened me on the ethical considerations vital for research, including the management of identifiable patient information and the secure storage of data.

The prevalence study was conducted at Bedfordshire Hospitals NHS Foundation Trust, which encompasses two hospitals: Luton & Dunstable University Hospital and Bedford Hospital. These institutions provide secondary care services to roughly 400,000 people within the local catchment area, which includes Luton, South Bedfordshire, and parts of Hertfordshire and Buckinghamshire. The hospital has been a foundation trust since 2006. It houses approximately 742 beds, of which 82 are designated for maternity, 18 for critical care, and high dependency beds, in addition to 18 contingency beds spread across 27 wards. Over twelve months, the Trust employed a headcount of 7,982 health professionals, recorded 86,676 inpatient admissions, and 442,113 outpatient attendances. Permission and support for data collection were obtained from the Chief Pharmacist and the pharmacy team at Bedfordshire Hospitals NHS Trust.

This Foundation Trust was chosen for several reasons: it received a 'Good' evaluation from CQC in 2022 (CQC, 2022), it has a sufficiently large population to extract data from 640 patient medical records from

2019 and 2020, and there was an adequate number of HCPs to participate in the survey study. Furthermore, the support from the AMS pharmacist and R&D department was instrumental in facilitating the conduct of the study. The hospital provided a welcoming environment; they granted me an honorary contract for two years, a secure NHS email, and Trust secure email access with a temporary username and password for data collection. I also received professional training on how to access and navigate the hospital system and the medicine management program. My principal supervisor, Prof. Zoe, recommended that I maintain diaries and write everything during the data collection period, which proved invaluable when writing the methods section for Study 2.

I also participated in sessions on SPSS data entry and analysis conducted by the UH Research Development Program (a list of attended courses is found in Appendix 1). As my work required regression analysis, the research team, along with Prof Neil Spencer, recommended a session with Dr Sue Baker. She provided thorough explanations that were essential for conducting the statistical tests and interpreting the data. Additionally, I benefited from valuable sessions in advanced Excel and R Programming with Dr Matt Coates at the De Havilland Campus.

Researchers must ensure the reliability and validity of their data. To this end, the research team and the hospital collaborator from the Trust—an AMS pharmacist—assisted me through various stages of data collection. This included the pilot phase, data entry, data extraction, and the development of the 'Data Extraction Tool.' Their support significantly increased my confidence in the research I conducted. Additionally, in seeking content validity, when I reached out to the RPS, the research team there provided invaluable feedback on the survey questionnaire. The AMS pharmacists for both hospitals within the Trust also offered their expert opinions on the survey alongside my supervisors, contributing to its face validity. Throughout the entire study conducted in the Trust, I requested the AMS pharmacist and the AMS lead, microbiology consultant within the Trust to allow me to attend the AMS ward rounds. This was to gain a deeper understanding of the antibiotic prescribing process, clinical judgment, and AMS implementation. They welcomed me, and I joined them for the AMS multidisciplinary ward rounds in ITU 1 and ITU 2 at Luton & Dunstable Hospital. The experience was impressive and greatly aided my comprehension of the data during the analysis phase, enhancing my understanding of the findings.

One of the most significant challenges I encountered during my retrospective medical records review was accessing the information, as I needed to extract data from 2019 and 2020. Many of the medical records had been archived, requiring me to liaise with IT support to retrieve them. Additionally, a system transition posed another complication; prior to the pandemic, the medicine management system known as JAC was in use but had since been deactivated. I had to contact IT support numerous times—more than ten, in fact—to have the system reactivated for my use. Since the system was obsolete and prone to blocking access, reactivation became a frequent necessity. Extracting data from this system was far from straightforward and was time-consuming, but eventually, I managed to obtain the necessary data. Fortunately, my prior computer skills and experience in data management endowed me with the patience needed to navigate the challenging period of data extraction. Survey questionnaire research is a new skill that I acquired during my PhD. I attended several face-to-face and virtual courses on qualitative research methods, analysis, and survey design both at UH and externally. These courses equipped me with the necessary skills, and I engaged in numerous discussions about qualitative analysis with the research team and my PhD peers. Recognising the value of maintaining diaries and reporting everything from the previous study, I continued this practice throughout my PhD research. During the survey, I observed that many participants were deeply engaged with the research, eager to learn about the findings, and curious about my prior work. They even invited me to join their AMS ward rounds, which made me feel immensely proud and emphasised the preliminary impact of my research. Furthermore, while I was placing the survey posters in the wards, several participants inquired about the survey. I explained to them the aim of the research and how crucial their participation was to address the knowledge gap and explore HCPs' knowledge and perceptions towards antibiotic prescribing and AMS practices during the pandemic.

Initially, while applying for HRA ethical approval, I did not fully recognise the significance of the documents required for the application, such as the Participant Information Sheet (PIS), consent form, invitation letter, and materials designed to attract HCPs and the public. However, once I began conducting the survey study, the importance of these documents became clear. They were instrumental during survey dissemination, and the posters, in particular, served as an effective tool to promote the survey among HCPs within the Trust, being displayed in the wards and on medicine trolleys.

At that point, I recognised the importance of patience during the HRA ethics application process. My initial submission was not accepted; however, after carefully addressing the comments from the first REC committee, I resubmitted to another REC committee. My principal supervisor, Prof. Zoe Aslanpour, conducted two mock sessions to review the documents. Along with my co-supervisor, Dr. Nkiruka Umaru, she provided invaluable feedback that significantly enhanced my application. Her motivation was inspiring, always reminding me that ‘PhD is a learning journey'. The revised submission to the second REC committee in Leicester South eventually led to final approval after one year.

This delay significantly delayed my timelines, necessitating adjustments to my Gantt Chart and delaying the second progression report (Appendix 2). Despite the initial disappointment, once my research commenced at the Foundation Trust, I appreciated the critical role that the REC ethical application played in ensuring the integrity and consistency of my research project. The preparation of these documents proved crucial; for instance, the participant information sheet offered detailed information to help potential participants make an informed decision about their involvement, providing necessary details, including contact information. Moreover, the posters succinctly summarised the research project, aiding its dissemination and enhancing survey response rates. For publication, I aimed to utilise multiple channels. Initially, I registered my systematic literature review with PROSPERO. Subsequently, I registered the study protocol with ISRCTN, aligning it with WHO criteria. This resulted in an invitation to write a blog post for ISRCTN during the WAAW in 2022. Following this, I was invited to submit my research to the ‘Springer

Community' in support of the United Nations 'Sustainable Development Goals', for which I created a visual video summarising my research project.

My passion for the publication and dissemination of my findings and knowledge mobilisation. This self-motivation paid off when 'PMC Public Health', a Springer publication, published my systematic literature review manuscript on the first submission. Additionally, as a member of the 'WHO AMR Community', I had the opportunity to share my systematic review and retrospective review study findings within the WHO AMR Community platform.

Additionally, study 2 has been successfully published in the Frontiers Microbiology Journal, the Journal of Global Antimicrobial Resistance (Elsevier), and the MDPI COVID Journals, as shown on page 6 of the thesis in the 'Research Dissemination' section.

After publishing my work, the Twitter account @ISRCTN, which has 4.1k followers, tweeted a link to my blog post. Additionally, @SN_Authors, with 8.5k followers, and @BioMedCentral, with 76.6k followers; the Elsevier account @IDAdvance, which has 6.4k; the Frontiers account @FrontiersIn, which has 94.1k, and the MDPI account @MDPIopenAccess which has 36.9k followers, all tweeted a link of the published papers. Furthermore, I successfully reviewed a paper for Antimicrobial Stewardship and Healthcare Epidemiology (ASHE), published by Cambridge University Press, and received recognition on the Web of Science for my review. Finally, I am delighted to prepare an educational practice article in the Pharmaceutical Journal, with CPD training, about 'The Contribution of Pharmacists in Antibiotic Review and Stewardship,' featuring case-based learning.

I also tweeted about my study. That was an unforgettable moment. It gave me the encouragement I needed to publish the prevalence study. The publication process taught me the importance of being critical and how to respond to reviewers' comments constructively. I have prepared the second paper of the retrospective study, which will be published in the BMJ journals in the coming days. I also presented poster presentations at several conferences, both nationally and internationally, including in the US, UK, EU, and Saudi Arabia. Throughout my PhD journey, I have published more than ten posters. For a detailed explanation of these presentations, please refer to page 19, 'Research Output' section, and Appendices 5, 15, 22, 28, 38, 39, 45, 47, 51, 53, 61 and 64.

In my first assessment viva, Prof Sam Salek advised me to consider how my PhD could contribute to knowledge and produce tangible products. This concept was new to me; I spent considerable time reflecting on how I could contribute to the body of knowledge. Prof Salek and Prof Zoe Aslanpour advised me to write down every idea and keep it until the completion of my PhD; consequently, I recorded everything. I also discussed these matters with my father, who, throughout my PhD journey, consistently reminded me of the importance of producing a tangible output from my studies. By the end of my PhD, I had developed several vital outputs, including the AMS roadmap, AMS dashboard, and an educational program, all of which were the result of my extensive deliberation and documentation of ideas.

Writing about my father is profoundly emotional for me; this is the first time I've put words to paper about him, and I do so through tears. Sadly, I lost him last year after a valiant battle with malignant pancreatic carcinoma. It's a long story, but in brief, I realise how fortunate I was to have understood all of his medicines, antibiotics, and to have taken an active role in his care. Despite my efforts in maintaining medicine optimisation, he passed away. He was a professor in management at the business school and the first person to encourage me to pursue a PhD. I still remember, four years ago, he questioned the significance of a PhD and its importance in contributing structured, evidence-based research. He was a pillar of strength throughout my journey, even though the difficulties of the ethics application process and the rigours of statistical analysis. After his passing, I was engulfed by depression and sadness. I decided to stop my PhD, and I lost my motivation to continue. The idea of writing this final page of my PhD without him in my life is unimaginable; he was my closest confidant and my most excellent role model. Nevertheless, I am deeply thankful to my supervisors for their support during these challenging times, to my PhD colleagues, and to my loving family, whose steadfast encouragement helped me to see my PhD through to completion. I wish he could be here now, reading this with me, just as he used to do before.

In concluding my PhD journey, I reflect on the profound insights and growth I have experienced. This research not only deepened my understanding of the subject of AMS but also highlighted the importance of selecting the appropriate theoretical framework, research paradigm, and research methodologies to meet the research aims, objectives, and answer the research questions. Despite the challenges, particularly in obtaining ethical approval, my scholarly mindset and commitment to excellence have guided me. As I am planning to contribute these findings to the wider academic community and beyond, I believe that different methods of dissemination are crucial to share the research findings in broader ways, by using a variety of dissemination methods, to include both health professionals and the public. I also believe in the role of technology and AI in fostering AMS implementation and providing evidence-based decision support AMS tools. I am reminded of the journey's significance—advancing knowledge and personal transformation. This thesis is not just the culmination of academic endeavours; it is the beginning of a new evidence-based scholarly life. It emphasises the importance of optimising antibiotic use, ensuring patient safety, and mitigating the threat of antimicrobial resistance to save lives and prepare healthcare professionals and settings for future emergencies or crises.

## 6.2. Future research

Globally, future research should prioritise understanding both the long- and short-term impacts of antimicrobial stewardship, especially its effects on clinical and non-clinical outcomes. This includes its efficacy in mitigating the antimicrobial resistance threat and safeguarding patients' lives. Furthermore, the efficacy of AMS practices and the suitability of AMS implementation across different healthcare settings should be explored.

The AMS survey population should be expanded to encompass hospitalised children. Given that caregivers, typically family members, play a vital role in administering treatment, it's pivotal to educate them about AMR and AMS. This education should be directed not only to children but also to older adults to ensure the correct use of antibiotics post-discharge or in outpatient settings. Furthermore, the perspectives of caregivers on AMR and AMS are invaluable. Therefore, interviews with older patients and their carers about post-discharge antibiotic use should be undertaken to gain a deeper understanding of their views on AMS. An extension of the AMS survey is necessary to explore AMS practices and antibiotic prescribing patterns following the implementation of the AMS programme.

Antimicrobial stewardship should be a cornerstone of the national action plan for AMR. Detailed discussions on AMS implementation and measures are vital to foster broad acceptance and execution of AMS interventions. This national action plan should be reviewed and approved by a local expert panel, incorporating the insights and experiences of diverse healthcare professionals and academics. Continued research is essential to evaluate AMS interventions and their outcomes, such as IV-to-Oral switches, de-escalation, and antibiotic reviews. It's also crucial to determine the most effective methods for promoting their implementation. Furthermore, it's vital to determine which interventions would be indispensable during any upcoming crisis or pandemic.

Future research is pivotal in assessing the impact of AMS education on its practical implementation, as well as its influence on the incidence of AMR in healthcare settings. It's also vital to identify the most effective methods of AMS education in order to increase engagement, enhance the outcomes of AMS education, and sustain the positive effects of this education on clinical practices while mitigating the AMR threat. Additionally, further research should be conducted to evaluate the effectiveness of virtual AMS education compared to traditional in-person or hands-on training.

Finally, evaluating the effectiveness of virtual AMS interventions, such as AMS ward rounds, is crucial to ensure their sustainability, especially during crises, emergencies, or periods of high workload. It's vital to assess the impact of these virtual rounds and identify ways to enhance them.

## 6.3. Recommendations

The recommendations are organised into three levels: healthcare policy, clinical practice, public health, and academic (Faculty of Medicine and Faculty of Pharmacy).

### 6.3.1. Recommendation for healthcare policy

- The antimicrobial stewardship multidisciplinary committee should be established in each Trust to discuss updates regarding AMS implementation, practices, and measures. Additionally, there should be a review of the AMS policy, infection prevention and control, and antibiogram, with subsequent necessary actions taken towards its implementation.
- Antibiograms inform appropriate antibiotic prescribing, ensuring the right antibiotic is given to the right patient at the right dose. They not only offer a visual tool for examining guidance but also present local resistance rates, facilitating a clearer understanding of patient therapy. Furthermore, local guidelines should be regularly updated based on antibiogram results and surveillance reports.
- AMS ward rounds should be established regularly, with tools provided to measure their effectiveness consistently. For instance, the AMS dashboard proposed in Chapter 6 might serve as a visual tool to evaluate AMS implementation and the efficacy of the AMS rounds.
- The principles of antibiotic safety, such as the 'Five Rights of Antibiotics', should be applied. Additionally, other safety communications should specify the roles of various HCP groups.
- A framework, proposed in Chapter 6, might be utilised to engage HCPs and healthcare systems in the process of developing antimicrobial stewardship communications.
- The electronic dissemination of information to HCPs, such as via NHS emails, is essential for enhancing AMS practices. An example of such communication is the outcome of this research, which is documented in the 'Antimicrobial Stewardship Report'. This report was distributed to HCPs at the Trust through the weekly newsletter titled 'Week' (see Appendix 60).
- Training should be provided to enhance the skills of the AMS lead, doctors, pharmacists, and nurses, with a focus on areas such as appropriate antibiotic prescribing and AMS implementation.
- There's also a need for skill mapping and acknowledging the expanded role of healthcare professionals to address the challenges of workload and limited time.
- Professionals should address the challenges of heavy workloads and constrained time.
- Promoting research into AMS implementation and identifying factors leading to inappropriate antibiotic prescribing is crucial.
- The development of a connection interface between secondary and primary care settings is essential.
- Implementing AMS measures in the electronic prescribing system can facilitate the sharing of recent insights and improvements based on AMS metrics.

- Consider conducting an AMS audit using the SSTF toolkit. Currently, UKHSA monitors AMR and reports on antibiotic resistance. Integrating these tools into daily practice is crucial. The proposed AMS Dashboard in Chapter 6 provides a visual tool to track AMS implementation regularly, accommodating seasonal fluctuations or emergencies, such as the COVID-19 pandemic.
- Documentation of patient counselling about the proper use of antibiotics should be enforced, particularly for antibiotics prescribed upon discharge. This ensures the streamline of the 'Five Rights of Antibiotic Safety' even post-discharge.

### 6.3.2. Recommendations for clinical practice

- Hospitals should designate a lead individual or an implementation team to assist in the effective implementation of AMS within the hospital and identify barriers to its introduction. AMS lead should also liaise with PHE, NHS England, and UKHSA to guarantee precise and appropriate communication, contributing to the national UK AMR action plan and surveillance data with AMS implementation insights and metrics.
- Regular antibiotic reviews and weekly AMS rounds should be conducted, especially in high-risk wards, such as ITU(s). Metrics should be established to assess the effectiveness of these rounds. These AMS rounds provide AMS education, leading by example, and raise awareness among HCPs. Outcomes or measures from these AMS rounds should be shared with other HCPs or published to further advocate for AMS implementation. For optimal effectiveness of the AMS rounds, it's recommended that they be a multidisciplinary team led to ensure robust AMS implementation.
- Promote antibiotic reviews after 48-72 hours of admission and again after 5-7 days. Such reviews encourage judicious antibiotic use, stopping unnecessary antibiotics, and advocating for de-escalation. This decreases the use of broad-spectrum antibiotics, reduces the risk of hospital-acquired infections, and lowers the prevalence of other infections, such as CDI.
- Enhance the documentation of AMS interventions, the anticipated duration of antibiotics during hospitalisation, and the accurate diagnosis. For instance, in the case of CAP, it is preferable to note the precise diagnosis rather than simply writing ‘pneumonia’ or ‘LRTIs’. Furthermore, it is advisable to detail the specific criteria for CAP, such as a CURB-65 score of 0, 1, or 2. This ensures the selection of an appropriate antibiotic plan in alignment with local antimicrobial guideline recommendations.
- Develop local policies to improve antibiotic prescribing in line with antibiogram updates and the AMS implementation policy. Also, incorporate toolkits and guidelines that improve prescribing practices, such as the SSTF toolkit from PHE, NICE antimicrobial clinical pathways, and national antimicrobial guidelines.

- Implement innovative, easy-to-access methods to make local antimicrobial guidelines easily accessible to HCPs, especially during daily practice. For instance, employ a unique QR code for each respiratory tract infection or incorporate the guidelines into secure NHS mobile applications, such as Microguide, which necessitates a secure login, and it has to be updated on a regular basis, especially during an emergency or crisis.
- It is recommended to keep updating the local guidelines and frequently update them with any change in the streamlining of the daily clinical practice. These updates can be made available in a digital book, on the Trust's intranet, or in easy-access locations within the Wards.
- Clearly document any antibiotics prescribed in primary care before hospital admission in the system. Prior antibiotic use significantly influences prescribing decisions. For example, if a patient received antibiotics five days before hospital admission, they are more likely to have a hospital-acquired infection rather than a community-acquired one. Recognising this can guide appropriate antibiotic prescribing upon admission, reducing the risk of antimicrobial resistance.
- HCPs should emphasise patient empowerment and public involvement to enhance AMS practices and reduce the threat of AMR.
- An audit for AMS implementation should be conducted to identify and ensure proper antibiotic prescribing, particularly during care transitions.
- Healthcare professionals training in AMS practices should occur regularly, particularly during a crisis or emergency. Additionally, utilise multiple training channels, including HCPs' morning meetings, case-based discussions, online lectures, webinars, and in-person education.
- Internally share the feedback from the annual information about antibiotic prescribing, AMS and AMR in an appealing manner, such as through posters and reports, and make them easily accessible through an electronic newsletter. This approach will help promote AMS implementation and updates.
- Externally, share annual information and results from AMR quality improvement projects with national initiatives such as the Antibiotic Guardian Award, conferences, publications, and reports.

### 6.3.3. Recommendations for pharmacists

- Actively collaborate with healthcare professionals and the AMS team in developing, reviewing, and updating antimicrobial guidelines to aid in preventing antimicrobial resistance in acute care settings.
- Extend roles in AMS beyond traditional duties by understanding and implementing strategies such as formulary restriction, antibiotic review, and prospective audits with feedback.
- Enhance AMS education and contribute to the development of antimicrobial guidelines, enabling the devising of tactical AMS strategies and supporting organisations in AMS implementation and AMR reduction.

- Support and alleviate the burden on emergency departments and intensive care units by aiding medical staff in developing antimicrobial guidelines and practice pathways.
- Diligently follow up on antibiotic dosages and microbiologic culture results, making informed decisions about de-escalating or stopping antibiotics.
- Monitor and prevent antibiotic-related allergies, adverse drug reactions, and drug-drug interactions, ensuring patient safety.
- Contribute to reducing unnecessary antimicrobial use while maintaining judicious use.
- Utilise surveillance data effectively to monitor patients' clinical information and verify ongoing treatments.
- Provide clinical advice to optimise antimicrobial prescriptions and usage.
- Monitor compliance with antimicrobial treatment guidelines and strengthen collaboration between healthcare teams.
- Address antimicrobial resistance by using antibiograms, revising guidelines to minimise misuse, and ensuring the continued efficacy and safety of existing antimicrobials.
- Regularly review prescription appropriateness and advise patients on correct antimicrobial usage to prevent misuse.
- Educate patients on effective antimicrobial use, provide guidance on self-care, explain how antimicrobials work, and distribute informative leaflets.
- Promote the best use of AMS resources, such as COVID-19 and influenza vaccination.
- Pledge to become an Antibiotic Guardian to support better antibiotic use.
- Actively participate in local AMS groups/networks and contribute to AMS initiatives.
- Conduct regular audits of AMS activities using guides for clinical audits in pharmacy.
- Ensure and maintain high standards of hand hygiene in the workplace, including the use of alcohol-based hand rubs and adherence to handwashing guidelines.

### 6.3.4. Recommendations for academia

- Antimicrobial stewardship should be incorporated into the current undergraduate curriculum for medicine, pharmacy, and nursing. Additionally, the concepts of antimicrobial utilisation and resistance surveillance should be emphasised.
- Interprofessional education at the undergraduate level should be promoted among HCPs, encompassing doctors, pharmacists, and possibly nurses, as well as those in pharmacy technician schools and diploma programs.
- Students should also be familiarised with these communications during their work-based placement experiences.
- An academic curriculum involving Antimicrobial Stewardship should also be considered for post-graduate students and continuing professional development.

- As there are current aspirations to establish registration programs for the pharmacy profession, it's pivotal to include an antimicrobial stewardship-focused registration program.
- Promote a lifelong learning mission in AMS among doctors, pharmacists, and nurses throughout their professional careers.
- Encourage AMS leads to deepen their understanding of AMS measures and metrics, such as AMS dashboards and key performance indicators (KPIs), to facilitate benchmarking both inter-hospital and nationally.
- AMS leads should also be familiarised with project management, quality improvement projects, and related tools. This will promote continuous improvement in antibiotic prescribing and AMS, ultimately reducing the threat of AMR.

### 6.3.5. Recommendations for public

- Public health campaigns should raise awareness about the importance of bringing antibiotic medicines when admitted to the hospital and the risks of taking unnecessary antibiotics, which can endanger both the individual and their family. They should emphasise the need to follow HCPs advice on antibiotic use and highlight that proper antibiotic use prevents antimicrobial resistance. Additionally, campaigns should clarify that antibiotics do not treat viral infections like flu or COVID-19 and encourage online health information-seeking behaviour. Promoting preventive measures such as vaccination and hand hygiene is also essential.
- Public health campaigns concerning antibiotics should operate year-round, not just during specific times like the WHO World Antibiotic Awareness Week (WAAW) from 18-24 November each year. These antibiotic campaigns should also adapt according to seasonal changes and emergencies. For example, in October, it's advisable to heighten campaigns that focus on vaccination, highlight that antibiotics don't combat viruses, and advocate for safety measures.
- Enhance and cultivate advocacy skills among the public to improve participation and drive action against AMR. Whether as patients or caregivers, HCPs play a crucial role in championing the proper use of antimicrobial medicines. By safeguarding these medicines, a more sustainable future is secured for all, particularly for those most vulnerable to untreatable infections.
- Ensure ongoing public and patient involvement in research studies. For instance, prior to initiating the research, the study protocol was submitted to representatives from the Citizens Senate, a patient care organisation with good representation from many older individuals.
- Provide attractive materials, such as posters and videos in patient visiting areas within healthcare systems to raise awareness about AMR and AMS. Utilising storytelling can be an effective method to promote public engagement.
- Public information can also be incorporated into Trust websites, especially in the inpatient and visitor sections, to enhance public engagement.

## 6.4. Conclusion

This research provided invaluable insights into antimicrobial stewardship implementation in acute care settings before and during the COVID-19 pandemic. Key AMS strategies that showed promising outcomes during the pandemic were ‘prospective audits with feedback’ and ‘antibiotic review’. Essential strategies such as ‘guidelines and clinical pathways’ and ‘education’ were crucial to maintaining AMS best practices. The integration of ‘computerised decision support systems’ and ‘surveillance’ is necessary for sustained AMS implementation. Maintaining appropriate antibiotic prescribing requires considering factors like antibiotic allergy and safety. Insights into HCPs’ knowledge, attitudes, and perceptions towards antimicrobial resistance, prescribing, and AMS were investigated, showing that interprofessional collaboration and continuous AMS education and training are vital for sustainable AMS practices. However, limited AMS knowledge and attitudes among healthcare professionals pose challenges to effective AMS interventions. The study highlighted that understanding the factors influencing knowledge, attitudes, and perceptions, including age, gender, professional background, and experience, is crucial. The absence of robust AMS educational programmes intensifies the AMR challenge, necessitating effective educational initiatives. Healthcare system facilitators like electronic prescribing, decision support tools, and educational resources are essential for successful AMS implementation.

The research emphasises the importance of regular AMS implementation and proposes the AMS roadmap and dashboard as structured tools for effective AMS practices. Future research should evaluate AMS interventions and education techniques, with public campaigns raising AMR and AMS awareness. Collaborative efforts among policymakers, healthcare systems, professionals, and the public are critical to ensure prudent antibiotic use and curb AMR. A paradigm shift is needed in the perception of pharmacists' roles in co-leading AMS implementation. Pharmacists should utilise their expertise to optimise antibiotic prescribing, reduce AMR, and improve patient outcomes. They require comprehensive AMS training, guidance on using dynamic dashboards, and easy access to AMS policies and guidelines through tools like the AMS card. This positions pharmacists as leaders in AMS, especially in the post-COVID-19 world, emphasising their role in educating healthcare professionals and the public on antimicrobial resistance. Their expertise is essential for sustained AMS efforts, appropriate antibiotic use, and ultimately improving global health, public health, patient safety, and quality of life. Implementing sustainable AMS practices and using dynamic dashboards to detect any incidents will promote the sustainability of AMS and fight the AMR threat, ultimately saving patients' lives.

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# Appendices

# Appendices

**Appendix 1.** Training and Development

The PhD student attended a series of sessions in the Research and Development (RDP) at the UH De-Havilland Campus in data analysis using Excel, SPSS, and R Programming. There is also a session about ‘Build a Research Website’, which helps the researcher to do a website for the research project (Appendix 1).

| Date | Session |
|---|---|
| 30/11/2020 | The WHO Webinar of the Impact of COVID-19 and Antimicrobial Stewardship |
| 20/01/2021 | Writing for, and submitting to, a Journal |
| 21/01/2021 | Inferential Statistics |
| 25/01/2021 | Research Cycle and Writing a Manuscript |
| 27/01/2021 | Systematic Review Critical Appraisal |
| 28/01/2021 | Developing your impact plan |
| 28/01/2021 | How to Cope with Stress |
| 18/02/2021 | COVID-19 and Antimicrobial Stewardship |
| 24/02/2021 | Leading creatively across the NHS in 2021 |
| 27/02/2021 | Project Management NHS Elect Training |
| 15/03/2021 | Healthcare Cultural Intelligence NHS Course |
| 17/03/2021 | Qualitative Data Analysis: Methods and Techniques |
| 17/03/2021 | CVs, Application Forms and Personal Statements |
| 24/03/2021 | Reference Management (Endnote, Mendeley and Zotero) |
| 25/03/2021 | Research Data Management\| Working with Supervisors |
| 25/03/2021 | Writers Block &How to Overcome It |
| 30/03/2021 | How to give a presentation |
| 15/07/2021 | Introduction to Office 365 for UH Researchers |
| 08/09/2021 | The British PhD: some key steps to success |
| 09/09/2021 | Research Data Management |
| 09/09/2021 | Qualitative and Quantitative Research Methods |
| 10/09/2021 | Supporting your well being |
| 10/09/2021 | The Challenges of your research |
| 15/09/2021 | Critical Thinking |
| 15/09/2021 | Raising the visibility of your research |
| 16/09/2021 | Critical Reading & Writing |
| 16/09/2021 | The Writer’s Block |

| | |
|---|---|
| 17/09/2021 | Conceptual Frameworks and concept mapping |
| 04/11/2021 | A Guide to Applying for External Research Funding |
| 30/11/2021 | Lean thinking methodology |
| 01/12/2021 | Quality Improvement projects |
| 07/12/2021 | Compassionate leadership |
| 10/02/2022 | Critical Reading & Writing |
| 10/03/2022 | Technical Writing Course |
| 14/03/2022 | Build a Research Website in Under 3 hours |
| 14/03/2022 | Social Media Bootcamp: Sharing and Connecting |
| 24/05/2022 | Conservational Analysis |
| 04/07/2022 | 4D research workshop |
| 06/07/2022 | 101: what, why and how research podcasting |
| 06/10/2022 | Introduction to Excel and SPSS |
| 03/11/2022 | Survey Design & Analysis 1: Collecting, Summarising & Analysing Survey Data No.1 |
| 09/11/2022 | Quantitative Data Analysis 1: Hypothesis Testing, Sample Size & Power No.1 (SPSS and Excel) |
| 23/11/2022 | Quantitative Data Analysis 2: Correlation & Regression Methods (SPSS and Excel) |
| 24/11/2022 | ANOVA using R Programming |
| 24/11/2022 | Rapid Reading |
| 30/11/2022 | Maximise your Memory |
| 30/11/2022 | Using Multiple Qualitative and Visual Methods in Research |
| 01/12/2022 | Getting to Know R No.1 |
| 08/12/2022 | Data Analysis in R No.2 |

In the second study, the PhD student has to extract data from 640 patient medical records. The PhD student completed the following modules at the Trust:

1. **Evolve prescribing system:** The researcher completed the training module of Evolve at L&D hospital.
2. **JAC medicines management system:** The researcher completed the training module of JAC at L&D hospital.
3. **Interactive Connectivity Establishment (ICE) system:** The training modules include:

- ICE Basic Online Training Module
- ICE Electronic Discharge Letter Training Module
- ICE MRSA Training Module

**Appendix 2**. PhD Research Project Gantt Chart (2020-2024): [Access the Complete Chart Here]

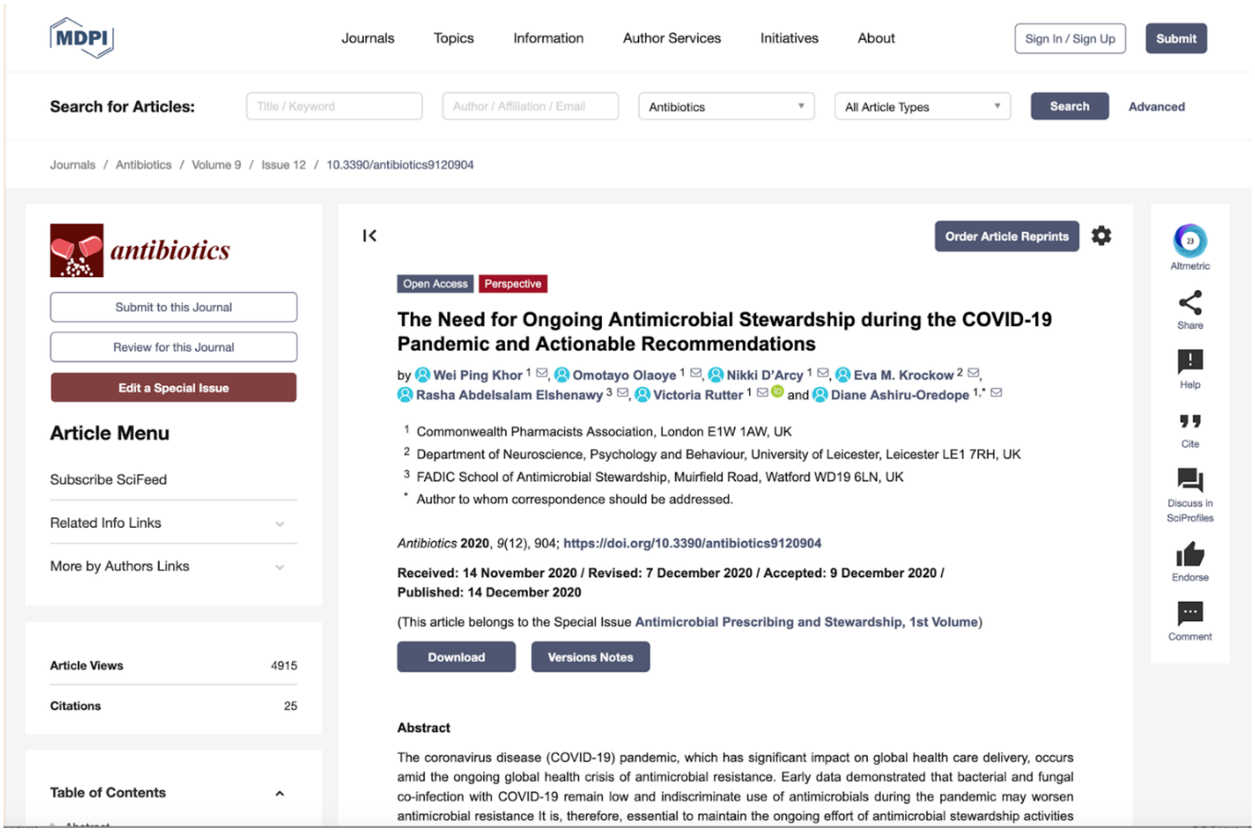
# GANTT CHART for 2020 - 2024

**Research Project: Investigating the Antimicrobial Stewardship Before and During the COVID-19 Pandemic in Acute Care Setting**

| Task name | Stard date | End date | Progress |
|---|---|---|---|
| **First Study: Systematic Literature Review** | 1/11/2020 | 30/8/2021 | 100% |
| Systematic Review Registeration in Prospero | 1/11/2020 | 30/3/2021 | 100% |
| Writing the Fisrt Assessment Report | 30/3/2021 | 30/7/2021 | 100% |
| Initial Registeration Report | 30/7/2021 | 30/8/2021 | 100% |
| BMC Journal Submission | 1/10/2021 | 4/1/2023 | 100% |
| Global Pharmacist Role in AMS Manuscript & Publication | 1/7/2022 | 30/8/2022 | 100% |
| Prepare the Research Project Protocol | 1/10/2021 | 30/5/2022 | 100% |
| HRA Ethics Application First Submission | 30/9/2021 | 10/3/2022 | 100% |
| HRA Ethics Application Second Submission | 30/9/2021 | 10/10/2022 | 100% |
| **Second Study: Retrospective Medical Record Review** | 1/8/2021 | 1/9/2023 | 100% |
| Mock Second Progression Report | 19/1/2023 | 19/1/2023 | 100% |
| Second Progression Report | 19/1/2023 | 26/1/2023 | 100% |
| Data Extraction for Pilot Test | 1/1/2023 | 30/3/2023 | 100% |
| Pilot Test: Validity and Reliability | 1/3/2023 | 30/3/2023 | 100% |
| Review Pilot Tesr Results with Supervisory Team | 30/3/2023 | 15/4/2023 | 100% |
| Communicate with the IT support to Solve the Technical Issues | 15/4/2023 | 15/5/2023 | 100% |
| Complete Data Extraction | 1/1/2023 | 30/8/2023 | 100% |
| Data Cleaning | 5/1/2023 | 20/3/2023 | 100% |
| Data Anonymisation & Transfer to UH Secure System | 1/2/2023 | 2/2/2023 | 100% |
| Data Analysis using Excel, SPSS and R Programming | 10/3/2023 | 7/6/2023 | 100% |
| Results Finding | 3/4/2023 | 1/7/2023 | 100% |
| Review the Findings with Supervisory Team | 1/5/2023 | 1/6/2023 | 100% |
| Write Study 2, Chapter 4 of the theisis | 1/6/2023 | 1/8/2023 | 100% |
| Preparing Manuscript for Publication | 8/4/2023 | 29/5/2023 | 100% |
| **Third Study: Prospective Survey Questionnaire Study** | 14/4/2023 | 21/10/2023 | 100% |
| Send Ethics Approval to R&D | 14/6/2023 | 21/6/2023 | 100% |
| Review the PIS, Invitation Letter, Survey Questionnaire with R& | 14/6/2023 | 1/7/2023 | 100% |
| Send the Final Documents to R&D | 7/7/2023 | 10/7/2023 | 100% |
| Disseminate the Survey to HCPs at Bedfordshire Hospitals NHS T | 14/6/2022 | 5/9/2023 | 100% |
| Pilot Test: Validity and Reliability | 1/8/2023 | 20/8/2023 | 100% |
| Review Pilot Test Results with Supervisory Team | 25/8/2023 | 30/8/2023 | 100% |
| Re-send a Reminder Email with the Survey Link to Increase Resp | 1/9/2022 | 6/9/2023 | 100% |
| Extract the Response Data for Cleaning and Analysis | 10/9/2023 | 15/10/2023 | 100% |
| Results Finding and Analysis using Excel and SPSS | 10/9/2023 | 30/10/2023 | 100% |
| Review the Findings with Supervisory Team | 7/9/2023 | 18/9/2023 | 100% |
| Write Study 3, Chapter 5 of the Thesis | 18/9/2023 | 18/10/2023 | 100% |
| Preparing Manuscript for Publication | 30/9/2023 | 30/12/2023 | 100% |
| Writing up the Final Thesis | 1/2/2022 | 30/10/2023 | 100% |
| Review up the Final Thesis | 1/9/2023 | 1/12/2023 | 100% |
| Submit the Final Thesis | 1/12/2023 | 1/1/2024 | 100% |
| Preparing Manuscript for Publication | 1/3/2021 | 1/1/2024 | 100% |
| Final Dissertation | 20/3/2024 | 20/4/2023 | 100% |

| 2020 | | 2021 | | | | 2022 | | | | 2023 | | | | | | | | | | | | 2024 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Nov | Dec | Jan - Mar | Apr - June | Jul - Sep | Oct - Dec | Jan - Mar | Apr - June | Jul - Sep | Oct - Dec | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | Jan | Feb | Mar | Apr |

**Appendix 3.** The Need for Ongoing Antimicrobial Stewardship during the COVID-19 Pandemic and Actionable Recommendations. Published November 2020. Click Here to View the Full Article.



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**The Need for Ongoing Antimicrobial Stewardship during the COVID-19 Pandemic and Actionable Recommendations**

by Wei Ping Khor [1], Omotayo Olaoye [1], Nikki D'Arcy [1], Eva M. Krockow [2], Rasha Abdelsalam Elshenawy [3], Victoria Rutter [1] and Diane Ashiru-Oredope [1,*]

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*Antibiotics* **2020**, *9*(12), 904; https://doi.org/10.3390/antibiotics9120904

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(This article belongs to the Special Issue Antimicrobial Prescribing and Stewardship, 1st Volume)

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**Abstract**

The coronavirus disease (COVID-19) pandemic, which has significant impact on global health care delivery, occurs amid the ongoing global health crisis of antimicrobial resistance. Early data demonstrated that bacterial and fungal co-infection with COVID-19 remain low and indiscriminate use of antimicrobials during the pandemic may worsen antimicrobial resistance It is, therefore, essential to maintain the ongoing effort of antimicrobial stewardship activities

**Appendix 4.** Systematic Review Prospero Registration: Exploring Antimicrobial Stewardship Pre and During COVID-19 Pandemic, January 2021. View the Full Link Here.

NIHR | National Institute for Health and Care Research

**PROSPERO**
**International prospective register of systematic reviews**

Print | PDF

**An investigation into the effectiveness of antimicrobial stewardship during a pandemic- COVID-19 in acute care setting**

*Rasha Abdelsalam Elshenawy, Nkiruka Umaru, Dr Amal Bandar Alharbi, Zoe Aslanpour*

### Citation

Rasha Abdelsalam Elshenawy, Nkiruka Umaru, Dr Amal Bandar Alharbi, Zoe Aslanpour. An investigation into the effectiveness of antimicrobial stewardship during a pandemic- COVID-19 in acute care setting. PROSPERO 2021 CRD42021242388 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021242388

### Review question

1. What strategies have been employed for effective antibiotic utilization/antimicrobial stewardship during pandemics?
2. What challenges have arisen in the use of antibiotics due to pandemics?
3. What antibacterial stewardship strategies have been employed in the acute care setting during the COVID-19 pandemic?
4. What antibacterial stewardship strategies can be adapted for use in acute care settings during pandemics?

### Searches [1 change]

Firstly, rapid reviews in the PROSPERO were conducted for previously accepted systematic reviews, using different search terms that were used to carry out database searches for published articles from 2007 to March 2021. Then, the first search was completed on MEDLINE, using a comprehensive list of search terms, and this search was then amended or modified in the subsequent databases depending on the subject headings and keywords and their synonyms identified in the databases with more relevant and related keywords. A combination of keywords (searching the title and abstract) and index terms, as well as their synonyms where applicable, were used depending on the database. Spelling variations for different search terms were also employed. then search continued using the title field of the following databases: AMED (Allied and Complementary data Medicine); EMBASE; Embase classic; Global Health; HMIC (Health Management Information Consortium); International Pharmacutical Abstracts; Health and Psychosocial Instruments; PsycEXTRA; PsycINFO; Maternity & Infant Care Database (MIDIRS); PubMed; Scopus; Web of Science; CINAHL PLUS; OpenGrey. References of related publications were searched, and references of the included studies were also searched until no more relevant study could be retrieved.

### Types of study to be included

RCTs, non-randomized trials, CBA studies, interrupted time series designs, case–control studies and cohort studies.

### Condition or domain being studied

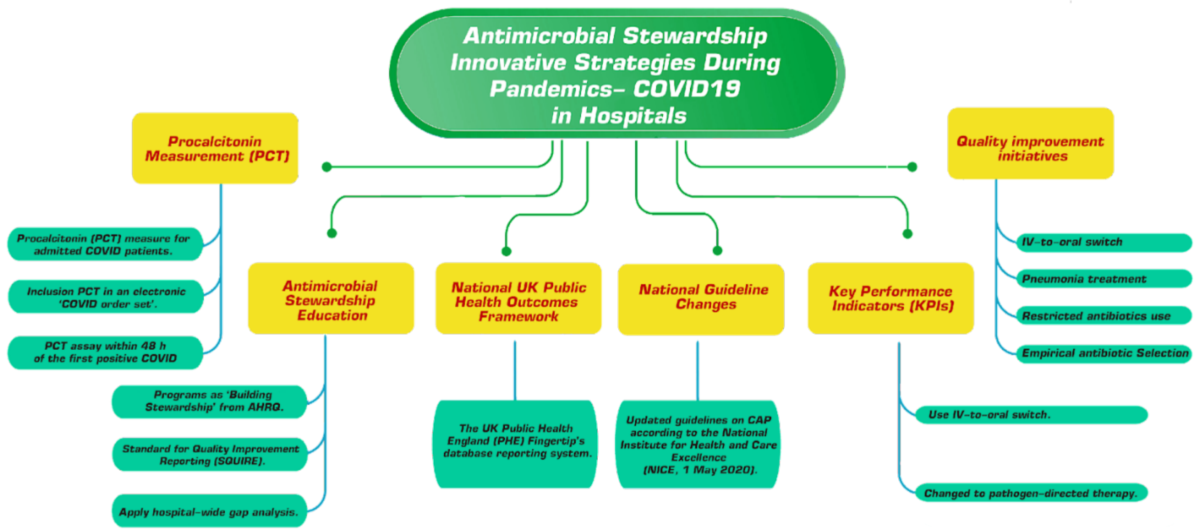
This systematic review aims to identify and describe the current evidence base of the effectiveness of antimicrobial stewardship strategies in acute care hospitals during a pandemic- - systematic review of antimicrobials—which have been utilised to ensure the (i) timely review of IV antibiotics; and subsequently (ii) timely IVOST; and (iii) the optimization of the duration of oral and IV antibiotics, it will be conducted at three different baseline times (pre-pandemics, during pandemics, and after the second wave of COVID-19 pandemics).

### Participants/population

COVID19 patients' use of antibiotics.

**Appendix 5:** Behavior Change Strategies to Influence Antimicrobial Stewardship During COVID-19 Pandemic in acute care settings. LMS Conference Poster Presentation: June 2021. [Access from this link.]

**Appendix 6:** Innovative Strategies for Antimicrobial Stewardship During COVID-19 (Systematic Review).



**Appendix 7.** The systematic review of the search terms in different databases.

| Database | *Search term* |
|---|---|
| **PubMed** | *((((((((((((((((antimicrobial stewardship[Title/Abstract]) OR ("antimicrobial utilization"[Title/Abstract])) OR ("antimicrobial use"[Title/Abstract])) OR ("antimicrobial stewardship strategies"[Title/Abstract])) OR ("antibiotic metrics"[Title/Abstract])) OR ("antimicrobial stewardship intervention"[Title/Abstract])) OR ("antimicrobial stewardship outcomes"[Title/Abstract])) OR ("antibiotic use"[Title/Abstract])) AND ("COVID19"[Title/Abstract])) OR ("coronavirus"[Title/Abstract])) OR ("SARS CoV2"[Title/Abstract])) OR ("severe acute respiratory infection"[Title/Abstract])) OR ("pandemic"[Title/Abstract])) AND ("antimicrobial resistance"[Title/Abstract])) OR ("antibiotic management"[Title/Abstract])) OR ("acute care settings"[Title/Abstract])) OR ("hospitals"[Title/Abstract])) Sorted by: best match* |
| **Scopus** | *( TITLE-ABS-KEY ( "antimicrobial stewardship" or "antimicrobial utilization" or "antimicrobial use" or "antimicrobial stewardship strategies" or "metrics" or "intervention" or "antibiotic use" and "COVID-19" or COVID19" or "coronavirus" or "SARS-CoV-2" or "severe acute respiratory infection" or "pandemic" and "antimicrobial resistance" or "antibiotic management" or "acute-care settings" or "hospitals" ) AND TITLE-ABS-KEY ( hospital OR hospitalized OR admitted OR admissions OR "secondary care" OR hospitalization ) ) AND ( LIMIT-TO ( LANGUAGE , "English" ) )* |
| **CINHAL PLUS** | *"Antimicrobial stewardship" OR "antimicrobial utilization" OR "antimicrobial use" OR "antimicrobial stewardship strategies" OR "antibiotic metrics" OR "antimicrobial stewardship intervention" OR "antimicrobial stewardship outcomes" OR "antibiotic use" AND "COVID19" OR "coronavirus" OR "SARS CoV2" OR "severe acute respiratory infection" OR "pandemic" AND "antimicrobial resistance" OR "antibiotic management" OR "acute care settings" OR "hospitals"* |
| **All OVID journals, PsycINFO and Web of Science** | *(("antimicrobial stewardship" or "antimicrobial utilization" or "antimicrobial use" or "antimicrobial stewardship strategies" or "metrics" or "intervention" "antibiotic use" and ("COVID-19" or COVID19" or "coronavirus" or "SARS-CoV-2" or "severe acute respiratory infection" or "pandemic") and ("antimicrobial resistance" or "antibiotic management" and "acute-care settings" or "hospitals"))* |
| **OpenGrey** | *""antimicrobial stewardship" OR "antimicrobial utilization" OR "antimicrobial use" OR "antimicrobial stewardship strategies" OR "antibiotic metrics" OR "antimicrobial stewardship intervention" OR "antimicrobial stewardship outcomes" OR "antibiotic use" AND "COVID19" OR "coronavirus" OR "SARS CoV2" OR "severe acute respiratory infection" OR "pandemic" AND "antimicrobial resistance" OR "antibiotic management" OR "acute care settings" OR "hospitals" AND admissions OR Hospital* OR hospital* OR admitted lang:"en"* |

**Appendix 8.** Antimicrobial Stewardship Core and Supplemental Strategies.

| **Core Strategies** | **Supplemental Strategies** |
|---|---|
| Formulary restrictions and pre-authorization | Streamlining / timely de-escalation of therapy |
| Prospective audit with feedback | Dose optimisation |
| Multidisciplinary stewardship team | Parenteral to oral conversion |
| | Guidelines and clinical pathways |
| | Antimicrobial order forms |
| | Education |
| | Computerized decision support, surveillance |
| | Laboratory surveillance and feedback |

**Appendix 9.** Definition of some of the AMS strategies.

| Intervention/ Strategies | Description |
|---|---|
| **Formulary restriction** | Antibiotics may be prescribed only:<br>● For specific approved clinical indications<br>● By certain physicians (i.e., infectious diseases specialists) |
| **Pre-authorisation** | Permission (from an ASP team member or infectious diseases specialist) is required for the release of certain antibiotics. Often implemented together with formulary restrictions. |
| **Prospective audit and feedback** | Case review by trained ASP team member and feedback of recommendations if reviewed antibiotics are deemed to be inappropriately prescribed. |
| **Clinical guidelines** | Treatment protocols for various infections – should be institution-specific |
| **Clinical decision support systems** | Information technology systems for improving antibiotic prescription. Requires existing electronic records and electronic prescribing system to be effective |
| **Microbiology laboratory susceptibility reporting** | Selective reporting of susceptibility profiles for positive cultures may dramatically alter prescribing patterns of physicians |

**Appendix 10.** AMS Strategies and their related outcomes.

| Strategy | Evidence Support Outcomes |
|---|---|
| Formulary restriction | Clinical Outcome<br>Economic Outcome<br>Resistance Outcome |
| Formulary review/streamlining | Clinical Outcome |
| General antimicrobial order forms | Clinical Outcome |
| Identification of inappropriate pathogen/antimicrobial combinations (bug-drug mismatch | Resistance Outcome |
| Improved rapid diagnostics | Clinical Outcome<br>Economic Outcome<br>Resistance Outcome |
| Intravenous to oral conversion | Clinical Outcome<br>Economic Outcome<br>Resistance Outcome |
| Prescriber education | Clinical Outcome<br>Economic Outcome<br>Resistance Outcome |
| Preventing treatment of non-infectious conditions | Resistance Outcome |
| Promotion of timely and appropriate microbiologic sampling | Resistance Outcome |
| Prospective audit with intervention and feedback | Clinical Outcome<br>Economic Outcome<br>Resistance Outcome |
| Scheduled antimicrobial reassessments ("antibiotic time-outs") | Economic Outcome<br>Resistance Outcome |
| Strategic microbiology results reporting | Resistance Outcome |
| Surgical antibiotic prophylaxis optimization | Clinical Outcome |
| Systematic antibiotic allergy verification | Clinical Outcome |
| Targeted review of patients with Clostridium difficile infection | Clinical Outcome<br>Resistance Outcome |
| Targeted review of patients with bacteremia/fungemia | Clinical Outcome<br>Resistance Outcome |
| Targeted review of therapeutic duplication | Economic Outcome |
| Therapeutic drug monitoring (with feedback) | Clinical Outcome |

**Appendix 11.** AMS measures/metrics Example

| **Metric** | **Definition** | **Example** |
|---|---|---|
| Outcome Measures (Antimicrobial Utilization Measures and Antimicrobial Resistance Measures) | | |
| Grams of antimicrobials | Grams of antimicrobial based on acquisition (purchased), dispensed, or administered over a defined time | Measure the grams of antimicrobials in three different baselines (pre-, during, after wave1 and wave 2 of pandemics |
| Antimicrobial Expenditures | Antimicrobial costs can be based on dispensed or administered over a defined time<br>Costs can be expressed as absolute £ value, percent of total (dispensed or administered) and/or per patient-days<br>Antimicrobials can be tracked monthly hospital wide, for specific clinical services (e.g., ICU), classes of antimicrobials (e.g., fluoroquinolones), individual drugs (e.g., linezolid), or types of infections/indications (e.g. ventilator associated pneumonia) | For example, Pharmacy drug budget of £3,000,000 Antimicrobial acquisition costs £750,000 (25% of budget)<br>Cost savings (percent reduction in antimicrobial costs):<br>a) overall antibiotic acquisition costs<br>During: £750,000<br>Post COVID: $675,000<br>Absolute decrease of £75,000, equals 10% reduction<br>b) ICU antibiotic acquisition costs<br>During pandemics: £100,000 (patient days = 2000, $50/patient-day)<br>Pre: £75,000 (patient days = 2000, £37.50/patient-day) Absolute decrease of $25,000, equivalent to a reduction of $12.50/patient-day |

| | | |
|---|---|---|
| Defined Daily Dose (DDD) | "The assumed average maintenance dose per day for a drug used for its main indication in adults" as specified by the World Health Organization (WHO). (e.g., Levofloxacin = 500mg daily)<br><br>DDD are often standardized to 1000 patient days (DDD/1000 patient days) to allow comparison of antibiotic use during pandemics and before it. | Refer to the WHO-approved Defined Daily Dose values<br><br>1 levofloxacin DDD = 0.5 g Rx: Levofloxacin 500mg po od x 7 days DDD = (0.5g dose / 0.5g DDD) x 7d = 1 DDD x 7d = 7 DDD<br><br>Rx: Levofloxacin 750mg po od x 7 days DDD = (0.75g dose / 0.5g DDD) x 7d = 1.5 DDD x 7d = 10.5 DDD Rx: Levofloxacin 750mg po q48h x 7 days DDD = (0.75g/0.5g DDD) x 4 (# days on which patient received a dose) = 6 DDD<br><br>Pre pandemics: hospital dispensed 13,000 grams of meropenem, WHO DDD for meropenem: 2 g = 6500 DDD (13,000 / 2) If 391,116 occupied bed days after pandemics then 6500 DDD / 391,116 X 1000 = 16.6 DDD / 1000 patient days |
| Days of Therapy (DOT) | The number of days that a patient receives an antimicrobial agent (regardless of dose). Any dose of an antibiotic that is received during a 24-hour period represents 1 DOT. The DOT for a given patient on multiple antibiotics will be the sum of DOT for each antibiotic that the patient is receiving. DOT is often standardized to 1000 patient days (DOT/1000 patient days) to allow | Rx: Levofloxacin 500mg po od x 7 days DOT = 1 DOT x 7d = 7 DOT<br><br>Rx: Levofloxacin 750mg po od x 7 days DOT = 1 DOT x 7d = 7 DOT<br><br>Rx: Levofloxacin 750mg po q48h x 7days = 4 DOT<br><br>Rx: Cefazolin 2 g q8h iv X 1 day = 1 DOT<br><br>Rx: Cefazolin 1 g iv X 1 dose = 1 DOT<br><br>Rx: Levofloxacin 750mg po od x 7 days + Vancomycin 1g iv q12h x 7 days:<br><br>DOT Levofloxacin = 1 DOT x 7d = 7 DOT<br><br>DOT Vancomycin = 1 DOT x 7d = 7 DOT<br><br>Total DOT = 14 DOT |

| | | |
|---|---|---|
| | comparison between hospitals or services of different sizes. | |
| Antimicrobial Resistance Trends | Number of patients with a specific drug-resistant organism divided by the total number of patients admitted to the ward, service, or unit of interest | Meropenem resistant Pseudomonas aeruginosa in critical care:<br><br>During the pandemics, of 500 patients admitted to critical care unit, 100 patients had meropenem resistant P. aeruginosa: 100/500 = 20%<br><br>60 patients with meropenem resistant P. aeruginosa in 2012 with 600 patients admitted to critical care unit pre pandemics: 60/600 = 10%<br><br>Therefore, the rate of meropenem-resistant P. aeruginosa was reduced from 20% in 2009 to 10% pre pandemics. |
| C. difficile Infection (CDI) rate | CDI rate per 1,000 patient days: Number of patients newly diagnosed with institution acquired CDI, divided by the number of inpatient days in that time, multiplied by 1,000<br><br>May also be expressed as the number of new CDI cases per 1000 patient admissions<br><br>For more information on the testing, management and surveillance of CDI see Annex C: Routine Practices and Additional Precautions | During pandemics: 75 cases C. difficile and 90,000 patient days in 2009 = (75/90,000) *1000 = 0.83<br><br>Before pandemics: 43 cases C. difficile and 85,000 patient days in 2011 = (43/85,000) *1000 = 0.5<br><br>Reduction in C. difficile rate = (0.83-0.5)/0.83 = 40% reduction in C. difficile rate in 2011 compared to 2009 |
| Hospital Associated Antibiotic Resistant Organism | New hospital associated Methicillin Resistant Staphylococcus aureus (MRSA) | 2 cases MRSA bacteremia<br><br>April - June<br><br>Patient days = 2100 |

<table>
<tr><td>(ARO)<br>Infection Rate</td><td>bacteremia rate per 1,000 patient days or new hospital associated<br><br>Vancomycin Resistant Enterococcus (VRE) bacteremia rate per 1,000 patient days</td><td colspan="5">Rate = (2/2100) *1000 = 0.95</td></tr>
<tr><td colspan="7">Process Measures</td></tr>
<tr><td>Interventions</td><td>Tally of the number and type of interventions made and acceptance rate</td><td colspan="5">1000 antimicrobial orders were reviewed by the stewardship team in pre pandemics and recommendations were made for 750 (75%)<br><br>The overall acceptance rate was 650/750 (87%)</td></tr>
<tr><td></td><td>Potential types of interventions are listed in the sample calculation</td><td colspan="5">The types of interventions and their acceptance rates were:</td></tr>
<tr><td></td><td></td><td>Dose optimization<br><br>n= 152/160 (95%)</td><td>Escalation of therapy<br><br>n=45/50 (90%)</td><td>De-escalation of therapy<br><br>n=250/300 (83%)</td><td>Route change (e.g., IV to PO)<br><br>n=89/100 (89%)</td><td>Discontinuation of therapy<br><br>n=112/140 (80%)</td></tr>
</table>

**Appendix 12. Data extraction Form for the systematic literature review**

1. **General information**

| | |
|---|---|
| **Title of the article** | |
| **First author and Date published** | |
| **Country of study, and country classification** | |
| **Conflict of interest** | |
| **Notes:** | |

**2. Eligibility**

| | |
|---|---|
| **Type of the study** | |
| **Population** | |
| **Primary and secondary outcomes measure** | |
| **Decision** | |
| **Notes:** | |

3. **If included.**

| | |
|---|---|
| **Quality assessment score** | |
| **Aim of the study** | |
| **Population and location description** | |

| | |
|---|---|
| **Design** | |
| **Study period** | |
| **Aim of the Study** | |
| **Total number of participants** | |
| **Location of the study, hospital, or department** | |
| **Results**<br>● **AMS strategies, measures, metrics, Quality Improvement and KPIs detected**<br>● **Strategies and measures of AMS used**<br>● **HCP or stakeholders involved**<br>● **Metrics of AMS**<br>● **Common Strategies used before and during COVID-19 pandemics**<br>● **Other results** | |
| **Authors Conclusion** | |
| **Strength of the study** | |
| **Limitation of the study** | |
| **Notes:** | |

**Appendix 13.** Dashboard used for studies analysis <u>Summarised</u> in one Image – Raw data from the systematic review. [The complete analysis is available in this link.]

| Study Papers | Pandemics/ Non- pandemics | Retrospective Vs Prospectives | Quantitative Vs Qualitative | RCT or Before/After or interventional study/ Cross sectional | Country | High or Low Income Counteries | Quantiative Studies in which Countries | Number of Patients | Secondary or tertiary settings | Hospital-wide or Departmental | which Department | Acceptance Rate | Intervention ASP Team |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Chung, 2013 | Non-pandemics | Prospective | Qualitative | Intervention | Singapore | HIC | | 0 | Secondary | Hospital-wide | | | |
| Mehta, 2014 | Non-pandemics | Prospective | Qualitative | Intervention | United States | HIC | | 55,336 | Secondary | Hospital-wide | | | |
| Ababneh, 2020 | Non-pandemics | Retrospective | Qualitative | Intervention | Jordan | LMIC | | 144 | Tertiary | Hospital-wide | | | |
| Moriyama, 2021 | Non-pandemics | Retrospective | Quantitative | Intervention | Japan | HIC | Quantiative | 0 | Both | Hospital-wide | | | Yes |
| Panditrao, 2021 | Non-pandemics | Prospective | Qualitative | Before/after | India | LMIC | | 337 | Tertiary | Departmental | Surgical Unit | | |
| Thakkar, 2021 | Non-pandemics | Retrospective | Quantitative | Intervention | Italy | HIC | Quantiative | 1366 | Tertiary | Departmental | Surgical Unit | | |
| Trivedi, 2013 | Non-pandemics | Retrospective | Quantitative | Cross sectional | United States | HIC | Quantiative | 223 | Both | Hospital-wide | | Yes | Yes |
| Spernovasilis, 2021 | Non-pandemics | Retrospective | Qualitative | Cross sectional | Greece | LMIC | | 342 | Secondary | Hospital-wide | | | |
| Guisado-Gil, 2020 | Pandemics | Retrospective | Qualitative | Intervention | Spain | HIC | | 282 | Tertiary | Hospital-wide | | | |
| Guerra, 2021 | Pandemics | Prospective | Qualitative | Intervention | Mexico | HIC | | 794 | Tertiary | Departmental | ICU | | |
| Williams, 2021 | Pandemics | Retrospective | Quantitative | Intervention | United Kingdom | HIC | Quantiative | 629 | Secondary | Hospital-wide | | | |
| Ashiru-Oredope, 2021 | Pandemics | Retrospective | Quantitative | Intervention | United Kingdom | HIC | Quantiative | 95 | Secondary | Hospital-wide | | | |
| Weston, 2012 | Non-pandemics | Prospective | Quantitative | Observational | United States | HIC | Quantiative | 0 | Both | Hospital-wide | | | |
| Kallen, 2017 | Non-pandemics | Prospective | Quantitative | RCT | Netherlands | HIC | Quantiative | 4245 | Both | Both | ICU | | |
| Surat, 2021 | Pandemics | Retrospective | Quantitative | Intervention | Germany | HIC | Quantiative | 767 | Tertiary | Departmental | Surgical Unit | | |
| Tamma, 2021 | Pandemics | Retrospective | Quantitative | Intervention | United States | HIC | Quantiative | 437 | Both | Hospital-wide | | | |

**Appendix 14.** Dashboard used for studies analysis <u>Detailed</u> in three Images - Raw data from the systematic review.

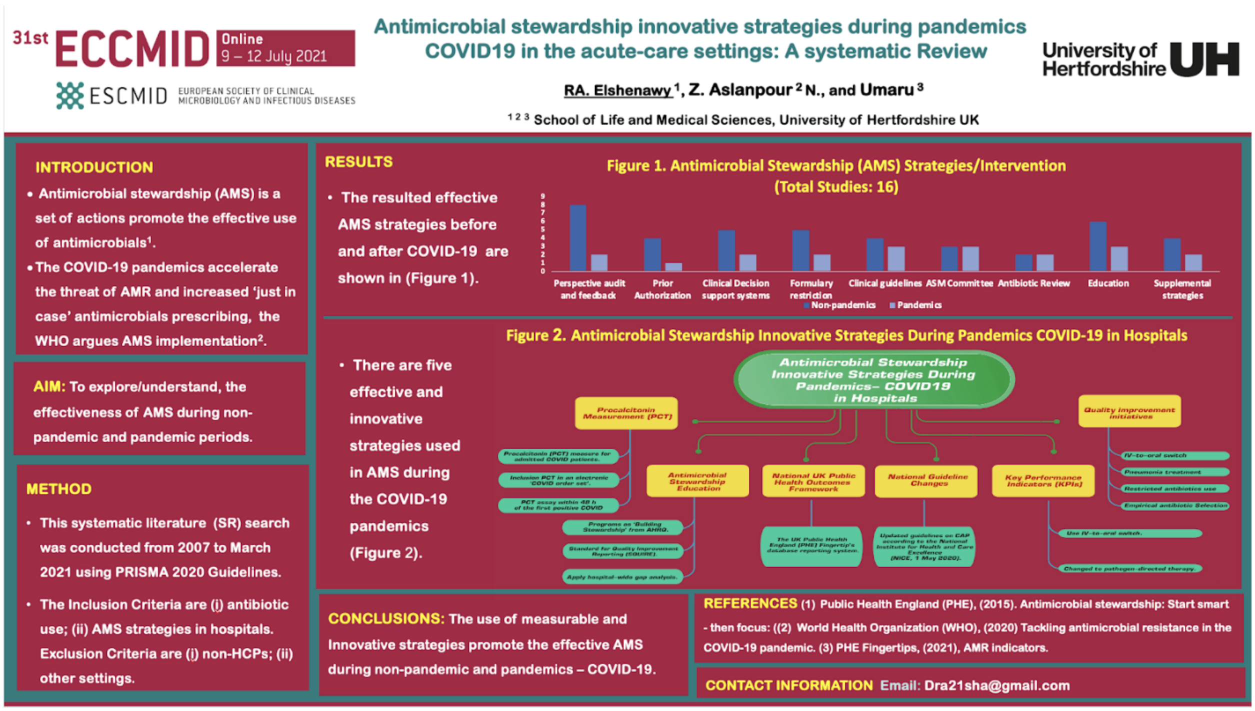
| Study Papers | Pandemics/ Non- pandemics | Retrospective Vs Prospectives | Quantitative Vs Qualitative | RCT or Before/After or interventional study/ Cross sectional |
|---|---|---|---|---|
| Chung, 2013 | Non-pandemics | Prospective | Qualitative | Intervention |
| Mehta, 2014 | Non-pandemics | Prospective | Qualitative | Intervention |
| Ababneh, 2020 | Non-pandemics | Retrospective | Qualitative | Intervention |
| Moriyama, 2021 | Non-pandemics | Retrospective | Quantitative | Intervention |
| Panditrao, 2021 | Non-pandemics | Prospective | Qualitative | Before/after |
| Thakkar, 2021 | Non-pandemics | Retrospective | Quantitative | Intervention |
| Trivedi, 2013 | Non-pandemics | Retrospective | Quantitative | Cross sectional |
| Spernovasilis, 2021 | Non-pandemics | Retrospective | Qualitative | Cross sectional |
| Guisado-Gil, 2020 | Pandemics | Retrospective | Qualitative | Intervention |
| Guerra, 2021 | Pandemics | Prospective | Qualitative | Intervention |
| Williams, 2021 | Pandemics | Retrospective | Quantitative | Intervention |
| Ashiru-Oredope, 2021 | Pandemics | Retrospective | Quantitative | Intervention |
| Weston, 2012 | Non-pandemics | Prospective | Quantitative | Observational |
| Kallen, 2017 | Non-pandemics | Prospective | Quantitative | RCT |
| Surat, 2021 | Pandemics | Retrospective | Quantitative | Intervention |
| Tamma, 2021 | Pandemics | Retrospective | Quantitative | Intervention |

Appendices

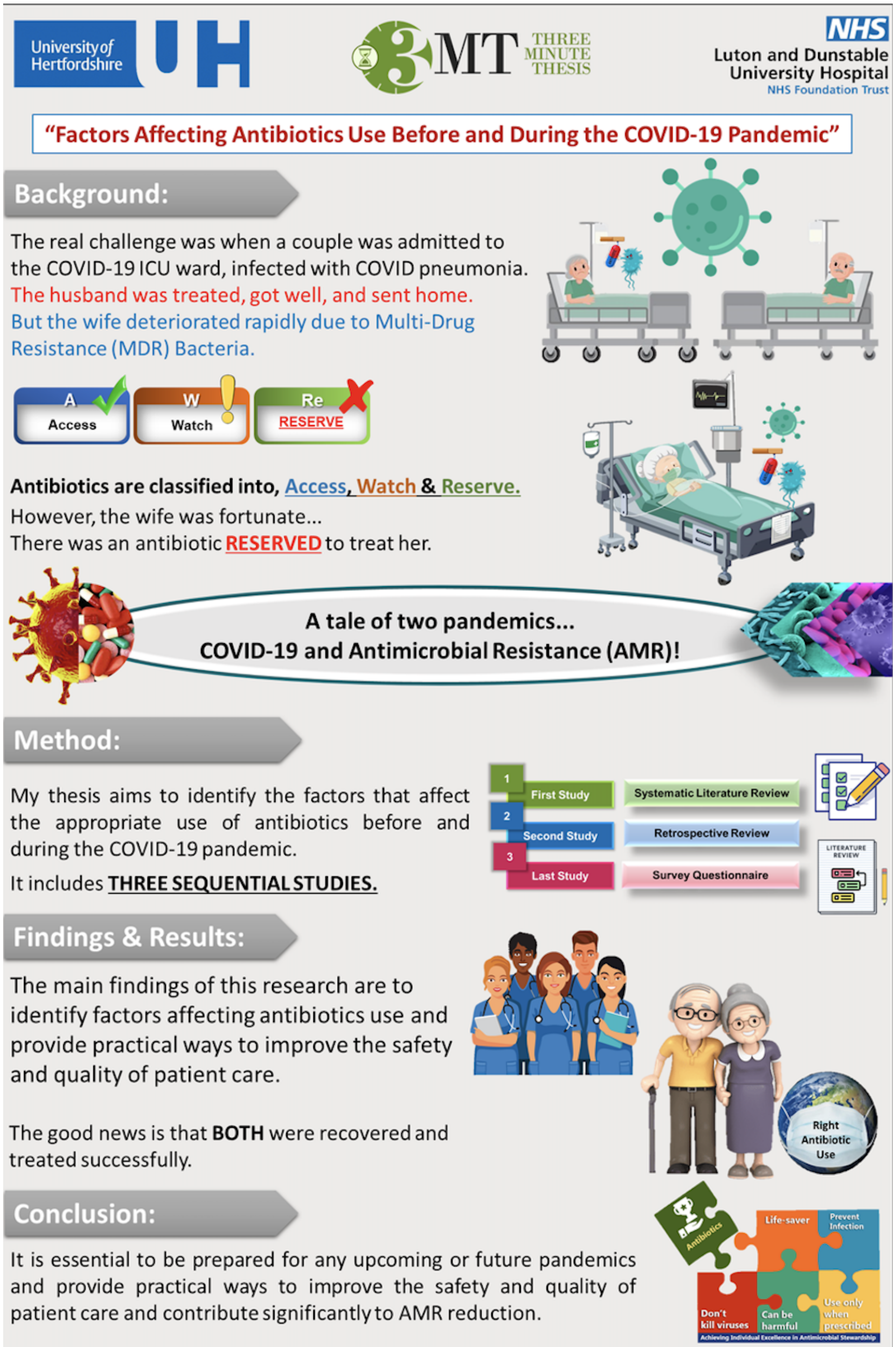
| Study Papers | Country | High or Low Income Counteries | Quantiative Studies in which Countries | Number of Patients |
|---|---|---|---|---|
| Chung, 2013 | Singapore | HIC | | 0 |
| Mehta, 2014 | United States | HIC | | 55,336 |
| Ababneh, 2020 | Jordan | LMIC | | 144 |
| Moriyama, 2021 | Japan | HIC | Quantiative | 0 |
| Panditrao, 2021 | India | LMIC | | 337 |
| Thakkar, 2021 | Italy | HIC | Quantiative | 1366 |
| Trivedi, 2013 | United States | HIC | Quantiative | 223 |
| Spernovasilis, 2021 | Greece | LMIC | | 342 |
| Guisado-Gil, 2020 | Spain | HIC | | 282 |
| Guerra, 2021 | Mexico | HIC | | 794 |
| Williams, 2021 | United Kingdom | HIC | Quantiative | 629 |
| Ashiru-Oredope, 2021 | United Kingdom | HIC | Quantiative | 95 |
| Weston, 2012 | United States | HIC | Quantiative | 0 |
| Kallen, 2017 | Netherlands | HIC | Quantiative | 4245 |
| Surat, 2021 | Germany | HIC | Quantiative | 767 |
| Tamma, 2021 | United States | HIC | Quantiative | 437 |

| Study Papers | Secondary or tertiary settings | Hospital-wide or Departmental | which Department | Acceptance Rate | Intervention ASP Team |
|---|---|---|---|---|---|
| Chung, 2013 | Secondary | Hospitalwide | | | |
| Mehta, 2014 | Secondary | Hospitalwide | | | |
| Ababneh, 2020 | Tertiary | Hospitalwide | | | |
| Moriyama, 2021 | Both | Hospitalwide | | | Yes |
| Panditrao, 2021 | Tertiary | Departmental | Surgical Unit | | |
| Thakkar, 2021 | Tertiary | Departmental | Surgical Unit | | |
| Trivedi, 2013 | Both | Hospitalwide | | Yes | Yes |
| Spernovasilis, 2021 | Secondary | Hospitalwide | | | |
| Guisado-Gil, 2020 | Tertiary | Hospitalwide | | | |
| Guerra, 2021 | Tertiary | Departmental | ICU | | |
| Williams, 2021 | Secondary | Hospitalwide | | | |
| Ashiru-Oredope, 2021 | Secondary | Hospitalwide | | | |
| Weston, 2012 | Both | Hospitalwide | | | |
| Kallen, 2017 | Both | Both | ICU | | |
| Surat, 2021 | Tertiary | Departmental | Surgical Unit | | |
| Tamma, 2021 | Both | Hospitalwide | | | |

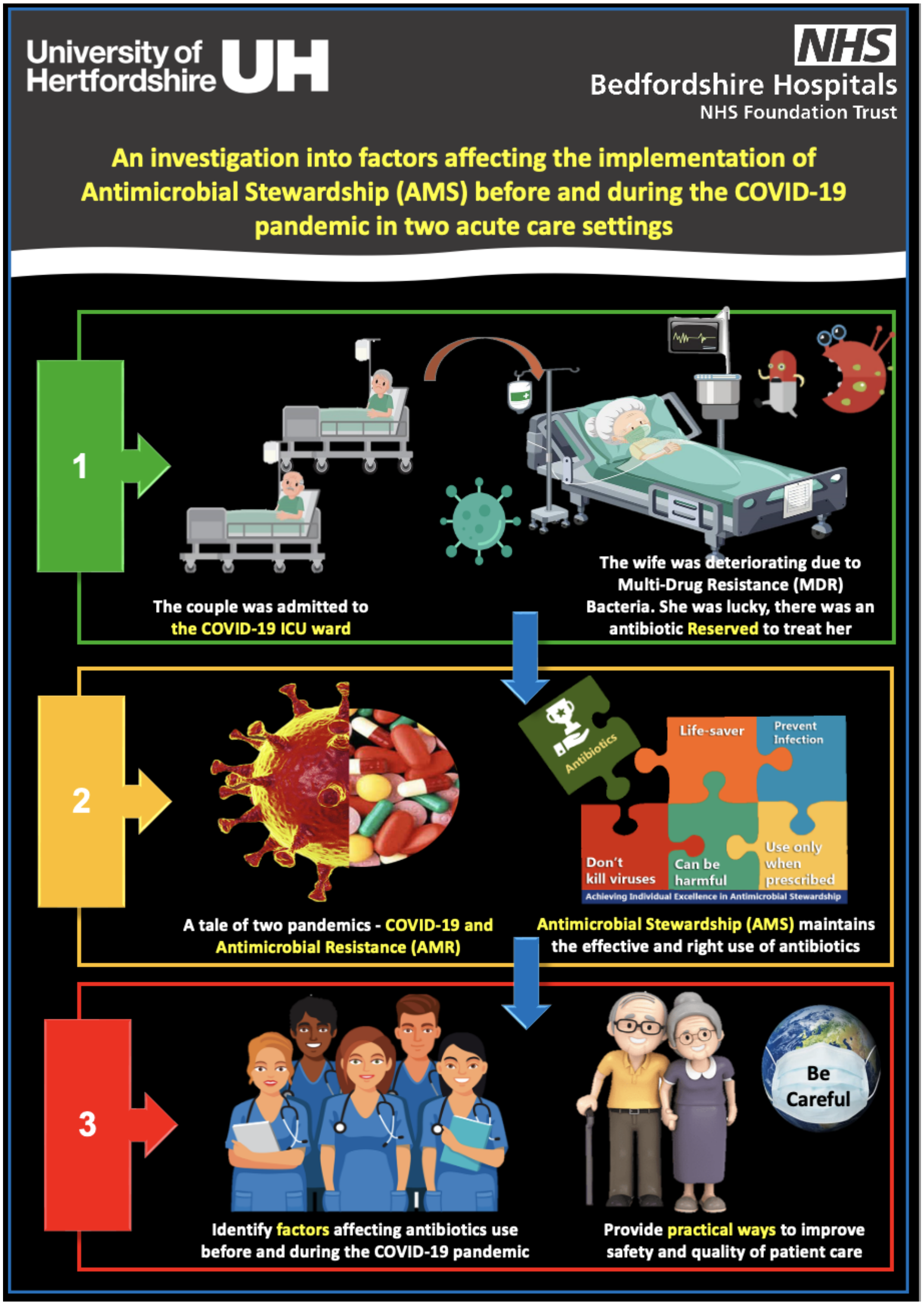
**Appendix 15.** Antimicrobial stewardship innovative strategies during pandemics - COVID-19 in the acute-care settings: A Systematic Review. European Congress of Clinical Microbiology & Infectious Diseases (ESCMID) Poster presentation - September 2021. [Access from this link.]



**Appendix 16.** Three-Minute Thesis (3MT) at UH



**Appendix 17. Research story at UH vision research story**



**Appendix 18:** Registering the study in the ISRCTN public database related to the WHO criteria. An investigation into factors affecting antibiotic use during the COVID-19 pandemic in two hospitals.

BMC
Part of Springer Nature

ISRCTN registry

Search | Advanced Search

View all studies | Why register? | Register your study | Update your record | Report your results

ISRCTN14825813 https://doi.org/10.1186/ISRCTN14825813

An investigation into factors affecting antibiotic use during the COVID-19 pandemic in two hospitals

**Submission date**
18/05/2022
**Registration date**
23/05/2022
**Last edited**
24/06/2022

**Recruitment status**
Not yet recruiting
**Overall trial status**
Ongoing
**Condition category**
Infections and Infestations

✓ Prospectively registered
✓ Protocol available
? SAP not yet available
– Results not yet expected
– Raw data not yet expected
✓ Record updated in last year

**Plain English Summary**

Background and study aims

Antimicrobial resistance (AMR) is a global crisis that requires urgent attention and action. More than 1.2 million people died worldwide in 2019 from infections caused by bacteria resistant to antibiotics, according to the last most extensive study on the issue to date. This is more than the annual death toll from malaria or Aids. The COVID-19 pandemic challenges all aspects of healthcare, especially the management of serious acute bacterial infections and effective delivery of antimicrobial stewardship. The World Health Organization (WHO) have declared AMR one of the biggest threats to global health and one of the biggest health challenges. Antimicrobial stewardship (AMS) is a set of actions to promote the effective use of antimicrobials. Public Health England AMS and NICE AMS guidelines urge the AMS implementation in the acute care settings to maintain the appropriate use of antibiotics and maintain the safety and quality of patient care.

The proposed study will investigate the factors affecting antimicrobial stewardship (AMS) implementation before and during the COVID-19 pandemic.

Who can participate?

Patients aged 18 years or older admitted at Bedfordshire Hospitals NHS Trust from 2019 to 2020, and healthcare professionals who worked during the OCVID-19 pandemic.

**Appendix 19:** Antimicrobial Stewardship Intervention Before and During The COVID-19 Pandemic in the Acute Care Settings: A Systematic Review - Poster Presentation at LMS Research Conference, July 2022.

University of Hertfordshire UH

School of Medical and Life Science

## Antimicrobial Stewardship Intervention Before And During The COVID-19 Pandemic in the Acute Care Settings: A Systematic Review

Elshenawy, R.,[1] Umaru, N.,[2] Aslanpour, Z.[3]

[1 2 3] Department of Pharmacy, School of Life and Medical Sciences, University of Hertfordshire, UK

### Introduction

An estimated 1.2 million people died in 2019 from antibiotic-resistant bacterial infections [1]. The COVID-19 pandemic has challenged the appropriate use of antibiotics. Antimicrobial stewardship (AMS) is a set of actions to promote effective antibiotic use. This systematic review explored AMS interventions before and during the COVID-19 pandemic in acute care settings.

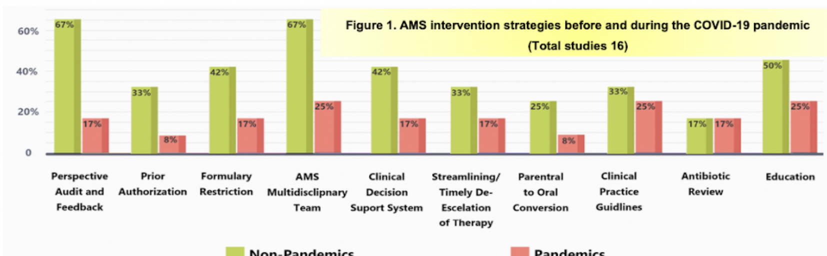
### Method

A systematic literature search from 2007 to 2021 using different databases, such as MEDLINE, Embase classic, OVID, International Pharmaceutical Abstracts, PsycINFO, PubMed, Scopus, CINAHL PLUS, OpenGrey, and Google Scholar. The inclusion criteria: (i) studies focused on antibiotic use in acute-care settings; (ii) AMS implementation strategies; (iii) adult patients of any gender; (iv) English language. This systematic review followed the guidelines for systematic reviews (PRISMA 2020 flow diagram and checklist). The authors used the data collection tool to independently extract and analyse the data.

### Results

- Sixteen articles met the inclusion criteria from an initial result of 8,763 identified article titles. To facilitate the interpretation of the results, The Public Health England (PHE) toolkit of AMS implementation strategies was used as a gold standard in the analysis of the extracted data before and during the COVID-19 pandemic [2].
- Prior to the COVID-19 pandemic, the most reported AMS strategies in 67% of studies were prospective audit, feedback, and AMS Multidisciplinary Team (MDT).
- During the COVID-19 pandemic, AMS education and MDT were the most written strategies implemented in 25% of studies. These were followed by antibiotic review and formulary restriction reported in 17% of studies (Figure 1).

Figure 1. AMS intervention strategies before and during the COVID-19 pandemic (Total studies 16)




### Conclusion

This systematic literature review showed promising outcomes in selecting the appropriate AMS intervention strategies. However, the ongoing global crisis of AMR must not be neglected. Urgent actions are required to ensure the effective implementation of AMS, especially during the COVID-19. In order to be better prepared for any future pandemics. Finally, advocacy for AMS must continue in the post-pandemic era to assure the safety of patient care.

### Reference

[1] Murray, C. J., et al. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The.Lancet.399(10325),629–655. https://doi.org/10.1016/S0140-6736(21)02724

[2] Antimicrobial stewardship: Start smart - then focus. (n.d.).GOV.UK|https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

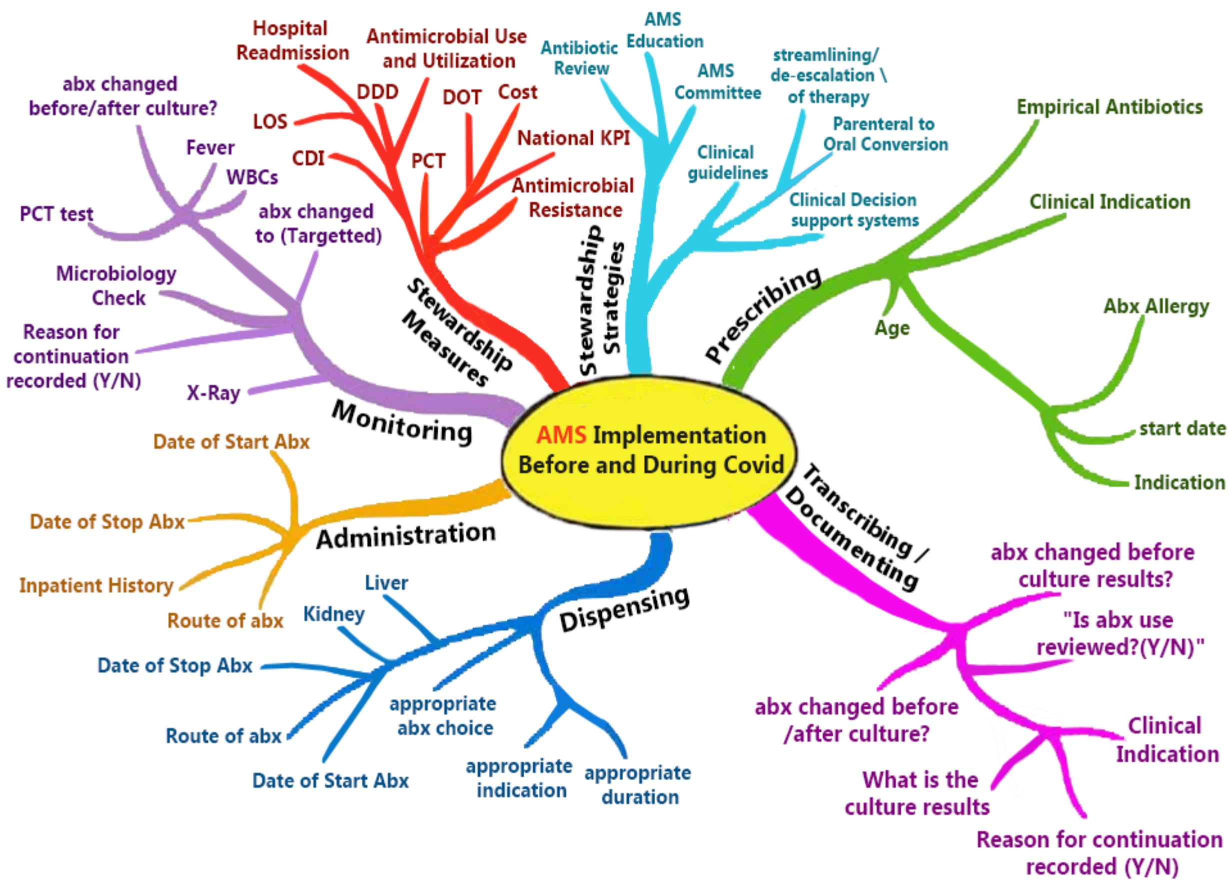
Funding None

Email: r.a.elshenawy@herts.ac.uk

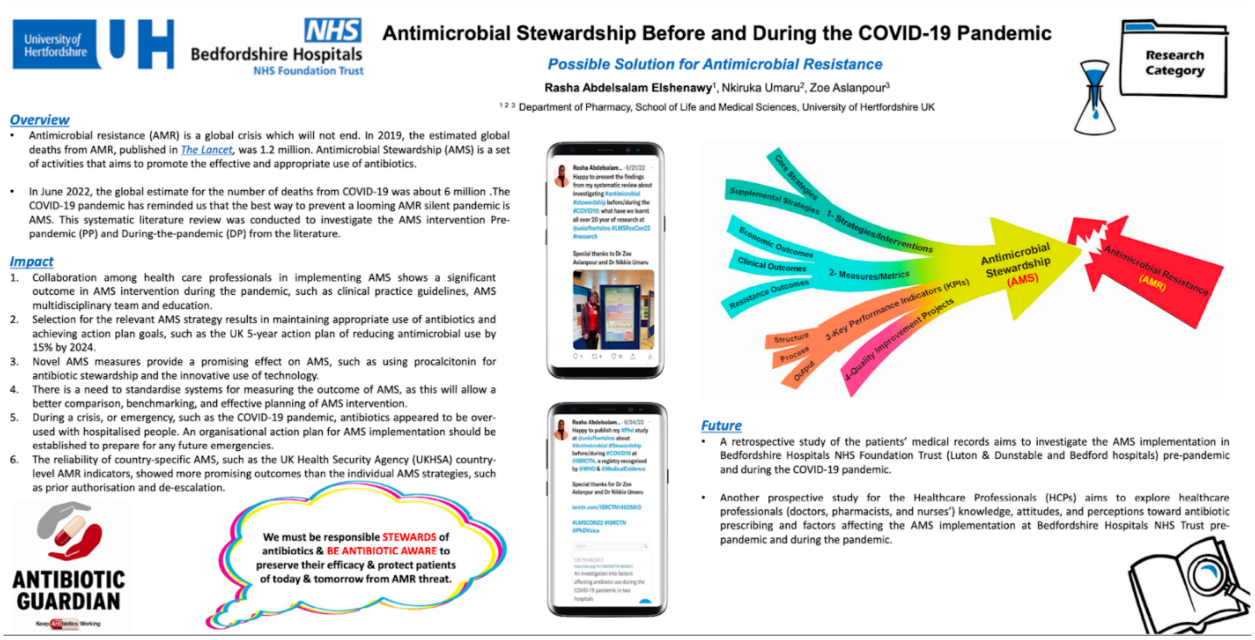
**Appendix 20:** Launched the Research Project Website, July 2022

https://stewardshipcovid.wordpress.com/

**Appendix 21.** Mind map for the study 2: retrospective medical records review



**Appendix 22.** Antibiotic Guardian Award Submission 2022: Tackling Antimicrobial Resistance through Antimicrobial Stewardship Pre and During the COVID-19 Pandemic - **[Accompanied by a Research Project Visual Video.]**



**Appendix 23.** Response to Comments from the Leicester Research Ethics Committee (REC) - Cover Letter.

Available Here.

**Chief Investigator:** Dr Zoe Aslanpour
**Principal Investigator:** Rasha Abdelsalam Elshenawy
**Sponsorship**: University of Hertfordshire
**IRAS Project ID:** 314805
**Research Ethics Committee (REC):** East Midlands - Leicester South
**Reference Number: 22/EM/0161**
**Email:** r.a.elshenawy@herts.ac.uk
**Work Number:** 07393530357
**Version #1**: 05/09/2022

Dear Sir or Madam,

First, we would like to thank the chair and the committee members for their time, constructive comments and guidance on improving our proposed study titled **'An investigation of the factors affecting the implementation of Antimicrobial Stewardship (AMS) before and during the COVID-19 pandemic at Bedfordshire Hospitals NHS Trust.'**

I and my supervisor Dr Zoe Aslanpour, the Chief Investigator, revised all the committee comments and updated all the required changes requested by the committee as tabled below.

We hope that the changes are now satisfactory.

Yours sincerely,
Rasha Abdelsalam Elshenawy

**Ethical Review – Further information required**

| Number | Action Required | Response from applicant |
|---|---|---|
| 1 | Revisit the **survey** to ensure any questions that could lead to the disclosure of potentially identifiable data are removed. For instance, job title could be specific enough so as to identify an individual. During the meeting you indicated staff could indicate their Band instead. | Completed. Please see page 2 of the survey questionnaire with yellow highlights. |

**Appendix 24.** HRA Approval Letter

https://drive.google.com/file/d/1fY_88nMtu6IXDTeJAysQ9FY00kTai5nv/view?usp=sharing

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr Zoe Aslanpour
Department of Pharmacy,
Pharmacology and Postgraduate Medicine
School of Life and Medical Sciences
University of Hertfordshire, Hatfield
AL10 9AB

Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk

19 October 2022

Dear Dr Aslanpour

**HRA and Health and Care Research Wales (HCRW) Approval Letter**

| | |
|---|---|
| **Study title:** | **An investigation into factors affecting the implementation of Antimicrobial Stewardship (AMS) before and during the COVID-19 pandemic in two acute care settings** |
| **IRAS project ID:** | **314805** |
| **Protocol number:** | **N/A** |
| **REC reference:** | **22/EM/0161** |
| **Sponsor** | **University of Hertfordshire** |

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

**How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?**

HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report

**Appendix 25.** A signed copy of the UH Full Sponsorship approval letter for the research study

University of Hertfordshire UH

University of Hertfordshire
Higher Education Corporation
Hatfield, Hertfordshire
AL10 9AB

Telephone +44 (0) 1707 284000
Fax +44 (0) 1707 284115
Website www.herts.ac.uk

John M Senior
BSc MSc DSc PGCE CEng FIET FRSA FHEA
Professor of Communication Networks
Pro Vice-Chancellor (Research and Enterprise)

Dr Zoe Aslanpour & Rasha Abdelsalam
Department of Pharmacy

21 October 2022

Dear Zoe

**Re: UNIVERSITY OF HERTFORDSHIRE SPONSORSHIP IN FULL for the following:**
**RESEARCH STUDY TITLE:** An investigation into factors affecting the implementation of Antimicrobial Stewardship (AMS) before and during the COVID-19 pandemic in two acute care settings
**NAME OF CHIEF INVESTIGATOR (Supervisor):** Dr Zoe Aslanpour
**NAME OF INVESTIGATOR (Student):** Rasha Abdelsalam
**UNIVERSITY OF HERTFORDSHIRE ETHICS PROTOCOL NUMBER:** LMS/PGR/NHS/02975
**HEALTH RESEARCH AUTHORITY REFERENCE: IRAS number:** 314805

This letter is to confirm your research study detailed above has been reviewed and accepted and I agree to give full University of Hertfordshire sponsorship, so you may now commence your research.

As a condition of receiving full sponsorship, please note that it is the responsibility of the Chief Investigator to inform the Sponsor at any time of any changes to the duration or funding of the project, changes of investigators, changes to the protocol and any future amendments, or deviations from the protocol, which may require re-evaluation of the sponsorship arrangements.

Permission to seek changes as outlined above should be requested from myself before submission to the Health Research Authority (HRA) Research Ethics Committee (REC) and I must also be notified of the outcome. It is also essential that evidence of any further NHS Trust or other site permissions is sent as soon as they are received. Copies of annual reports and the end of study report as submitted to the HRA also need to be provided. Please do this via email to research-sponsorship@herts.ac.uk

**Please note that University Sponsorship of your study is invalidated if this process is not followed.**

In the meantime, I wish you well in pursuing this interesting research study.

Yours sincerely

Professor J M Senior
Pro Vice-Chancellor (Research and Enterprise)

University of Hertfordshire Higher Education Corporation is an exempt charity

**Appendix 26.** Meeting minutes and communication between the PhD student and Bedfordshire Hospitals NHS Foundation Trust

| Meetings | Person(s) | Details |
|---|---|---|
| 21/11/2021<br><br>(Online) | • Mrs Patricia Edward: lead pharmacist<br>• Mr Patel Sanil: AMS pharmacist<br>• Dr Nkiruka Umaru: Supervisor<br>• Mrs Rasha Elshenawy: Principal Investigator (PI) or research student | • Dr Nikkie introduced Rasha, the research student. Then, the research student provided a summary of the research project.<br>• Patricia and Patel asked about the details of the data extraction.<br>• They agreed that the research student has to access all the patient information, including the protected information, in order to extract the required data that will answer the research question.<br>• They also agreed to proceed with the Honorary Contract application process till they received Ethical approval. |
| 2/12/2021<br><br>(L&D hospital) | • Mrs Patricia Edward: lead pharmacist<br>• Dr Muhammed Wasil: Director of R&D at Bedfordshire Hospitals NHS Trust.<br>• Dr Nkiruka Umaru: Supervisor<br>• Mrs Rasha Elshenawy: PI/ research student | • The research student provided a synopsis and summary for the research project.<br>• The research student provided all the required documents for the Honorary Contract and signed it for 2 years.<br>• The research student signed the agreement and the Honorary Contract and received the hospital ID after the meeting. |
| 7/9/2022<br><br>(L&D hospital) | • Mrs Patricia Edward: lead pharmacist<br>• Mrs Rasha Elshenawy: PI/ research student | • After receiving a favourable opinion from the NHS ethics, the research student met with Patricia to start the awareness process for the hospital system.<br>• The research student received the Hospital Account details and NHS secure email.<br>• The research student also received the required portal training modules for the hospital systems, ICE and Evolve. The research student has to finish all these modules and provide the successful certificates to the IT service desk in order to activate her access to these programs, to extract the required data from them. |
| 20/09/2022<br><br>(L&D hospital) | • Mr Faisal Khan: AMS pharmacist<br>• Mrs Rasha Elshenawy: PI/ research student | • The research student provided a synopsis, summary, and the NHS ethics favourable opinion of the new AMS pharmacist, Faisal Khan.<br>• The student also provided a copy of the data extraction tool and discussed every item in this tool and how the extraction tool will answer the research questions.<br>• The AMS pharmacist suggested re-arranging some items, to be easily extracted with regards to the hospital system, such as co-morbities column and the lab results. |

| | | |
|---|---|---|
| 15/9/2022<br><br>(Online) | • Azad Kasar: Specialist ePMA Pharmacist | • The student asked to obtain access to the old pharmacy dispensing system, JAC.<br><br>• This program was used in 2019 and 2020, but no longer used any more.<br><br>• Kaser asked to finish the training modules of this program, and then the access can be obtained. |
| 27/9/2022<br><br>(L&D hospital) | • Mr Faisal Khan: AMS pharmacist at L&D hospital<br><br>• Mrs Rasha Elshenawy: PI/ research student<br><br>• Azad Kasar: Specialist ePMA Pharmacist<br><br>• Juel Miah: Senior Pharmacy Technician - Medicine Management | • The student reviewed the last draft of the extraction tool with the AMS pharmacist.<br><br>• The AMS pharmacists showed the student how to extract the data from the hospital system in an organised manner.<br><br>• The student provided the successful certificate to Juel, in order to obtain the access to the JAC program.<br><br>• Unfortunately, remote access is not easy for JAC. The research student has to contact the IT service desk for three weeks, in order to solve this issue.<br><br>• The IT service desk could not solve the issue, and asked to refer the issue to the pharmacy department. |
| 28/09/2022<br><br>(Bedford hospital) | • Mr Abdul Mohamed: AMS pharmacist at Bedford hospital<br><br>• Mrs Alli Hickson: Pharmacy Office Manager at Pharmacy Department in Bedford hospital<br><br>• Mrs Rasha Elshenawy: PI/ research student | • The research student provided a synopsis, summary, and the NHS ethics favourable opinion of the AMS pharmacist at Bedford hospital, Abdul Mohamed.<br><br>• Abdul requested new hospital account for the research student, and a NHS secure email at Bedford hospital.<br><br>• The student also received the required portal training modules for hospital systems, Medichart and Viper.<br><br>• The research student has to finish all these modules and provide the successful certificates to the IT service desk in order to activate her access to these programs, to extract the required data from them. |
| 4/10/2022<br><br>(Online) | • Mr Abdul Mohamed: AMS pharmacist at Bedford hospital<br><br>• Mrs Rasha Elshenawy: PI/ research student | • Abdul provided the student with the account details and NHS email at Bedfordshire hospitals. |
| 7/10/2022<br><br>(Online) | • Mrs Gemma McGuigan: Lead pharmacist at Bedford hospital.<br><br>• Mrs Rasha Elshenawy: PI/ research student | • The student provided an introductory discussion on the PhD Research project<br><br>• She offered her help if there is any issue related to the data extraction process. |
| 15/10/2022<br><br>(Online) | • Mr Faisal Khan: AMS pharmacist at L&D hospital<br><br>• Mrs Rasha Elshenawy: PI/ research student | • Faisal extracted data from patient medical records, 6 patients.<br><br>• The research student compares this extracted data with her extracted one, there was more than 80% agreement between them. |

| | | |
|---|---|---|
| | | • They also discussed and ensured the validity of the data extraction tool. |
| 1/11/2022<br><br>(Online) | • Mr Faisal Khan: AMS pharmacist at L&D hospital<br><br>• Mrs Rasha Elshenawy: PI/ research student | • Faisal extracted data from 4 additional patients.<br><br>• The research student compares this extracted data with her extracted one, there was more than 80% agreement between them.<br><br>• There were three important issues:<br><br>1. The main diagnosis was written in some patient records in a generalised diagnosis, such as pneumonia not 'community acquired pneumonia (CAP)', which would be difficult to the research student to judge if the antibiotic is appropriate or not. The AMS pharmacists recommend the student to do the assessment based on CURB65 score and then determine if the antibiotic is appropriate or not. The research student aggreged for this step. But mentioned that the main diagnosis should be written as it is provided in the medical records. The student asked the supervisor.<br><br>2. The second issue is related to the initial antibiotic used, as in medical records, the antibiotics was not written in appropriate way (right dose, route, frequency, and duration), in many patients, only the name and route. Faisal recommended to take this information from the pharmacy system, as this is the dispensary system. The research student agreed for that but mentioned that she will extract the initial antibiotic from both systems, to compare the prescribing system with the doctors and the dispensing system with the pharmacist. The student asked the supervisor.<br><br>3. The third issue is related to JAC program, Faisal mentioned that the seniors and executive directors only has access for this program, but it is mandatory for the student to access this program to avoid missing items in the data extraction, and refer the issue to Juel Miah, Senior Pharmacy Technician - Medicine Management. |
| 2/11/2022<br>(Online) | • Juel Miah: Senior Pharmacy Technician - Medicine Management<br><br>• Mrs Rasha Elshenawy: PI/ research student | • Rasha asked Juel to solve her problem with JAC.<br><br>• Juel sent Rasha an instruction file to be able to access the old JAC program. It is mandatory to install new program in her system.<br><br>• Rasha fail to access JAC in her system.<br><br>• Juel referred this issue to Peter Seymour, Lead Directorate Pharmacist |
| 3/11/2022<br><br>(Online) | • Peter Seymour: Lead Directorate Pharmacist<br><br>• Juel Miah: Senior Pharmacy Technician - Medicine Management | • Rasha provide summary and synopsis of the research project and copy of Ethical approval.<br><br>• Rasha Asked Peter for help in solving the JAC access problem. |

| | | |
|---|---|---|
| | • Mrs Rasha Elshenawy: PI/ research student | • Peter welcomed Rasha and referred the issue to Hamza Saleemi, the Pre-Registration Pharmacist to solve the issue with Rasha.<br><br>• Rasha thanked Peter for the help and support in this issue. |
| 4/11/2022<br><br>(Online) | • Mrs Rasha Elshenawy: PI/ research student<br><br>• Matthew Parker: IT service desk | • Rasha asked Matthew to solve her problem, to obtain remote access to Bedford hospital. She had 'authentication failure' issue.<br><br>• Matthew tried to solve the issue with her, but it didn't work.<br><br>• He had to reset all her passwords, with no solve unfortunately. |
| 7/11/2022<br><br>(Online) | • Hamza Saleemi, the Pre-Registration Pharmacist<br><br>• Mrs Rasha Elshenawy: PI/ research student | • Hamza sent Rasha the instructions on how to access JAC.<br><br>• He followed up with Rasha, that the access of JAC should be from Windows 7.<br><br>• Rasha tried to obtain the 'Remote Desktop Connection' application on her computer.<br><br>• This can usually be located by searching when she clicked 'Start' (Windows 7)<br><br>• Rasha also contacted the IT for authorisation to server 'jac-rds-srv'.<br><br>• Finally Rasha obtained the JAC access successfully. |
| 8/11/2022<br><br>(Online) | • Mrs Rasha Elshenawy: PI/ research student<br><br>• Matthew Parker: IT service desk | • Rasha tried so many times to obtain the access, it was not working.<br><br>• Mattew also tried, the problem is still working.<br><br>• Mattew asked Rasha, to download new browser 'Microsoft Edge' and new 'Remote program', then reset the passwords again.<br><br>• Finally Rasha obtained the remote access successfully to Bedford hospital. |

**Appendix 27.** ISRCTN Blog Article: World Antibiotic Awareness Week 2022, Released on 18th November 2022. **Click Here for the Full Article Link.**

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# On Medicine

About this blog

## Antimicrobial stewardship before and during the COVID-19 pandemic

In a blog for World Antimicrobial Awareness Week, Rasha Abdelsalam Elshenawy, Dr Nikkie Umaru, and Dr Zoe Aslanpour discuss their study, registered with the ISRCTN registry, investigating the factors affecting the Antimicrobial Stewardship (AMS) implementation in two acute care settings before and during the COVID-19 pandemic.

Rasha Abdelsalam Elshenawy 18 Nov 2022


Rasha Abdelsalam Elshenawy

Rasha Abdelsalam Elshenawy is a Clinical Pharmacist doing her PhD at the University of Hertfordshire in the UK. She is an Antimicrobial Stewardship Global Lead. She has an American Board of Pharmacy with 20 years of experience and is certified in AMS. She has special interests in antimicrobial resistance (AMR) and antimicrobial stewardship (AMS). She led AMS and put measures against antibiotic-resistant bacteria. She is a director of the Antimicrobial Stewardship School, which was shortlisted for the Antibiotic Guardian award (2020), and the AMR challenge of the Centre for Disease Control and Prevention (CDC). Realising the global burden of AMR has fulfilled her

**Appendix 28.** Springer Community Article: Explained the research project of Antimicrobial Stewardship Implementation Before and During the COVID-19 Pandemic in Acute-care settings - informed by the Sustainable Development Goals framework of the United Nations target goals. Includes Video. Released Dec 13, 2022. [Access the Complete Article Here.]

BMC

Health and well-being for all COVID-19

# Antimicrobial Stewardship Implementation Before and During the COVID-19 Pandemic in Acute-care settings

In this invited "SDG 3 and me", I explain the research project of investigating the Antimicrobial Stewardship Implementation Before and During the COVID-19 Pandemic to tackle the Antimicrobial Resistance threat -and is informed by- the Sustainable Development Goals framework of the United Nations target goals.

Published Dec 13, 2022

Rasha
PhD Research in Antimicrobial Stewardship and COVID-19 Pandemic, University of Hertfordshire

Follow

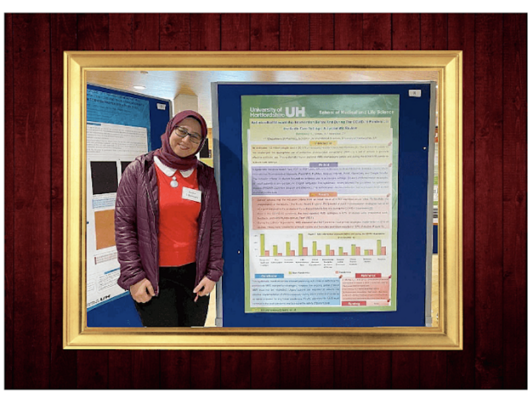


Read the paper

Processing
The data is being processed.

I am a Clinical Pharmacist by background doing my PhD at the University of Hertfordshire in the UK. I am an Antimicrobial Stewardship (AMS) Global Lead. I have an American Board of Pharmacy with 20 years of experience, and I am certified in Antimicrobial Stewardship. I have special interests in antimicrobial resistance (AMR) and antimicrobial stewardship (AMS). I led AMS and put measures against antibiotic-resistant bacteria and 5-years AMS strategic plan. I am a director of FADIC Antimicrobial Stewardship School, which was shortlisted for the Antibiotic Guardian award (2020). This school was shared in the Centre for Disease Control and Prevention (CDC) AMR challenge in 2018. Realising the global burden of AMR has fulfilled my passion for finding possible solutions to AMR through effective implementation of AMS and improving antibiotic prescribing and education. I presented this research project at the University of Hertfordshire, School of Life and Medical Science (LMS) annual meeting in 2022 (Figure 1).

**Figure 1. Poster presentation at the University of Hertfordshire School of Life and Medical Sciences (LMS) annual meeting in 2022**



What SDG3 target(s) in my work and the work of the organization most closely aligned with?

**Appendix 29.** Data Extraction from 40 Patient Records in March 2019: A Single-Time Point (1/4). Access the Link for Complete Raw Data

| Dempgraphic Characteristics | | | | | | |
|---|---|---|---|---|---|---|
| Serial No | Study ID | Date of Admission | Date of Discharge | LOS (Days) | Patient Outcome (1 Discharged, 2&4 Diseased) | Abx Allergy |
| 1 | BBM1 | 03/03/2019 17:00:00 | 3/21/19 17:00 | 18 | 1 | 0 |
| 2 | BBM2 | 03/07/2019 00:00:00 | 3/11/2019 18:10 | 3 | 1 | 0 |
| 3 | BBM3 | 03/03/2019 00:00:00 | 3/21/2019 17:00 | 18 | 1 | 0 |
| 4 | BBM4 | 03/02/2019 00:00:00 | 3/6/2019 19:30 | 4 | 1 | 0 |
| 5 | BBM5 | 03/02/2019 00:00:00 | 3/6/2019 14:00 | 4 | 1 | 0 |
| 6 | BBM6 | 03/03/2019 21:18:00 | 3/8/2019 15:30 | 4 | 1 | CLARITHROMYCIN, |
| 7 | BBM7 | 03/06/2019 00:00:00 | 3/27/2019 11:55 | 21 | 1 | PENICILLINS |
| 8 | BBM8 | 03/06/2019 20:02:00 | 3/18/2019 14:50 | 11 | 1 | CO-TRIMOXAZOLE, |
| 9 | BBM9 | 03/07/2019 05:22:00 | 3/10/2019 17:15 | 3 | 4 | erythromycin |
| 10 | BBM10 | 03/09/2019 00:00:00 | 3/22/2019 10:50 | 12 | 4 | 0 |
| 11 | BBM11 | 03/09/2019 23:44:00 | 3/14/2019 11:36 | 4 | 1 | 0 |
| 12 | BBM12 | 03/10/2019 00:00:00 | 3/21/2019 15:25 | 11 | 1 | chloramphenicol, |
| 13 | BBM13 | 03/10/2019 00:00:00 | 3/14/2019 17:12 | 4 | 1 | AMOXICILLIN |
| 14 | BBM14 | 03/11/2019 11:18:00 | 3/15/2019 18:53 | 4 | 1 | 0 |
| 15 | BBM15 | 03/11/2019 00:00:00 | 3/18/2019 12:20 | 6 | 1 | 0 |
| 16 | BBM16 | 03/11/2019 00:00:00 | 3/18/2019 20:30 | 6 | 1 | 0 |
| 17 | BBM17 | 3/13/2019 16:47 | 3/21/2019 15:00 | 7 | 1 | 0 |
| 18 | BBM18 | 3/13/2019 22:22 | 3/22/2019 18:30 | 8 | 1 | 0 |
| 19 | BBM19 | 3/14/2019 0:25 | 5/16/2019 17:10 | 63 | 1 | 0 |
| 20 | BBM20 | 3/14/2019 18:18 | 3/27/2019 14:30 | 12 | 1 | CLARITHROMYCIN, |
| 21 | BBM21 | 3/15/2019 16:30 | 3/20/2019 13:00 | 4 | 1 | PENICILLINS, |
| 22 | BBM22 | 3/15/2019 23:29 | 3/29/2019 11:53 | 13 | 1 | 0 |
| 23 | BBM23 | 3/15/2019 23:48 | 4/11/2019 09:15 | 26 | 4 | 0 |
| 24 | BBM24 | 3/16/2019 8:22 | 3/19/2019 7:00 | 2 | 4 | 0 |
| 25 | BBM25 | 3/16/2019 20:33 | 3/19/2019 18:30 | 2 | 1 | 0 |
| 26 | BBM26 | 3/17/2019 2:03 | 3/21/2019 13:40 | 4 | 1 | FLUCLOXACILLIN, |
| 27 | BBM27 | 3/17/2019 12:31 | 3/24/2019 11:40 | 6 | 4 | 0 |
| 28 | BBM28 | 3/19/2019 2:53 | 3/28/2019 14:15 | 9 | 1 | 0 |
| 29 | BBM29 | 3/19/2019 19:59 | 4/3/2019 10:30 | 14 | 1 | 0 |
| 30 | BBM30 | 3/19/2019 23:03 | 4/18/2019 10:30 | 29 | 1 | 0 |
| 31 | BBM31 | 3/21/2019 18:33 | 4/7/2019 18:00 | 16 | 1 | 0 |
| 32 | BBM32 | 3/22/2019 17:56 | 4/2/2019 17:00 | 10 | 1 | 0 |
| 33 | BBM33 | 3/22/2019 23:44 | 3/30/2019 21:31 | 7 | 4 | PENICILLINS - |
| 34 | BBM34 | 3/23/2019 1:17 | 4/5/2019 09:30 | 13 | 1 | meropenem |
| 35 | BBM35 | 3/25/2019 3:40 | 4/8/2019 13:50 | 14 | 1 | 0 |
| 36 | BBM36 | 3/25/2019 22:54 | 3/29/2019 19:10 | 3 | 1 | 0 |
| 37 | BBM37 | 3/26/2019 3:54 | 3/31/2019 17:00 | 5 | 1 | erythromycin |
| 38 | BBM38 | 3/26/2019 11:43 | 4/6/2019 16:30 | 11 | 4 | 0 |
| 39 | BBM39 | 3/27/2019 6:58 | 3/29/2019 9:00 | 2 | 1 | CO-AMOXICLAV |
| 40 | BBM40 | 3/29/2019 19:18 | 4/4/2019 13:45 | 5 | 1 | 0 |

**Cont. Appendix 30.** Data Extraction from 40 Patient Records in March 2019: A Single-Time Point (2/4)

| Start Smart | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Symptoms on Admission | Confusion (Y=1, N=0)? | Clinical Indication | Initial Antibiotics | Frequency | Duration (Days) | Is comply with local guidelines (Y/N) | Is Abx selected for appropriate indication? (Y/N) | Is Abx dose is appropriately selected? (Y/N) | Is the duration of Abx is appropriate? (Y/N) | Is the Frequency of Abx is appropriate? (Y/N) | Route (Oral= 1, IV= 2, Both=3) | Is Route Appropriate? (Y=1, N=0)? | If IV, is there a switch to PO within 72hrs? (Y=1, N=0)? |
| | | COPD infective exacerbation | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 500 mg Oral TWICE a day (08:30, 22:00) for 7 days | 7 | 1 | 1 | 1 | Y | Y | | | |
| | | LRTI | Piperacillin-tazobactam IV 4.5g (Tazocin) + | 4.5 g Intravenous Every EIGHT | 1 | 0 | 1 | 0 | N | N | | | |
| | | COPD infective exacerbation | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 500 mg Oral TWICE a | 7 | 1 | 1 | 1 | Y | Y | | | |
| | | Community Acquired Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 4 | 0 | 0 | 0 | N | Y | | | |
| | | Community Acquired Pneumonia | Amoxicillin 1g Injection + Clarithromycin 500 mg | DOSE: 1 g Intravenous THREE | 2 | 1 | 1 | 1 | Y | Y | | | |
| SOB | | COPD infective exacerbation | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg Oral TWICE a | 4 | 1 | 1 | 1 | N | Y | 2 | 1 | N |
| | | Community Acquired Pneumonia | Levofloxacin PO 500mg | DOSE: 500 mg Oral In the | 2 | 1 | 1 | 1 | N | Y | 1 | 1 | |
| | | LRTI | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 4 | 1 | 1 | 1 | 0 | 1 | 2 | 2 | 0 |
| | | Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 3 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 |
| | | LRTI | Amoxicillin IV 500mg | DOSE: 500 mg Intravenous | 3 | 1 | 1 | 1 | 0 | 1 | 1 | | |
| | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1.2 g Intravenous Every | 4 | 1 | 1 | 1 | 0 | 1 | 3 | 1 | 0 |
| | | Hospital Acquired Pneumonia | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 |
| SOB | | Chest Infection | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 3 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| SOB, Cough | | Chest Infection | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 3 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 1 |
| | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1200 mg Intravenous | 5 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 0 |
| | | Chest Infection | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 |
| | | LRTI | Co-amoxiclav 500/125mg Tablets | DOSE: 1 Tablet Oral THREE | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| SOB,fever=38.4, | | Pneumonia | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 |
| | | Hospital Acquired Pneumonia | Levofloxacin PO 500mg | DOSE: 500 mg Oral TWICE a | 4 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | |
| SOB, Cough | | Viral Pneumonia | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 2 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 1 |
| | | Ventilator Pneumonia (VAP) | Ciprofloxacin 500 mg | DOSE: 500 mg Oral TWICE a | 4 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | |
| | | Chest Infection | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 2 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| | | LRTI | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 3 | 0 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1200 mg Intravenous | 3 | 0 | 1 | 1 | 0 | 1 | 3 | 0 | 1 |
| | | Hospital Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| | | Chest Infection | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 5 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 |
| | | LRTI | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 3 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| | | LRTI | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| | | Hospital Acquired Pneumonia | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 3 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| | | COPD infective exacerbation | Co-amoxiclav IV 1.2 | DOSE: 1200 mg Intravenous | 7 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 0 |
| SOb, cough, | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1200 mg Intravenous | 4 | 1 | 1 | 1 | 0 | 1 | 3 | 1 | 0 |
| | | Community Acquired Pneumonia | Levofloxacin PO 500mg | DOSE: 500 mg Oral TWICE a | 2 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | |
| | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 4 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 0 |
| | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1200 mg Intravenous | 2 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| | | Chest Infection | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 |
| | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1.2 g Intravenous Every | 6 | 1 | 1 | 1 | 1 | 1 | 3 | 1 | 0 |
| | | Chest Infection | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 2 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 1 |
| SOB, Cough, | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1200 mg Intravenous | 5 | 0 | 1 | 1 | 1 | 1 | 3 | 0 | 0 |
| | | Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 7 | 0 | 1 | 1 | 1 | 1 | 2 | 1 | 0 |
| | | LRTI | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1200 mg Intravenous | 3 | 0 | 1 | 1 | 0 | 1 | 3 | 1 | 1 |

**Cont. Appendix 30.** Data Extraction from 40 Patient Records in March 2019: A Single-Time Point (3/4)

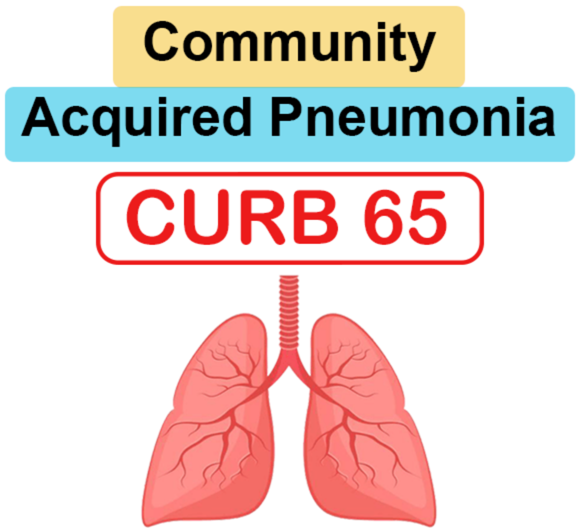
| Then Focus | | | | Co-morbiditis | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day of review | Type of intervention (Change, De-escalate, IV-to-Oral, Stop) | Name of antibiotic changed | Is Abx selected after reviewing appropriate? (Y=1, N=0)? | HTN | PE | Hypotension | AF | HF | Hypercholesterimia | DM | Hypothyroidism or Thyroid | Kidney | Liver | Malignancy | Bronchiectasis | OA | Asthma | COPD | Dementia | Epilepsy | Depression |
| 7 | IV-to-Oral Switch | Co-amoxiclavIV 1.2g | | | | | | | | | | | | | | | | | | | |
| 1 | IV-to-Oral Switch | Co-amoxiclavIV | | | | | | | | | | | | | | | | | | | |
| 7 | IV-to-Oral Switch | Co-amoxiclavIV | | | | | | | 1 | 1 | | | | | 1 | | | | | | |
| 4 | Continue Antibiotics | Piperacillin 4g + | | | | | | | | | | | | | | | | | | | |
| 2 | IV-to-Oral Switch | | | | | | | | | | | | | | | 1 | 1 | | | | 1 |
| 4 | IV-to-Oral Switch | | | 1 | | | | | | | 1 | | | | | 1 | | 1 | | | |
| 2 | Stop Antibiotics | | | | | 1 | | | | | | | | | | | 1 | 1 | | | |
| 4 | IV-to-Oral Switch | | | 1 | 1 | | | | | | | | | | 1 | | 1 | | | | |
| 3 | Change antibiotic | metronidazole | | 1 | 1 | | | | | | | 1 | | 1 | | | | | | | |
| 3 | Escalation | piperacillin 4g + | | | | | | | | | | | | | | | | | | | |
| 4 | De-escalation | | | | | | 1 | | 1 | | | | | | | 1 | | | 1 | 1 | |
| 2 | IV-to-Oral Switch | | | 1 | | | | | | | | | | | | | 1 | | 1 | | |
| 3 | IV-to-Oral Switch | | | 1 | 1 | | | | | | | | | | | | | | | | |
| 3 | IV-to-Oral Switch | | | 1 | | | | | | 1 | | | | | | | | | | | |
| 5 | IV-to-Oral Switch | | | 1 | | | | | 1 | | | | | | | | | | | | |
| 2 | Escalation | piperacillin 4g + | not appro | 1 | | | | | 1 | | | | | | | | | | | | |
| 7 | Stop Antibiotics | | | | | | | 1 | | | | | | | | | | | | | |
| 2 | Change antibiotic | piperacillin 4g + | | | | | | | | | | | | | | | 1 | | | | |
| 4 | Continue Antibiotics | | | | | | 1 | | | | | | | | | 1 | | | | | |
| 2 | Stop Antibiotics | | | 1 | | | | | | 1 | 1 | | | | | | | | | | |
| 4 | Escalation | vancomycin | 1 | 1 | | | 1 | | 1 | 1 | | 1 | | | | | 1 | | | | |
| 2 | Change antibiotic | meropenem | 1 | | | | | | | | | | | | | | | | | | |
| 3 | Stop Antibiotics | | | | | | | | | | | 1 | | 1 | | | | | 1 | | |
| 3 | Stop Antibiotics | | | | | | 1 | | | | | | | | | | | | | | |
| 2 | IV-to-Oral Switch | | | | | | | | | | | | | | | | | | 1 | | |
| 2 | Escalation | piperacillin 4g + | 1 | 1 | | | | | | | | | | | 1 | | | | | | |
| 5 | Stop Antibiotics | | | | | | | | 1 | | | | | | | | | | | | |
| 3 | Stop Antibiotics | | | | | | | | | | | | | | | | | | | | |
| 2 | IV-to-Oral Switch | | | | | | | | 1 | 1 | | | | | | 1 | | | | | |
| 3 | IV-to-Oral Switch | | | 1 | | | | | | | | | | | | | 1 | | | | |
| 7 | Stop Antibiotics | | | 1 | | | | | | | | | | | | | 1 | 1 | | | |
| 4 | Escalation | piperacillin 4g + | 0 | | | | 1 | | 1 | 1 | | 1 | | | | | | | | | |
| 2 | Escalation | levofloxacin | 1 | 1 | | | | | 1 | | | | | | | | | | | | |
| 2 | IV-to-Oral Switch | | | | | | | | | | | 1 | | | | | | | | | |
| 4 | Escalation | piperacillin 4g + | 0 | | | | | | | | | | | | | | | | | | |
| 2 | Escalation | piperacillin 4g + | 0 | 1 | | | | 1 | | | | | | | | | | | | | |
| 2 | Stop Antibiotics | | | | | | | | | | | | | | | | | | | | |
| 6 | Escalation | piperacillin 4g + | | | | 1 | 1 | | | | | | | 1 | | | | 1 | | | |
| 2 | Stop Antibiotics | | | | | | | | | | | | | | | | | | | | |
| 5 | Stop Antibiotics | | | 1 | | | 1 | | | | | | | | | | | | | | |
| 7 | IV-to-Oral Switch | | | | | | | | | | | | | | | | | | | | |
| 3 | Escalation | piperacillin 4g + | | | | | | | | | 1 | | | | | | | | | | |

**Cont. Appendix 30.** Data Extraction from 40 Patient Records in March 2019: A Single-Time Point (4/4)

| Blood Culture | | | Investigation | | | | | | | Orher Factors | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Did culture sent to Mic prior to Abx (Y/N) | Culture Time Collection | Blood Culture Result | X-Ray Finding | WBCs count | PCT | CRP | D Dimer | Urea | Creatinine | CDI (Y/N) | CURB-65 Score | Probiotics | Comments |
| | C.T:3/3/2019 09:30 ---- | No growth | T.X-RAY: 2/3/2019 01:38 ---- T.R: | 2.4 | 0 | 155 | | | | | | | |
| | C.T: 6/3/2019 9:30 ---- R.T: | No growth | T.X.RAY:2/3/2019 ---- T.R: | 2.8 | 0 | 9 | | | | 1 | | | |
| | | | | | 0 | | | | 60 | | | | |
| | C.T: 8/3/2019 9:30 ---- R.T: | N.A | T.X-RAY: 5/3/2019 22:53 ---- T.R: | 7.2 | 0 | 36 | | | | | | | |
| NA | | | | | 0 | | | | 58 | | | | Pseudomonas infection |
| NA | | | | | 0 | | | | 159 | | | | Previous Pneumonia + Died MDR |
| 1 | C.T: 10/3/2019 18:45 ---- | N.A | T.X-RAY: 9/3/2019 21:00 ---- T.R: | 17 | 0 | 321 | | | | | | | |
| NA | | | | | 0 | | | | | | | | Community Acquired Pneumonia (not fully |
| 1 | C.T: 12/3/2019 11:18 ---- | N.A | T.X-RAY: 10/3/2019 05:18 ---- | 14.1 | 0 | 87 | | | | | | | |
| 1 | C.T: 10/3/2019 16:14 ---- | N.A | T.XRAY: 10/3/2019 18:46 ---- | 12.9 | 0 | 95 | | | 73 | | | | |
| NA | | | | | 0 | | | | | | | | |
| 1 | C.T: 13/3/2019 09:40 ---- | N.A | T.X-RAY Shoulder: 12:3:2019 | 11 | 0 | 94 | | | | | | | |
| 0 | C.T: 13/3/2019 02:51 --- | N.A | | 11.2 | 0 | 149 | | | 214 | | | | |
| 0 | 15/03/2019 11:54- Result: | | The left base is not well | 10.6 | 0 | 90 | | | | | | | |
| 1 | 13/03/2019 19:25- Result: | | XR chest: There is worsening of | 10.2 | 0 | 103 | | | 61 | | | | TB |
| 1 | 15/03/2019 10:45- | | XR Hip Lt : there is an impacted | 6,9 | 0 | | | | 52 | | | | |
| 0 | 23/03/2019 09:30- Result: | | XR chest: Cardiomegaly noted, | 19.5 | 0 | 23 | | | | | | | |
| na | | | XR chest : chronic bronchitic type | 9.5 | 0 | 137 | | | | | | | |
| na | | | XR chest : there is some linear | 2.1 | 0 | 192 | | | | | | | |
| 1 | 15/3/2019 20:50 | | XR chest: there is perhaps some | 8.4 | 0 | 60 | | | 11 | | | | |
| na | | | | | 0 | | | | | | | | |
| na | | | XR chest : there is linear | 17.4 | 0 | 60 | | | 171 | | | | |
| na | | | | | 0 | | | | | | | | |
| na | | | | | 0 | | | | 70 | | | | |
| na | | | | | 0 | | | | | | | | |
| 0 | 24/3/2019 9:30- Result : N.A | | XR Lumbar spine : Bones are | 5.1 | 0 | 16 | | | 115 | | | | |
| na | | | | | 0 | | | | | | | | |
| na | | | | | 0 | | | | | | | | |
| na | | | | | 0 | | | | 239 | | | | |
| 1 | 23/03/2019 16:15:00 - | | | 14 | 0 | 39 | | | | | | | |
| na | | | | | 0 | | | | | | | | |
| na | | | | | 0 | | | | 90 | | | | |
| 0 | 28/3/2019 2:00 Result: No | | This plain film chest x-ray has | 9.2 | 0 | 22 | | | | | | | |
| na | | | | | 0 | | | | | | | | |
| na | | | XR shoulder Rt : there is a loss of | 15.3 | 0 | 179 | | | | | | | |
| na | | | | | 0 | | | | | | | | |
| 0 | 30/3/2019 2:50 Result: N.A | | XR Chest: No frank consolidation | 6.6 | 0 | 34 | | | | | | | |
| NA | 3/6/2019 11:30 | N.A | | | 0 | | | | | | | | |
| 1 | 19/6/2019 18:00 | No growth | | 9.7 | 0 | 176 | | | | | | | |
| NA | 24/6/2019 08:50 | N.A | | 9 | 0 | 36 | | | | | | | |
| 1 | 8/6/2019 11:10 | N.A | XR Chest: There is dense | 14 | 0 | 242 | | | | | | | |
| na | 2/6/2019 15:30 | N.A | XR Knee Rt: The bone have a | 13.4 | 0 | 164 | 3.8 | | | | | | |
| 1 | 6/6/2019 10:10 | N.A | XR Chest: Hearrt size cannont | 8.7 | 0 | 37 | | | | | | | |

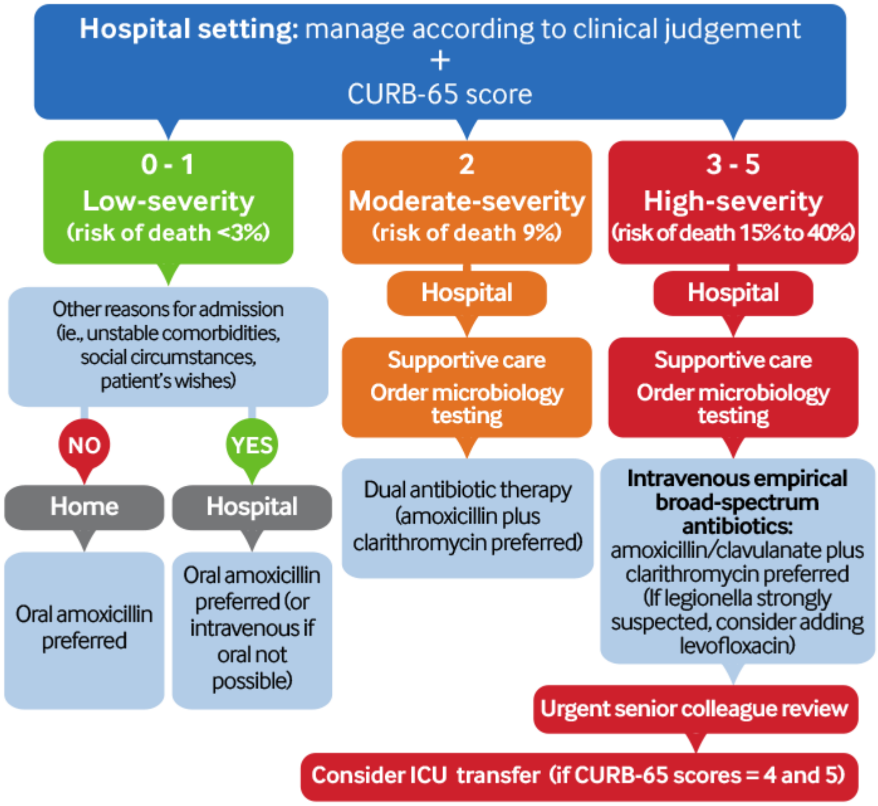
**Appendix 31.** OCTOPUS Publication, May 2023: Impact of the COVID-19 pandemic on antibiotic prescribing and antimicrobial stewardship in acute care settings (**Seven Articles**). [Access the full article by clicking here].

**Appendix 32.** The CURB-65 Risk Assessment Framework for Community-Acquired Pneumonia




| CURB-65 | Clinical Feature | Points |
|---|---|---|
| C | Confusion | 1 |
| U | Urea>7 mmol/L | 1 |
| R | RR≥30 | 1 |
| B | SBP≤90 mm Hg OR DBP≤60 mm Hg | 1 |
| 65 | Age>65 | 1 |

**Appendix 33.** Risk assessment and management of CAP in the first 4 hours of admission in an acute care setting (Bestpractice.bmj.com, 2020)



**Appendix 34.** Anonymous raw data from 640 patient medical records in 2019 and 2020. [Access from this link]

| Dempgraphic Characteristics | | | | | | | Start Smart | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Serial No | Study ID | Date of Admission | Date of Discharge | LOS (Days) | Patient Outcome (1 Discharged, 2&4 Diseased) | Abx Allergy | Symptoms on Admission | Confusion (Y=1, N=0)? | Clinical Indication | Initial Antibiotics | Frequency | Duration (Days) | Is comply with local guidelines (Y/N) | Is Abx selected for appropriate indication? (Y/N) | Is Abx dose is appropriately selected? (Y/N) | Is the duration of Abx is appropriate? (Y/N) | Is the Frequency of Abx is appropriate? (Y/N) | Route (Oral= 1, IV= 2, Both=3) | Is Route Appropriate? (Y=1, N=0)? | If IV, is there a switch to PO within 72hrs? (Y=1, N=0)? |
| 1 | BBM1 | 03/03/2019 17:00:00 | 3/21/19 17:00 | 18 | 1 | 0 | | | COPD infective exacerbation | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 500 mg Oral TWICE a day (08:30, 22:00) for 7 days | 7 | 1 | 1 | 1 | Y | Y | | | |
| 2 | BBM2 | 03/07/2019 00:00:00 | 3/11/2019 18:10 | 3 | 1 | 0 | | | LRTI | Piperacillin-tazobactam IV 4.5g (Tazocin) + | 4.5 g Intravenous Every EIGHT | 1 | 0 | 1 | 0 | N | N | | | |
| 3 | BBM3 | 03/03/2019 00:00:00 | 3/21/2019 17:00 | 18 | 1 | 0 | | | COPD infective exacerbation | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 500 mg Oral TWICE a | 7 | 1 | 1 | 1 | Y | Y | | | |
| 4 | BBM4 | 03/02/2019 00:00:00 | 3/6/2019 19:30 | 4 | 1 | 0 | | | Community Acquired Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 4 | 0 | 0 | 0 | N | Y | | | |
| 5 | BBM5 | 03/02/2019 00:00:00 | 3/6/2019 14:00 | 4 | 1 | 0 | | | Community Acquired Pneumonia | Amoxicillin 1g Injection + Clarithromycin 500 mg | DOSE: 1 g Intravenous THREE | 2 | 1 | 1 | 1 | Y | Y | | | |
| 6 | BBM6 | 03/03/2019 21:18:00 | 3/8/2019 15:30 | 4 | 1 | CLARITHROMYCIN, | SOB | | COPD infective exacerbation | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg Oral TWICE a | 4 | 1 | 1 | 1 | N | Y | 2 | 1 | N |
| 7 | BBM7 | 03/06/2019 00:00:00 | 3/27/2019 11:55 | 21 | 1 | PENICILLINS | | | Community Acquired Pneumonia | Levofloxacin PO 500mg | DOSE: 500 mg Oral In the | 2 | 1 | 1 | 1 | N | Y | 1 | 1 | |
| 8 | BBM8 | 03/06/2019 20:02:00 | 3/18/2019 14:50 | 11 | 1 | CO- | | | LRTI | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 4 | 1 | 1 | 1 | 0 | 1 | 2 | 2 | 0 |
| 9 | BBM9 | 03/07/2019 05:22:00 | 3/10/2019 17:15 | 3 | 4 | erythromycin | | | Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 3 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 |
| 10 | BBM10 | 03/09/2019 00:00:00 | 3/22/2019 10:50 | 12 | 4 | 0 | | | LRTI | Amoxicillin IV 500mg | DOSE: 500 mg Intravenous | 3 | 1 | 1 | 1 | 0 | 1 | 1 | | |
| 11 | BBM11 | 03/09/2019 23:44:00 | 3/14/2019 11:36 | 4 | 1 | 0 | | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1.2 g Intravenous Every | 4 | 1 | 1 | 1 | 0 | 1 | 3 | 1 | 0 |
| 12 | BBM12 | 03/10/2019 00:00:00 | 3/21/2019 15:25 | 11 | 1 | chloramphenicol, | | | Hospital Acquired Pneumonia | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 |
| 13 | BBM13 | 03/10/2019 00:00:00 | 3/14/2019 17:12 | 4 | 1 | AMOXICILLIN | SOB | | Chest Infection | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 3 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| 14 | BBM14 | 03/11/2019 11:18:00 | 3/15/2019 18:53 | 4 | 1 | 0 | SOB, Cough | | Chest Infection | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 3 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 1 |
| 15 | BBM15 | 03/11/2019 00:00:00 | 3/18/2019 12:20 | 6 | 1 | 0 | | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1200 mg Intravenous | 5 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 0 |
| 16 | BBM16 | 03/11/2019 00:00:00 | 3/18/2019 20:30 | 6 | 1 | 0 | | | Chest Infection | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 |
| 17 | BBM17 | 3/13/2019 16:47 | 3/21/2019 15:00 | 7 | 1 | 0 | | | LRTI | Co-amoxiclav 500/125mg Tablets | DOSE: 1 Tablet Oral THREE | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 18 | BBM18 | 3/13/2019 22:22 | 3/22/2019 18:30 | 8 | 1 | 0 | SOB,fever=38.4, | | Pneumonia | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 |
| 19 | BBM19 | 3/14/2019 0:25 | 5/16/2019 17:10 | 63 | 1 | 0 | | | Hospital Acquired Pneumonia | Levofloxacin PO 500mg | DOSE: 500 mg Oral TWICE a | 4 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | |
| 20 | BBM20 | 3/14/2019 18:18 | 3/27/2019 14:30 | 12 | 1 | CLARITHROMYCIN, | SOB, Cough | | Viral Pneumonia | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 2 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 1 |
| 21 | BBM21 | 3/15/2019 16:30 | 3/20/2019 13:00 | 4 | 1 | PENICILLINS, | | | Ventilator Pneumonia (VAP) | Ciprofloxacin 500 mg | DOSE: 500 mg Oral TWICE a | 4 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | |
| 22 | BBM22 | 3/15/2019 23:29 | 3/29/2019 11:53 | 13 | 1 | 0 | | | Chest Infection | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 2 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| 23 | BBM23 | 3/15/2019 23:48 | 4/11/2019 09:15 | 26 | 4 | 0 | | | LRTI | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 3 | 0 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| 24 | BBM24 | 3/16/2019 8:22 | 3/19/2019 7:00 | 2 | 4 | 0 | | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1200 mg Intravenous | 3 | 0 | 1 | 1 | 0 | 1 | 3 | 0 | 1 |
| 25 | BBM25 | 3/16/2019 20:33 | 3/19/2019 18:30 | 2 | 1 | 0 | | | Hospital Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| 26 | BBM26 | 3/17/2019 2:03 | 3/21/2019 13:40 | 4 | 1 | FLUCLOXACILLIN, | | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| 27 | BBM27 | 3/17/2019 12:31 | 3/24/2019 11:40 | 6 | 4 | 0 | | | Chest Infection | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 5 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 |
| 28 | BBM28 | 3/19/2019 2:53 | 3/28/2019 14:15 | 9 | 1 | 0 | | | LRTI | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 3 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| 29 | BBM29 | 3/19/2019 19:59 | 4/3/2019 10:30 | 14 | 1 | 0 | | | LRTI | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| 30 | BBM30 | 3/19/2019 23:03 | 4/18/2019 10:30 | 29 | 1 | 0 | | | Hospital Acquired Pneumonia | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 3 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 1 |
| 31 | BBM31 | 3/21/2019 18:33 | 4/7/2019 18:00 | 16 | 1 | 0 | | | COPD infective exacerbation | Co-amoxiclav IV 1.2 | DOSE: 1200 mg Intravenous | 7 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 0 |
| 32 | BBM32 | 3/22/2019 17:56 | 4/2/2019 17:00 | 10 | 1 | 0 | SOb, cough, | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1200 mg Intravenous | 4 | 1 | 1 | 1 | 0 | 1 | 3 | 1 | 0 |
| 33 | BBM33 | 3/22/2019 23:44 | 3/30/2019 21:31 | 7 | 4 | PENICILLINS - | | | Community Acquired Pneumonia | Levofloxacin PO 500mg | DOSE: 500 mg Oral TWICE a | 2 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | |
| 34 | BBM34 | 3/23/2019 1:17 | 4/5/2019 09:30 | 13 | 1 | meropenem | | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| 35 | BBM35 | 3/25/2019 3:40 | 4/8/2019 13:50 | 14 | 1 | 0 | | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 4 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 0 |
| 36 | BBM36 | 3/25/2019 22:54 | 3/29/2019 19:10 | 3 | 1 | 0 | | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1200 mg Intravenous | 2 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 1 |
| 37 | BBM37 | 3/26/2019 3:54 | 3/31/2019 17:00 | 5 | 1 | erythromycin | | | Chest Infection | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 2 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 |
| 38 | BBM38 | 3/26/2019 11:43 | 4/6/2019 16:30 | 11 | 4 | 0 | | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1.2 g Intravenous Every | 6 | 1 | 1 | 1 | 1 | 1 | 3 | 1 | 0 |
| 39 | BBM39 | 3/27/2019 6:58 | 3/29/2019 9:00 | 2 | 1 | CO-AMOXICLAV | | | Chest Infection | levofloxacin 500mg/100ml Infusion | DOSE: 500 mg (100ml) | 2 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 1 |
| 40 | BBM40 | 3/29/2019 19:18 | 4/4/2019 13:45 | 5 | 1 | 0 | SOB, Cough, | | Community Acquired Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1200 mg Intravenous | 5 | 0 | 1 | 1 | 1 | 1 | 3 | 0 | 0 |
| 41 | BBJ1 | 06/03/2019 13:46:00 | 6/26/2019 15:30 | 23 | 1 | 0 | | | Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 7 | 0 | 1 | 1 | 1 | 1 | 2 | 1 | 0 |
| 42 | BBJ2 | 6/19/2019 19:44 | 6/23/2019 15:00 | 5 | 1 | 0 | | | LRTI | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1200 mg Intravenous | 3 | 0 | 1 | 1 | 0 | 1 | 3 | 1 | 1 |
| 43 | BBJ3 | 6/21/2019 1:13 | 6/26/2019 20:15 | 5 | 1 | 0 | | | Community Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1.2 g Intravenous Every | 4 | 0 | 1 | 1 | 1 | 1 | 2 | 1 | 0 |
| 44 | BBJ4 | 06/06/2019 04:20:00 | 06/08/2019 20:13:00 | 2 | 1 | METRONIDAZOLE | | | Pneumonia | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1.2 g Intravenous | 1 | 0 | 1 | 1 | 0 | 1 | 3 | 1 | 1 |
| 45 | BBJ5 | 06/01/2019 00:06:00 | 06/12/2019 16:50:00 | 11 | 1 | 0 | | | LRTI | Co-amoxiclavIV 1.2g + Clarithromycin Oral 500mg | DOSE: 1.2 g Intravenous Every | 0 | 0 | Y | N | N | Y | 0 | 0 | 0 |
| 46 | BBJ6 | 06/03/2019 16:49:00 | 6/18/2019 17:10 | 15 | 1 | CO-TRIMOXAZOLE | | | Hospital Acquired Pneumonia | Co-amoxiclav IV 1.2 | DOSE: 1200 mg Intravenous | 10 | 0 | N | N | Y | Y | 2 | 1 | 0 |
| 47 | BBJ7 | 06/03/2019 16:49:00 | 6/30/2019 10:55 | 26 | 4 | 0 | | | Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 1 | 0 | N | N | N | Y | 2 | 1 | 1 |
| 48 | BBJ8 | 06/03/2019 17:37:00 | 06/09/2019 18:58:00 | 6 | 4 | 0 | | | Aspiration Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 2 | 0 | N | N | N | Y | 2 | 1 | 1 |
| 49 | BBJ9 | 06/03/2019 20:58:00 | 06/12/2019 13:15:00 | 8 | 4 | 0 | | | Community Acquired Pneumonia | Piperacillin-tazobactam IV 4.5g (Tazocin) | DOSE: 4.5 g Intravenous Every | 9 | 0 | N | N | N | Y | | | |

| Then Focus | | | | Co-morbiditis | | | | | | | | | | | | | | | | | | Blood Culture | | | Investigation | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day of review | Type of intervention (Change, De-escalate, IV-to-Oral, Stop) | Name of antibiotic changed | Is Abx selected after reviewing appropriate? (Y=1, N=0)? | HTN | PE | Hypotension | AF | HF | Hypercholesterimia | DM | Hypothyroidism or Thyroid | Kidney | Liver | Malignancy | Bronchiectasis | OA | Asthma | COPD | Dementia | Epilepsy | Depression | Did culture sent to Mic prior to Abx (Y/N) | Culture Time Collection | Blood Culture Result | X-Ray Finding | WBCs count | PCT | CRP | D Dimer | Urea |
| 7 | IV-to-Oral Switch | Co-amoxiclavIV 1.2g | | | | | | | | | | | | | | | | | | | | Y | | | Increase in airspace opacification | 15.8 | 0 | 264 | | |
| 1 | IV-to-Oral Switch | Co-amoxiclavIV | | | | | | | | | | | | | | | | | | | | | 7/3 at 15:52 | S | No active lung biology seen | 16.7 | 0 | 142 | | |
| 7 | IV-to-Oral Switch | Co-amoxiclavIV | | | | | | | 1 | 1 | | | | | 1 | | | | | | | Y | C.T: | N.A | T.X-RAY: 3/3/2019 3:14 ----- T.R: 9/3/2019 13:10 | 15.8 | 0 | 246 | | |
| 4 | Continue Antibiotics | Piperacillin 4g + | | | | | | | | | | | | | | | | | | | | | C.T:3/3/201 | No growth | T.X-RAY: 2/3/2019 01:38 ---- T.R: 5/3/2019 15:11 | 2.4 | 0 | 155 | | |
| 2 | IV-to-Oral Switch | | | | | | | | | | | | | | | 1 | 1 | | | | 1 | | C.T: | No growth | T.X.RAY:2/3/2019 ---- T.R: 5/3/2019 15:13 Lungs are clear | 2.8 | 0 | 9 | | |
| 4 | IV-to-Oral Switch | | | 1 | | | | | | | 1 | | | | | 1 | | 1 | | | | | | | | | 0 | | | |
| 2 | Stop Antibiotics | | | | | 1 | | | | | | | | | | | 1 | 1 | | | | | C.T: | N.A | T.X-RAY: 5/3/2019 22:53 ---- T.R: 10/3/2019 13:30 | 7.2 | 0 | 36 | | |
| 4 | IV-to-Oral Switch | | | 1 | 1 | | | | | | | | | | 1 | | 1 | | | | | NA | | | | | 0 | | | |
| 3 | Change antibiotic | metronidazole | | 1 | 1 | | | | | | | 1 | | 1 | | | | | | | | NA | | | | | 0 | | | |
| 3 | Escalation | piperacillin 4g + | | | | | | | | | | | | | | | | | | | | 1 | C.T: | N.A | T.X-RAY: 9/3/2019 21:00 ---- T.R: 12/3/2019 08:40 Injury to right lower | 17 | 0 | 321 | | |
| 4 | De-escalation | | | | | | 1 | | 1 | | | | | | | 1 | | | 1 | 1 | | NA | | | | | 0 | | | |
| 2 | IV-to-Oral Switch | | | 1 | | | | | | | | | | | | | 1 | | 1 | | | 1 | C.T: | N.A | T.X-RAY: 10/3/2019 05:18 ---- T.R: 10/3/2019 11:37 The lungs are | 14.1 | 0 | 87 | | |
| 3 | IV-to-Oral Switch | | | 1 | 1 | | | | | | | | | | | | | | | | | 1 | C.T: | N.A | T.XRAY: 10/3/2019 18:46 ---- T.R:14/3/2019 21:04 | 12.9 | 0 | 95 | | |
| 3 | IV-to-Oral Switch | | | 1 | | | | | | 1 | | | | | | | | | | | | NA | | | | | 0 | | | |
| 5 | IV-to-Oral Switch | | | 1 | | | | | 1 | | | | | | | | | | | | | 1 | C.T: | N.A | T.X-RAY Shoulder: 12:3:2019 11:26 --- T.R: 12/3/2019 12:30 ///// T.X- | 11 | 0 | 94 | | |
| 2 | Escalation | piperacillin 4g + | not appro | 1 | | | | | 1 | | | | | | | | | | | | | 0 | C.T: | N.A | | 11.2 | 0 | 149 | | |
| 7 | Stop Antibiotics | | | | | | | 1 | | | | | | | | | | | | | | 0 | 15/03/2019 | | The left base is not well demonstrated due to overlying cardiac | 10.6 | 0 | 90 | | |
| 2 | Change antibiotic | piperacillin 4g + | | | | | | | | | | | | | | | 1 | | | | | 1 | 13/03/2019 | | XR chest: There is worsening of the previosly described appearance of | 10.2 | 0 | 103 | | |
| 4 | Continue Antibiotics | | | | | | 1 | | | | | | | | | 1 | | | | | | 1 | 15/03/2019 | | XR Hip Lt : there is an impacted fracture through the neck of the left | 6.9 | 0 | | | |
| 2 | Stop Antibiotics | | | 1 | | | | | | 1 | 1 | | | | | | | | | | | 0 | 23/03/2019 | | XR chest: Cardiomegaly noted, CTR= 0.54 the lungs are clear | 19.5 | 0 | 23 | | |
| 4 | Escalation | vancomycin | 1 | 1 | | | 1 | | 1 | 1 | | 1 | | | | | 1 | | | | | na | | | XR chest : chronic bronchitic type chest with emphysema.small bilateral | 9.5 | 0 | 137 | | |
| 2 | Change antibiotic | meropenem | 1 | | | | | | | | | | | | | | | | | | | na | | | XR chest : there is some linear opacification in the lower zone | 2.1 | 0 | 192 | | |
| 3 | Stop Antibiotics | | | | | | | | | | | 1 | | 1 | | | | | 1 | | | 1 | 15/3/2019 | | XR chest: there is perhaps some increased airapaceopacification in the | 8.4 | 0 | 60 | | |
| 3 | Stop Antibiotics | | | | | | 1 | | | | | | | | | | | | | | | na | | | | | 0 | | | |
| 2 | IV-to-Oral Switch | | | | | | | | | | | | | | | | | | 1 | | | na | | | XR chest : there is linear atelectasis across the left lung mid zone. some | 17.4 | 0 | 60 | | |
| 2 | Escalation | piperacillin 4g + | 1 | 1 | | | | | | | | | | | 1 | | | | | | | na | | | | | 0 | | | |
| 5 | Stop Antibiotics | | | | | | | | 1 | | | | | | | | | | | | | na | | | | | 0 | | | |
| 3 | Stop Antibiotics | | | | | | | | | | | | | | | | | | | | | na | | | | | 0 | | | |
| 2 | IV-to-Oral Switch | | | | | | | | 1 | 1 | | | | | | 1 | | | | | | 0 | 24/3/2019 | | XR Lumbar spine : Bones are generally osteopaenic with a loss of | 5.1 | 0 | 16 | | |
| 3 | IV-to-Oral Switch | | | 1 | | | | | | | | | | | | | 1 | | | | | na | | | | | 0 | | | |
| 7 | Stop Antibiotics | | | 1 | | | | | | | | | | | | | 1 | 1 | | | | na | | | | | 0 | | | |
| 4 | Escalation | piperacillin 4g + | 0 | | | | 1 | | 1 | 1 | | 1 | | | | | | | | | | na | | | | | 0 | | | |
| 2 | Escalation | levofloxacin | 1 | 1 | | | | | 1 | | | | | | | | | | | | | 1 | 23/03/2019 | | | 14 | 0 | 39 | | |
| 2 | IV-to-Oral Switch | | | | | | | | | | | 1 | | | | | | | | | | na | | | | | 0 | | | |
| 4 | Escalation | piperacillin 4g + | 0 | | | | | | | | | | | | | | | | | | | na | | | | | 0 | | | |
| 2 | Escalation | piperacillin 4g + | 0 | 1 | | | | 1 | | | | | | | | | | | | | | 0 | 28/3/2019 | | This plain film chest x-ray has been surperseded by a HRCT scan dated | 9.2 | 0 | 22 | | |
| 2 | Stop Antibiotics | | | | | | | | | | | | | | | | | | | | | na | | | | | 0 | | | |
| 6 | Escalation | piperacillin 4g + | | | | 1 | 1 | | | | | | | 1 | | | | 1 | | | | na | | | XR shoulder Rt : there is a loss of subacromial space with the right | 15.3 | 0 | 179 | | |
| 2 | Stop Antibiotics | | | | | | | | | | | | | | | | | | | | | na | | | | | 0 | | | |
| 5 | Stop Antibiotics | | | 1 | | | 1 | | | | | | | | | | | | | | | 0 | 30/3/2019 | | XR Chest: No frank consolidation or pulmonary oedema. No significant | 6.6 | 0 | 34 | | |
| 7 | IV-to-Oral Switch | | | | | | | | | | | | | | | | | | | | | NA | ########## | N.A | | | 0 | | | |
| 3 | Escalation | piperacillin 4g + | | | | | | | | | 1 | | | | | | | | | | | 1 | ########## | No growth | | 9.7 | 0 | 176 | | |
| 4 | Escalation | piperacillin 4g + | | | | | | | | | | | | | | | | | | | | NA | ########## | N.A | | 9 | 0 | 36 | | |
| 1 | IV-to-Oral Switch | | | | | | | | | | | | | | | | | | | | | 1 | ########## | N.A | XR Chest: There is dense Consolidation of the right lower zone | 14 | 0 | 242 | | |
| 0 | No Intervention | | | | | | | | | | | | | | | | | | | | | na | ########## | N.A | XR Knee Rt: The bone have a dysplastic appearance and are generally | 13.4 | 0 | 164 | 3.8 | |
| 10 | Escalation | piperacillin 4g + | | 1 | | | | | | | | | | | | | | | | | | 1 | ########## | N.A | XR Chest: Hearrt size cannont accurately be assessed. There is | 8.7 | 0 | 37 | | |
| 1 | IV-to-Oral Switch | Co-amoxiclav | | | | | | | | | | | | | | | | | | | | 1 | ########## | N.A | | 8.6 | 0 | 83 | | |
| 2 | Stop Antibiotics | | | 1 | | | 1 | | | | | 1 | | | | | | | | | | na | 3/6/2019 | Growth | | 8.3 | 0 | 127 | | |
| 9 | Change antibiotic | Clarithromycin | | 1 | | | | | | | | 1 | | 1 | | | | | | | | 0 | ########## | N.A | XR Chest: There is background pulmonary congestion. There is | 10.4 | 0 | 50 | | 12.9 |

**Appendix 35.** Antimicrobial Stewardship Case Presentation #1

**Introduction:**

Study ID: LDM37

Patient Age: 42

Diagnosis: COVID Pneumonia

Gender: Male

**Case Presentation:**

A 42-year-old male was admitted on 21/04/2023 due to haemoptysis, shortness of breath, and cough. He reported testing positive for COVID-19 four weeks prior to admission. A CTPA revealed superadded cystic lung disease with cysts in the right lung, large bullae, and possible blood within the bullae. A CT scan suggested chronic Langerhans histiocytosis. He was treated with tranexamic acid, PRN adrenaline nebs, and IV antibiotics. His condition improved after completing a 14-day course of antibiotics, and he was deemed medically fit for discharge.

**Co-morbidities:** Hypertension, Heart failure and Diabetes Mellitus

**Symptoms on Admission:** Fever 38 C, Cough and Shortness of Breath (SOB)

**Lab Tests and Investigations:**

- Serum Creatinine: 66 μmol/L

- Urea: 4.4 mmol/L

- WBCs: 9.2 x 10^9/L

- CRP: 145 mg/L

- D Dimer: 1.31 μg/mL

- X-Ray: No focal area of consolidation is identified. No pleural effusion

- CT Scan: Chronic Langerhans histiocytosis

- CT Neck (24/04): Left-sided loculated pneumothorax, new dense bi-basal consolidation, left pleural effusion, decreased pneumomediastinum volume, large locule of gas para oesophagus, reactive nodes.

- Culture Results: No growth

**Treatment and Actions Taken:**

1. Co-amoxiclav IV: 5 days (21/04 - 25/04)

2. Clarithromycin PO: 4 days (22/04 - 25/04)

3. Tazocin and Linezolid for lung abscess:

   - Linezolid: 13 days (25/04 - 07/05)

- Tazocin: 9 days (25/04 - 03/05)

4. Meropenem: 5 days (03/05 - 07/05)

5. Co-amoxiclav PO: Started 08/05, continued for 2 weeks post-discharge

**Result:**

The patient completed a 14-day course of antibiotics, showing significant improvement with no further haemoptysis. His chest pain subsided, and his breathing improved. He remained stable on room air, with stable observations and blood test results. He was deemed medically fit for discharge.

**Discussion:**

This case study of a 42-year-old male diagnosed with COVID-19 pneumonia highlights the importance of a personalised and adaptive approach to antimicrobial therapy. The patient's complex presentation, including comorbidities such as hypertension, heart failure, and diabetes mellitus, as well as the presence of chronic Langerhans histiocytosis, posed a challenge in determining the most effective treatment regimen.

The patient was treated with multiple antibiotics, including Co-amoxiclav, Clarithromycin, Tazocin, Linezolid, and Meropenem. The antibiotics were prescribed based on the patient's clinical presentation, results from imaging studies, and culture results. The treatment regimen was periodically adjusted based on the patient's progress, with the addition or removal of specific antibiotics as needed.

The patient's improvement following the 14-day course of antibiotics demonstrates the effectiveness of this approach. The resolution of haemoptysis, chest pain, and breathing difficulties, as well as stable blood test results and observations, indicate successful management of the infection.

**Conclusion:**

In conclusion, this case study emphasises the importance of an individualised and dynamic approach to antimicrobial stewardship in patients with complex presentations. By carefully monitoring the patient's progress, assessing the effectiveness of the antibiotic regimen, and adjusting treatment as needed, healthcare providers can optimise the management of infections and ensure the best possible outcomes for their patients. This case also highlights the importance of a multidisciplinary approach, with input from various healthcare professionals, in managing patients with complicated infections like COVID-19 pneumonia.

**Appendix 36.** Antimicrobial Case Study 2: BDS30

**Patient Profile:**

- Age: 80
- Gender: Male
- Diagnosis: Community-acquired pneumonia (CAP)
- Medical History: COPD, previous NSTEMI (2017), angina, CKD, AF, last echo (2017) with good LV function

**Clinical Presentation:**

The patient presented with a three-week history of general malaise, fatigue, lethargy, shortness of breath, non-productive cough, intermittent sharp chest pain (worse with deep inspiration and coughing), diarrhoea, vomiting, reduced appetite, and fever. He was unable to leave the house due to shortness of breath. Upon paramedic arrival, the patient was hypotensive (84/50 mmHg) and mildly hypoxic (93% $SpO_2$).

**Lab Tests:**

- Serum Creatinine: Decreased from 221 to 159 µmol/L
- CRP: Decreased from 180 to 41 mg/L

**Investigation:**

- X-ray: No confluent consolidation or collapse, chronic background changes, no pneumothorax, heart size assessment inconclusive.

**Treatment and Management:**

The patient was initially started on Levofloxacin for lower respiratory tract infection. Upon review by the pharmacist, the medication was ceased due to a hazy CXR and blood results showing the patient was in AKI. The patient was treated with intravenous fluids (IVF) for AKI, which resolved, with serum creatinine decreasing from a peak of 221 to 159 µmol/L. The patient's CRP levels also decreased from 180 to 41 mg/L.

**Outcome:**

The patient's AKI resolved, and he was discharged to complete a 10-day course of Levofloxacin 500mg tablets for the treatment of CAP.

**Discussion:**

The key points to consider in this case are the patient's age, medical history, and the multidisciplinary approach taken to manage the community-acquired pneumonia (CAP) and acute kidney injury (AKI).

1. Age and medical history: The patient's age and complex medical history, including COPD, previous NSTEMI, angina, CKD, and AF, made him more susceptible to CAP and potential complications during treatment. These factors likely contributed to the patient's severe symptoms, such as shortness of breath and hypotension. It is essential to consider the patient's medical history and potential comorbidities when selecting appropriate antimicrobial treatment.

2. Diagnosis and investigation: The diagnosis of CAP was supported by the patient's clinical presentation, with symptoms such as fever, cough, and shortness of breath. However, the X-ray findings were not conclusive for CAP, and the patient's AKI complicated the diagnosis. This highlights the importance of using both clinical and laboratory findings to support the diagnosis and treatment of CAP.

3. Treatment and management: Levofloxacin, a fluoroquinolone, was initially chosen to treat the lower respiratory tract infection. Fluoroquinolones are broad-spectrum antibiotics and are often used to treat CAP. However, this case demonstrates the importance of a multidisciplinary approach, with the pharmacist reviewing the patient's medication and recognising the potential for drug-induced AKI. The decision to cease Levofloxacin and treat it with intravenous fluids was crucial in managing the patient's AKI and allowing for renal recovery.

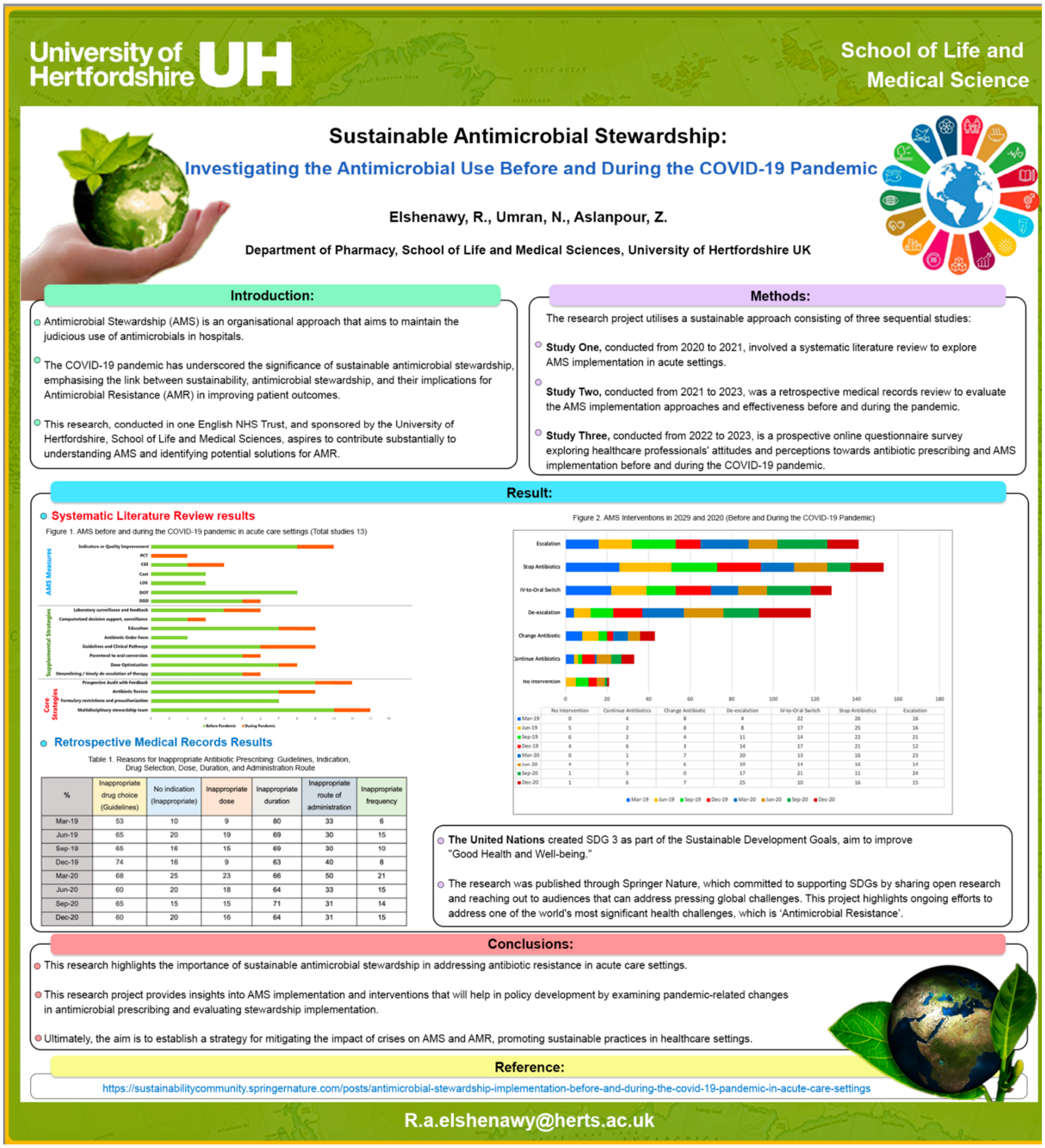
4. Outcome and follow-up: With the resolution of AKI, the patient was discharged to complete a 10-day course of Levofloxacin. This highlights the importance of monitoring and adjusting treatment based on patient response and clinical parameters. The multidisciplinary team's collaboration and timely interventions were crucial in achieving a positive outcome for the patient.

5. Implications for practice: This case highlights the importance of a multidisciplinary approach when managing patients with complex medical histories and conditions, such as CAP and AKI. Timely review and adjustments to antibiotic treatment, as well as close monitoring of renal function, are essential for optimising patient outcomes. Healthcare professionals should be vigilant in recognising and managing potential complications and tailor treatment to the specific needs and medical history of the patient.

**Conclusion:**

In this case of an 80-year-old male with a complex medical history, the patient was successfully treated for community-acquired pneumonia (CAP) and acute kidney injury (AKI). The multidisciplinary approach, including timely pharmacist review and adjustment of the antibiotic regimen, was crucial in achieving a positive outcome for the patient.

**Appendix 37.** Sustainable Antimicrobial Stewardship: Investigating the Antimicrobial Use Before and During the COVID-19 Pandemic - Awarded 2nd Place in Poster Presentation, June 2023.



**Appendix 38.** Poster Presentation at LMS: Antibiotic Prescribing: A Retrospective Study from One English National Health Service (NHS) Foundation Trusts Before And During The COVID-19 Pandemic, June 2023.

University of Hertfordshire UH

Department of Pharmacy
School of Life and Medical Sciences

## ANTIBIOTIC PRESCRIBING: A RETROSPECTIVE STUDY FROM ONE ENGLISH NATIONAL HEALTH SERVICE (NHS) FOUNDATION TRUSTS BEFORE AND DURING THE COVID-19 PANDEMIC

Author: Elshenawy **R.**; Supervisors: Umaru **N.**, Aslanpour **Z.**
Department of Pharmacy, School of Life and Medical Sciences, University of Hertfordshire, UK

**Introduction**

The global increase in multi-drug-resistant infections presents a substantial health risk, leading to heightened disease, death, and economic impact. A UK review in 2016 estimated a devastating 10 million deaths annually by 2050 due to Antimicrobial Resistance (AMR). This study seeks to understand the antibiotic prescribing practices and Antimicrobial Stewardship (AMS) before and during the COVID-19 pandemic in acute care settings within the context of the growing threat posed by AMR.

**Method**

In an English NHS Trust, a cross-sectional retrospective study was carried out to assess antibiotic prescribing practices. The study analysed data retrieved from the electronic medical records of adult patients diagnosed with Respiratory Tract Infections (RTIs). In order to evaluate antibiotic prescribing and determine the impact of COVID-19 on such practices, data were drawn from eight-time points across 2019 and 2020 before and during the COVID-19 pandemic. The gold standard, Access, Watch, Reserve (AWaRe) classification of the World Health Organisation (WHO), which provides short clinical guidance on the management of common infections, is used in this study to analyse antibiotic categorisation (www.who.int, 2021).

**Result**

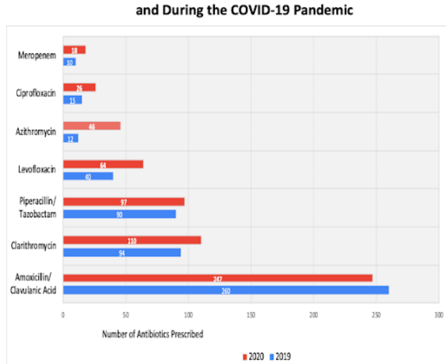
**Table 1.** The heatmap for antibiotic use in 2019 and 2020 is based on AWaRe criteria.

WHO Access, Watch, Reserve (AWaRe) classification for antibiotics evaluation and monitoring before and during the COVID-19 pandemic

| | Mar-19 | Jun-19 | Sep-19 | Dec-19 | Mar-20 | Jun-20 | Sep-20 | Dec-20 |
|---|---|---|---|---|---|---|---|---|
| **Access** | | | | | | | | |
| Amoxicillin | 2 | 1 | 2 | 3 | 6 | 6 | 0 | 1 |
| Amoxicillin/clavulanic acid | 67 | 61 | 56 | 76 | 25 | 70 | 86 | 66 |
| Benzylpenicillin | 1 | 0 | 2 | 0 | 3 | 0 | 0 | 0 |
| Doxycycline | 1 | 1 | 3 | 2 | 1 | 2 | 0 | 1 |
| Flucloxacillin | 2 | 2 | 3 | 2 | 0 | 5 | 2 | 1 |
| Gentamicin | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 |
| Metronidazole | 3 | 7 | 2 | 0 | 4 | 4 | 2 | 4 |
| Sulfamethoxazole/Trimethoprim | 0 | 1 | 1 | 0 | 4 | 2 | 0 | 0 |
| Clindamycin | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cephalexin | 0 | 0 | 2 | 1 | 1 | 0 | 0 | 0 |
| **Watch** | | | | | | | | |
| Azithromycin | 0 | 1 | 2 | 0 | 13 | 19 | 3 | 11 |
| Ceftazidime | 2 | 2 | 0 | 0 | 0 | 1 | 0 | 0 |
| Ceftriaxone | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 |
| Cefuroxime | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Ciprofloxacin | 3 | 3 | 1 | 8 | 7 | 5 | 9 | 5 |
| Clarithromycin | 14 | 21 | 26 | 33 | 32 | 21 | 25 | 32 |
| Levofloxacin | 12 | 9 | 8 | 11 | 14 | 13 | 14 | 23 |
| Meropenem | 2 | 0 | 1 | 1 | 5 | 4 | 4 | 5 |
| Piperacillin/Tazobactam | 29 | 30 | 15 | 16 | 29 | 21 | 22 | 25 |
| Teicoplanin | 0 | 0 | 1 | 0 | 3 | 0 | 0 | 0 |
| Vancomycin | 1 | 4 | 0 | 1 | 0 | 1 | 0 | 0 |
| **Reserve** | | | | | | | | |
| Aztreonam | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| Cefazidime/Azobactam | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| Linezolid | 3 | 2 | 1 | 1 | 0 | 0 | 1 | 1 |

0: Absence of antibiotic usage
1 - 9: Minimal antibiotic consumption
0 - 29: Moderate level of antibiotic usage
30 and above: High level of antibiotic consumption

**Figure 1.** The Seven Most Commonly Prescribed Antibiotics Before and During the COVID-19 Pandemic




**Conclusion**

The COVID-19 pandemic has influenced antibiotic prescription patterns, leading to increased use of specific antibiotics, such as Azithromycin and Amoxiclav. Such shifts in practice, if unchecked, may potentiate antimicrobial resistance and endanger patient lives. Therefore, the continuous implementation of antimicrobial stewardship measures is paramount to sustain the judicious use of antibiotics and mitigate the associated risks.

**Reference**

www.who.int. (2021). 2021 AWaRe classification. [online] Available at: https://www.who.int/publications/i/item/2021-aware-classification.

R.a.elshenawy@herts.ac.uk

**Appendix 39.** Achievement Certificate: E-Learning Refresher on Good Clinical Practice (GCP), June 2, 2023.

NIHR | National Institute for Health and Care Research

*Issued by:*
Clinical Research Network
Coordinating Centre

# CERTIFICATE OF ACHIEVEMENT

**Rasha Abdelsalam Elshenawy**

has completed the course:

**Good Clinical Practice (GCP) Refresher ELearning**

June 2, 2023

**Modules Completed**

- Good Clinical Practice (GCP) Refresher: Revisiting Key Concepts
- GCP Refresher Hot Topics
- Good Clinical Practice (GCP) Refresher: Reflecting on your own practice and experience

This course is worth 3 CPD Credits

CPD®
The CPD Certification Service

Version: May 2022

**Appendix 40.** Letter of Confirmation: Research Project Capacity and Capability at Bedfordshire Hospitals NHS Foundation Trust, June 2023. Available Here.

NHS
Bedfordshire Hospitals
NHS Foundation Trust

www.bedfordshirehospitals.nhs.uk

**Re: IRAS No: 314805** **7th June 2023**

**Confirmation of Capacity and Capability at Luton and Dunstable University Hospital**

**Full Study Title: An investigation into factors affecting the implementation of Antimicrobial Stewardship (AMS) before and during the COVID-19 pandemic in two acute care settings**

This letter confirms that **Bedfordshire Hospitals NHS Foundation Trust** has the capacity and capability to deliver the above referenced study. Please find attached our agreed Organisation Information Document as confirmation.

We agree to start this study on 12th June 2023.

I would like to take this opportunity of informing you that should any amendments be made to the study, e.g. Protocol, Information Sheet, Consent Form, etc. it is your responsibility to inform not only the Health Research Authority / Research Ethics Committee but also the Research & Development Department of these changes at Research.Development@bedsft.nhs.uk .

Please ensure that, Research and Development are copied into all monitoring correspondence, including requesting monitoring visits and monitoring reports. At the end of the study, please send documented evidence that the findings of the study have been published.

**NOTE TO PRINCIPAL INVESTIGATOR:** You are required to recruit the first participant within 30 days of this confirmation email.

If you wish to discuss further, please do not hesitate to contact the Research & Development Department.

Kind regards.

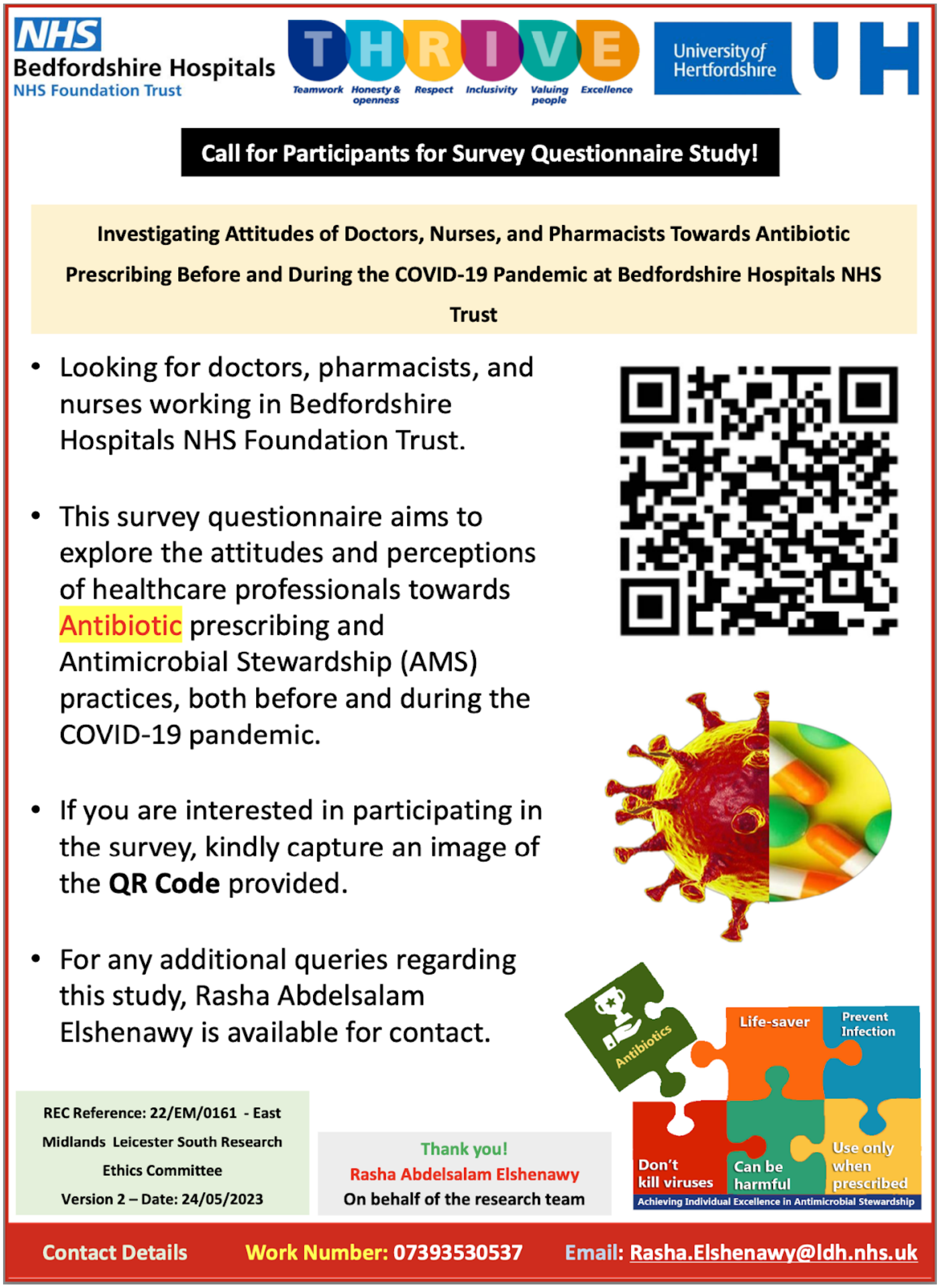
Louise Tate

Margaret Louise Tate
Research and Development Manager
Luton and Dunstable University Hospital
Lewsey Road
Luton
LU4 0DZ

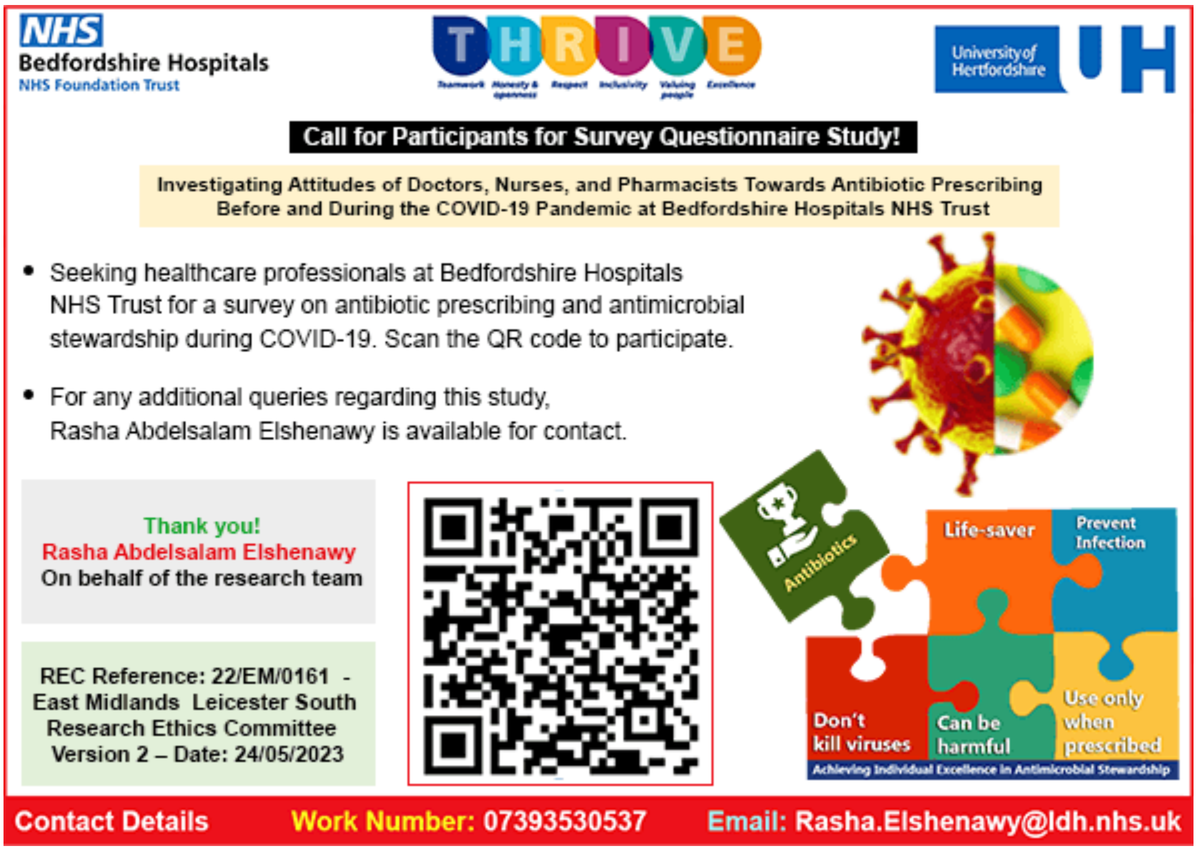
Contact:
R&D Manager - Margaret Louise Tate
Tel: - 01582 718242
Email: - margaret.tate@bedsft.nhs.uk

Chair: Simon Linnett
Chief Executive: David Carter

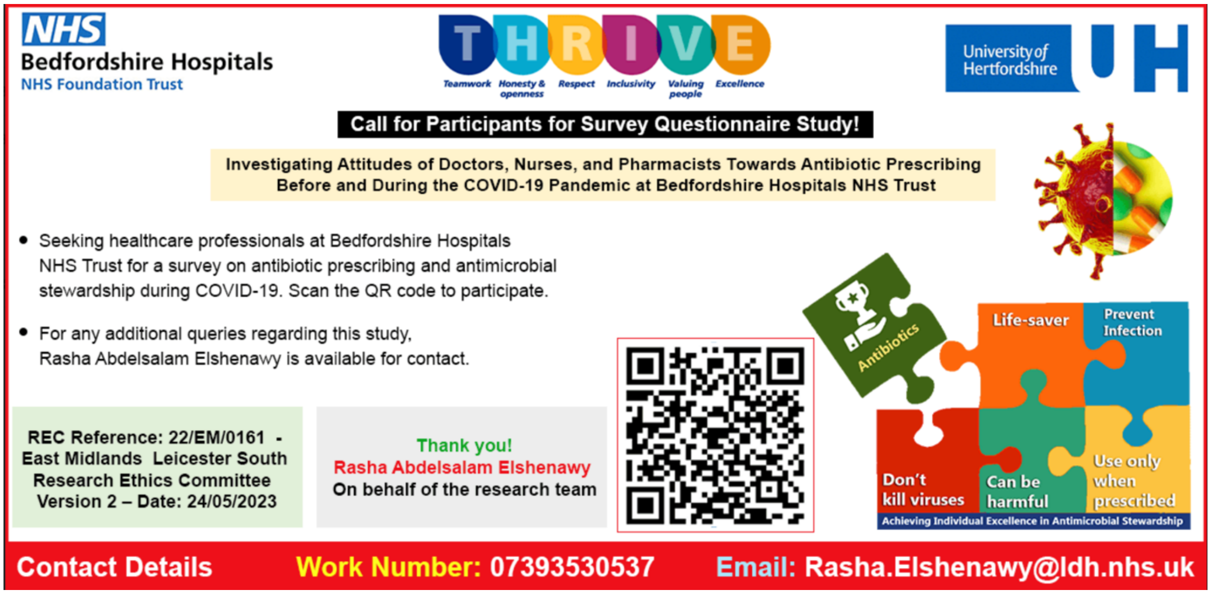
**Appendix 41.** Professional A4 Poster for Healthcare Professionals: Distributed Across All Wards and Departments of Bedfordshire Hospitals NHS Foundation Trust, Including Luton and Dunstable Hospital and Bedfordshire Hospital.



**Appendix 42.** A5 Professional Poster for Healthcare Staff: Displayed at Nurses' Stations, Staff Lounges, Medicine Trolleys, Main Workstations, MDT Rooms, Beside Doctors' Desks, and Notice Boards. Further placements include Medicine Rooms, IV Antibiotic Cabinets in Clean and Treatment Rooms, ensuring widespread visibility across Bedfordshire Hospitals NHS Foundation Trust - Luton & Dunstable Hospital, and Bedfordshire Hospital.



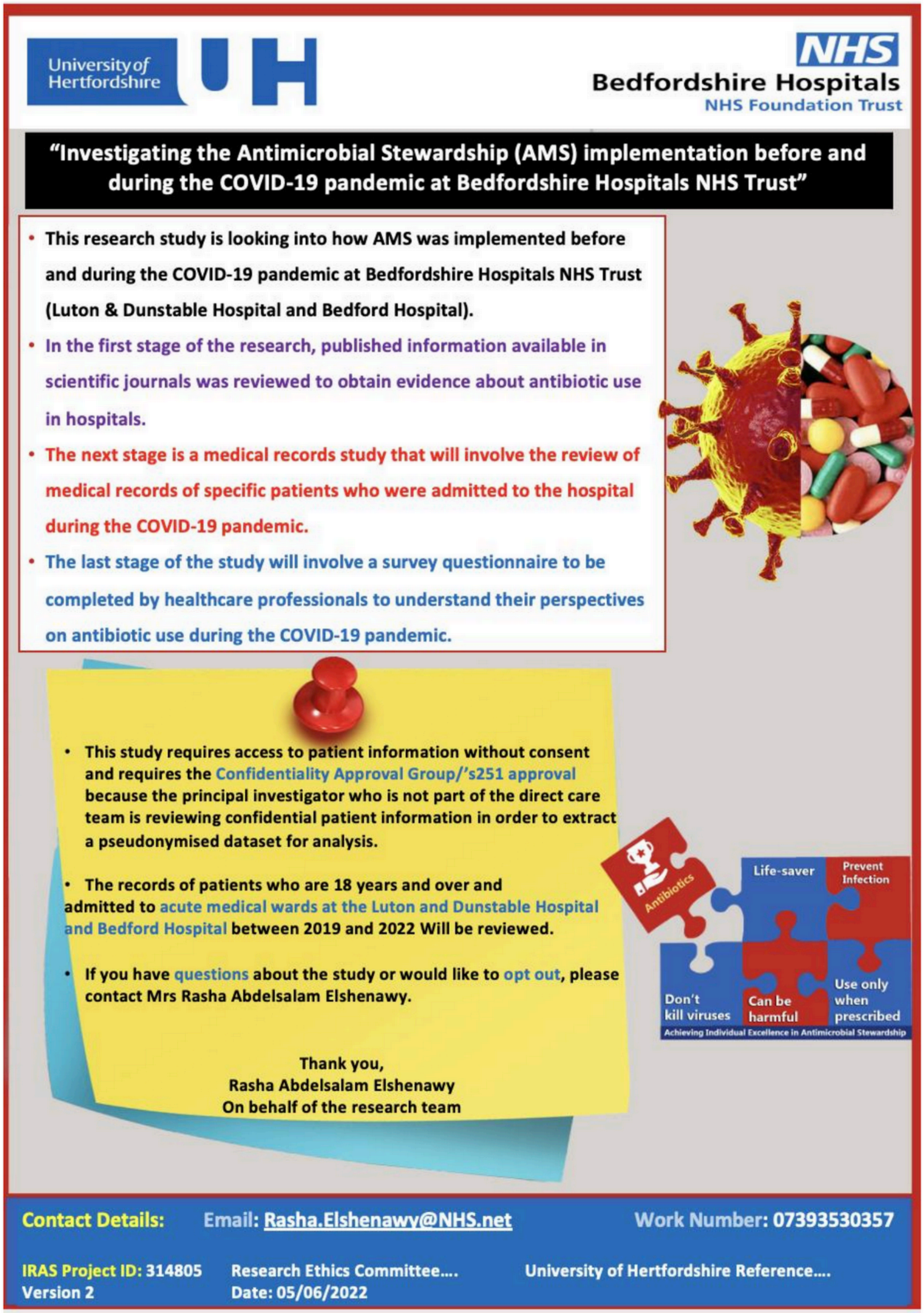
**Appendix 43.** Poster Image: Used as an Email Header by R&D to Encourage Consultants and Ward Managers to Promote the Survey Link Amongst Trust Health Professionals.



**Appendix 44.** Maximising Survey Participation in AMR Research: Comprehensive Poster on Novel Distribution Strategies.

**Appendix 45.** QR Code Distribution for Survey: Shared in Weekly Trust Newsletter and Group Emails to All Healthcare Professionals.

**Appendix 46.** Patient and public poster ‘Investigating the Antimicrobial Stewardship Before and During the COVID-19 Pandemic at Bedfordshire Hospitals NHS Foundation Trust’.



**Appendix 47.** Survey Successfully Shared with Healthcare Professionals in Bedfordshire: Refer to the 'Weekly News Updates' Screenshot.

**The Week: 23 June 2023**

Previously this service was restricted to chronic obstructive pulmonary disease (COPD) patients but has developed to include bronchiectasis, interstitial lung disease (ILD), chronic asthma, and patients requiring oxygen at home as they recover from pulmonary embolisms (PE's) and pneumonia.

To request a patient review please contact the team on bleep 451 / 566. If they meet the criteria we can admit them to the Virtual Ward on discharge from hospital or through GP referral.

**Call for participants for antibiotic survey questionnaire study**

Bedfordshire Hospitals Trust and the University of Hertfordshire are conducting a survey to investigate the attitudes of doctors, nurses and pharmacists towards antibiotic prescribing before and during the COVID-19 pandemic.

To take park in the survey, scan the QR code or visit the Herts website. If you have any further questions, please contact Rasha Abdelsalam Elshenawy.

**Appendix 48.** Information Sheet for Healthcare Professional Participants. Available Here.

**Version 2** **14/06/2023**

University of Hertfordshire UH

NHS Bedfordshire Hospitals NHS Foundation Trust

## Healthcare Professional Information Sheet

**Chief Investigator:** Dr Zoe Aslanpour
**Principal Investigator:** Rasha Abdelsalam Elshenawy
**Sponsorship**: University of Hertfordshire
**Research Ethics Committee:** East Midlands Leicester South
**REC Reference:** 22/EM/0161
**Email:** r.a.elshenawy@herts.ac.uk
**Work Number:** 07393530357
**Version #2**: 14/06/23

**Title of Project:** Exploring Antibiotic Prescribing Perceptions, Attitudes, and Knowledge among Doctors, Nurses, and Pharmacists at Bedfordshire Hospitals NHS Trust during the COVID-19 Pandemic.

**Introduction:**
UK health authorities have raised concerns about antimicrobial resistance (AMR), a "hidden pandemic" potentially emerging post-COVID-19 if antibiotics aren't prescribed responsibly. This study aims to investigate the perspectives of doctors, nurses, and pharmacists on antibiotic prescription practices, both before and amidst the COVID-19 pandemic. The research revolves around the concept of 'antimicrobial stewardship,' a term defined by the NICE guidelines as a healthcare system-wide initiative promoting and tracking the prudent use of antimicrobials to ensure their future efficacy. Our objective is to explore the factors influencing the decisions made concerning antibiotic prescriptions before and during the COVID-19 crisis. We invite you to participate in this study at the Bedfordshire Hospitals NHS Trust to identify the factors affecting the implementation of AMS and the prescribing behaviour, perceptions, and attitudes towards antibiotics during this pandemic. Your participation will provide valuable insights into antibiotic prescribing behaviour, aiding us in identifying strategies to enhance antibiotic prescribing practices and ensure their appropriate and judicious use.

This PhD research study was conducted per the University of Hertfordshire's regulation, UPR RE01. You can review UH's regulations by following this link: https://www.herts.ac.uk/about-us/governance/university-policies-and-regulations-uprs/uprs. Once you have accessed this link, please scroll down to Letter S, where you'll find the 'Studies Involving the Use of Human Participants' regulation. We kindly request that you carefully review the following information before deciding to participate. If anything is unclear or if you require further information, please do not hesitate to ask us.

We appreciate your time spent reading this. Thank you.

Page **1** of **4**

**Appendix 49.** Survey Participation Invitation Letter for Healthcare Professionals.

Version 2 Invitation Letter (HCP Name)
**IRAS ID: 314805** 16/05/2023

University of Hertfordshire UH

NHS
Bedfordshire Hospitals
NHS Foundation Trust

Dear colleague

You are invited to participate in a survey titled **"Healthcare professionals' knowledge, attitudes, and perceptions towards antibiotic prescribing before and during the COVID-19 pandemic in Bedfordshire Hospitals NHS Foundation Trust."** This survey aims to investigate the antibiotic prescribing practices of healthcare professionals at Bedfordshire Hospitals NHS Foundation Trust.

Your participation will contribute to our understanding of knowledge, perception, and attitudes towards antimicrobial prescribing and factors influencing Antimicrobial Stewardship (AMS) implementation during the pandemic. The NHS Research Ethics Committee, the University of Hertfordshire and R&D have approved this study. Your input and support are greatly appreciated!

The survey is anonymous and confidential. It is open to doctors, pharmacists, and nurses who have worked at Luton and Dunstable Hospital and/or Bedford Hospital before and during the COVID-19 pandemic.

The survey consists of three domains with a total of **12 questions.**

1. Knowledge
2. Attitudes and Perceptions
3. Practice

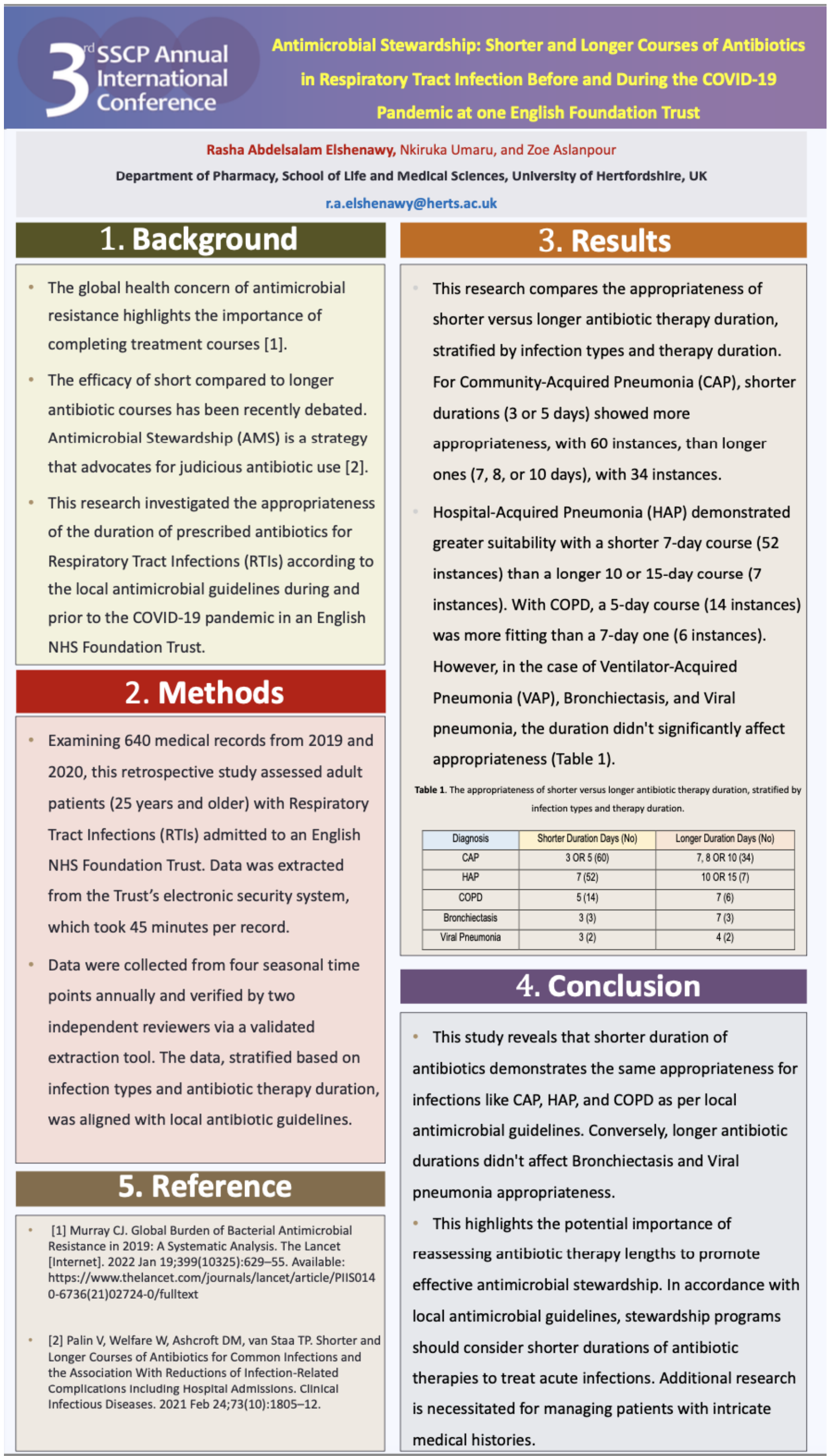
Please read the attached Participant Information Sheet (PIS) for comprehensive details about the study. If you want to participate, kindly click the provided survey link. The survey will take approximately 15 minutes to complete. Participation in this survey implies your consent to be part of the study.

If you have any additional questions, please feel free to contact Rasha Abdelsalam Elshenawy, PhD Candidate/Principal Investigator at the University of Hertfordshire.

Email: r.a.elshenawy@herts.ac.uk

Thank you!

**Appendix 50.** Poster Presentation at Saudi Society for the Clinical Pharmacy (SSCP) Conference: Antimicrobial Stewardship: Shorter and Longer Courses of Antibiotics in Respiratory Tract Infection Before and During the COVID-19 Pandemic at one English Foundation Trust.



3rd SSCP Annual International Conference

**Antimicrobial Stewardship: Shorter and Longer Courses of Antibiotics in Respiratory Tract Infection Before and During the COVID-19 Pandemic at one English Foundation Trust**

**Rasha Abdelsalam Elshenawy,** Nkiruka Umaru, and Zoe Aslanpour
Department of Pharmacy, School of Life and Medical Sciences, University of Hertfordshire, UK
r.a.elshenawy@herts.ac.uk

## 1. Background

- The global health concern of antimicrobial resistance highlights the importance of completing treatment courses [1].
- The efficacy of short compared to longer antibiotic courses has been recently debated. Antimicrobial Stewardship (AMS) is a strategy that advocates for judicious antibiotic use [2].
- This research investigated the appropriateness of the duration of prescribed antibiotics for Respiratory Tract Infections (RTIs) according to the local antimicrobial guidelines during and prior to the COVID-19 pandemic in an English NHS Foundation Trust.

## 2. Methods

- Examining 640 medical records from 2019 and 2020, this retrospective study assessed adult patients (25 years and older) with Respiratory Tract Infections (RTIs) admitted to an English NHS Foundation Trust. Data was extracted from the Trust's electronic security system, which took 45 minutes per record.
- Data were collected from four seasonal time points annually and verified by two independent reviewers via a validated extraction tool. The data, stratified based on infection types and antibiotic therapy duration, was aligned with local antibiotic guidelines.

## 5. Reference

- [1] Murray CJ. Global Burden of Bacterial Antimicrobial Resistance in 2019: A Systematic Analysis. The Lancet [Internet]. 2022 Jan 19;399(10325):629–55. Available: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext
- [2] Palin V, Welfare W, Ashcroft DM, van Staa TP. Shorter and Longer Courses of Antibiotics for Common Infections and the Association With Reductions of Infection-Related Complications Including Hospital Admissions. Clinical Infectious Diseases. 2021 Feb 24;73(10):1805–12.

## 3. Results

- This research compares the appropriateness of shorter versus longer antibiotic therapy duration, stratified by infection types and therapy duration. For Community-Acquired Pneumonia (CAP), shorter durations (3 or 5 days) showed more appropriateness, with 60 instances, than longer ones (7, 8, or 10 days), with 34 instances.
- Hospital-Acquired Pneumonia (HAP) demonstrated greater suitability with a shorter 7-day course (52 instances) than a longer 10 or 15-day course (7 instances). With COPD, a 5-day course (14 instances) was more fitting than a 7-day one (6 instances). However, in the case of Ventilator-Acquired Pneumonia (VAP), Bronchiectasis, and Viral pneumonia, the duration didn't significantly affect appropriateness (Table 1).

**Table 1**. The appropriateness of shorter versus longer antibiotic therapy duration, stratified by infection types and therapy duration.

| Diagnosis | Shorter Duration Days (No) | Longer Duration Days (No) |
|---|---|---|
| CAP | 3 OR 5 (60) | 7, 8 OR 10 (34) |
| HAP | 7 (52) | 10 OR 15 (7) |
| COPD | 5 (14) | 7 (6) |
| Bronchiectasis | 3 (3) | 7 (3) |
| Viral Pneumonia | 3 (2) | 4 (2) |

## 4. Conclusion

- This study reveals that shorter duration of antibiotics demonstrates the same appropriateness for infections like CAP, HAP, and COPD as per local antimicrobial guidelines. Conversely, longer antibiotic durations didn't affect Bronchiectasis and Viral pneumonia appropriateness.
- This highlights the potential importance of reassessing antibiotic therapy lengths to promote effective antimicrobial stewardship. In accordance with local antimicrobial guidelines, stewardship programs should consider shorter durations of antibiotic therapies to treat acute infections. Additional research is necessitated for managing patients with intricate medical histories.

**Appendix 51:** Presentation of a poster at the American College of Clinical Pharmacy (ACCP) Annual Meeting on 13 November 2023. The poster can be viewed at the following link:

https://www.accp.com/meetings/am23/posters.aspx?aid=63388

**Appendix 52.** Link to the Survey Consisting of 12 Questions. Access from this link.

University of Hertfordshire UH

NHS Bedfordshire Hospitals NHS Foundation Trust

**Chief Investigator:** Dr Zoe Aslanpour

**Principal Investigator:** Rasha Abdelsalam Elshenawy

**Research Ethics Committee (REC):** East Midlands - Leicester South

**Work Number:** 07393530357

**Sponsorship:** University of Hertfordshire

**Email:** r.a.elshenawy@herts.ac.uk

**Reference Number:** 22/EM/0161

Dear colleague,

Dear Colleague, You are invited to participate in our survey titled "Exploring the Knowledge, Attitudes, and Perceptions of Healthcare Professionals Towards Antibiotic Prescribing Pre and During the COVID-19 Pandemic at Bedfordshire Hospitals NHS Foundation Trust."

This survey aims to explore antibiotic prescribing behaviours within the trust. Your valuable participation will significantly contribute to our understanding of the knowledge, attitudes, and perceptions towards antimicrobial prescribing, allowing us to identify factors that may influence the implementation of Antimicrobial Stewardship (AMS) before and during the COVID-19 pandemic.

We are interested to hear from all doctors, pharmacists, or nurses who were working at Luton and Dunstable Hospital and/or Bedford Hospital before and during the COVID-19 pandemic and who are still currently employed at one or two of these hospitals.

This survey contains a total of 12 questions, and it should take no more than 20 minutes to complete. Responses will be completely anonymous and kept confidential. By answering the questions in this survey, you indicate your implied consent to participate in this study.

This study has received approvals from the NHS Research Ethics Committee (REC): East Midlands - Leicester South, and the University of Hertfordshire (UH) - Reference Number: 22/EM/0161.

If you have any questions, please contact Rasha Abdelsalam Elshenawy, PhD student/Principal Investigator at the University of Hertfordshire.

**Email:** r.a.elshenawy@herts.ac.uk



References

1. Public Health England. (2015, February 18). Antibiotic prescribing and behaviour change in healthcare settings. GOV.UK. https://www.gov.uk/government/publications/antibiotic-prescribing-and-behaviour-change-in-healthcare-settings

2. Antimicrobial stewardship: Start smart - then focus. (n.d.). GOV.UK. https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

## Demographic Information:

**Q1 of 12. What is your age?**

- 25-31 years old
- 32-41 years old
- 42-51 years old
- 52-61 years old
- 62-75 years
- more than 75 years

**Q2 of 12: What is your gender?**

- Male
- Female,
- Prefer not to say

**Q3 of 12: What is the highest educational degree you have completed?**

- Undergraduate degree
- Postgraduate degree (master/doctoral)
- Other ... (Please specify)

**Q4 of 12. What is your professional background?**

- Nurse
- Pharmacist
- Doctor
- Other ... (Please specify)

**Q5 of 12: What is your job banding?**

- Band 4
- Band 5
- Band 6
- Band 7
- Band 8a
- Band 8b
- Band 8c
- Band 9

**Q6 of 12: What is your speciality? Please type your answer in the box below.**

**Q7 of 12: How many years of professional experience do you have?**



References

1. Public Health England. (2015, February 18). Antibiotic prescribing and behaviour change in healthcare settings. GOV.UK. https://www.gov.uk/government/publications/antibiotic-prescribing-and-behaviour-change-in-healthcare-settings

2. Antimicrobial stewardship: Start smart - then focus. (n.d.). GOV.UK. https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

- Less than five years
- Six to 20 years
- More than 20 years.

## Knowledge

**This question has got statements that we would like you to indicate your level of agreement with**

**Q8 of 12. This question entails 10 statements. Please indicate the level of agreement with the following statements:**

| Item | Strongly disagree | Disagree | Neutral | Agree | Strongly agree |
|---|---|---|---|---|---|
| Empty antibiotics pipeline results in an unlikely solution to AMR to be found soon. | ☐ | ☐ | ☐ | ☐ | ☐ |
| AMR is a public health problem that affects clinical practice. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Actions in combating AMR within the trust will affect society and future generations. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Implementing Antimicrobial Stewardship promotes the judicious use of antibiotics. | ☐ | ☐ | ☐ | ☐ | ☐ |
| The implementation of Antimicrobial Stewardship enhances patient outcomes within the Trust. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Intravenous antibiotic therapy proved more effective than oral options during the COVID-19 pandemic. | ☐ | ☐ | ☐ | ☐ | ☐ |
| According to hospital antimicrobial guidelines, a shorter antibiotic treatment duration is preferable over a longer one. | ☐ | ☐ | ☐ | ☐ | ☐ |
| A blood culture test should be requested upon patient admission prior to initiating any antibiotic therapy. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Delayed antibiotic prescribing strategy contributes to effective Antimicrobial Stewardship. | ☐ | ☐ | ☐ | ☐ | ☐ |



1. Public Health England. (2015, February 18). Antibiotic prescribing and behaviour change in healthcare settings. GOV.UK. https://www.gov.uk/government/publications/antibiotic-prescribing-and-behaviour-change-in-healthcare-settings

2. Antimicrobial stewardship: Start smart - then focus. (n.d.). GOV.UK. https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

## Perceptions & Attitudes

**There are two questions under this section, and each has got statements that we would like you to indicate your level of agreement with**

**Q9 of 12. Please indicate the level of agreement with the following statements:**

| Item | Strongly disagree | Disagree | Neutral | Agree | Strongly agree |
|---|---|---|---|---|---|
| During the pandemic, the antibiotic guidelines in my trust were updated. | ☐ | ☐ | ☐ | ☐ | ☐ |
| The changing clinical conditions of Covid patients influenced antibiotic prescribing during the COVID-19 pandemic. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Time pressure challenges affected antibiotic decision-making during the COVID-19 pandemic | ☐ | ☐ | ☐ | ☐ | ☐ |
| During the COVID-19 pandemic, clinical judgment was prioritised over antimicrobial guidelines. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Prescribing broad-spectrum antibiotics is often viewed as more effective when dealing with resistant pathogens. | ☐ | ☐ | ☐ | ☐ | ☐ |
| During the COVID-19 pandemic, patients should continue antibiotics even with negative culture. | ☐ | ☐ | ☐ | ☐ | ☐ |
| During the pandemic, communication with microbiologists and AMS team supported more informed decisions about antibiotic use. | ☐ | ☐ | ☐ | ☐ | ☐ |

**Q10 of 12. Which of these AMS strategies has an impact on antibiotic prescribing during the COVID-19 pandemic?**

**This question has got seven statements.**



1. Public Health England. (2015, February 18). Antibiotic prescribing and behaviour change in healthcare settings. GOV.UK. https://www.gov.uk/government/publications/antibiotic-prescribing-and-behaviour-change-in-healthcare-settings

2. Antimicrobial stewardship: Start smart - then focus. (n.d.). GOV.UK. https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

| Item | Negative | Positive | No impact |
|---|---|---|---|
| AMS ward rounds | ☐ | ☐ | ☐ |
| Antibiotic Review | ☐ | ☐ | ☐ |
| Prospective audit and feedback | ☐ | ☐ | ☐ |
| Regular antimicrobial use surveillance | ☐ | ☐ | ☐ |
| AMS education and training | ☐ | ☐ | ☐ |
| Intravenous-to-oral antibiotic switch | ☐ | ☐ | ☐ |
| Multidisciplinary team meetings (MDTMs) | ☐ | ☐ | ☐ |

## Antimicrobial Stewardship Practices

**This question has got statements that we would like you to indicate your level of agreement with**

**Q11 of 12: Please indicate how much you agree with the following statements regarding AMS practices in your trust during Covid.**



1. Public Health England. (2015, February 18). Antibiotic prescribing and behaviour change in healthcare settings. GOV.UK. https://www.gov.uk/government/publications/antibiotic-prescribing-and-behaviour-change-in-healthcare-settings

2. Antimicrobial stewardship: Start smart - then focus. (n.d.). GOV.UK. https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

| Item | Strongly disagree | Disagree | Neutral | Agree | Strongly agree |
|---|---|---|---|---|---|
| Antibiotic prescribing was complied with the local antimicrobial guidelines. | ☐ | ☐ | ☐ | ☐ | ☐ |
| I was informed of the resistance pattern in my Trust. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Overuse/misuse of antimicrobials during Covid could impact Antimicrobial Resistance (AMR). | ☐ | ☐ | ☐ | ☐ | ☐ |
| Review the use of IV antibiotics post- receipt of culture results. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use of technology platforms like Zoom, Teams, or Skype for multidisciplinary meetings. | ☐ | ☐ | ☐ | ☐ | ☐ |

**Q12 of 12: Are there any key messages you have learnt during the Covid that you would like to share, e.g. Antimicrobial Stewardship?**

We thank you for your time spent taking this survey.

Your response has been recorded.

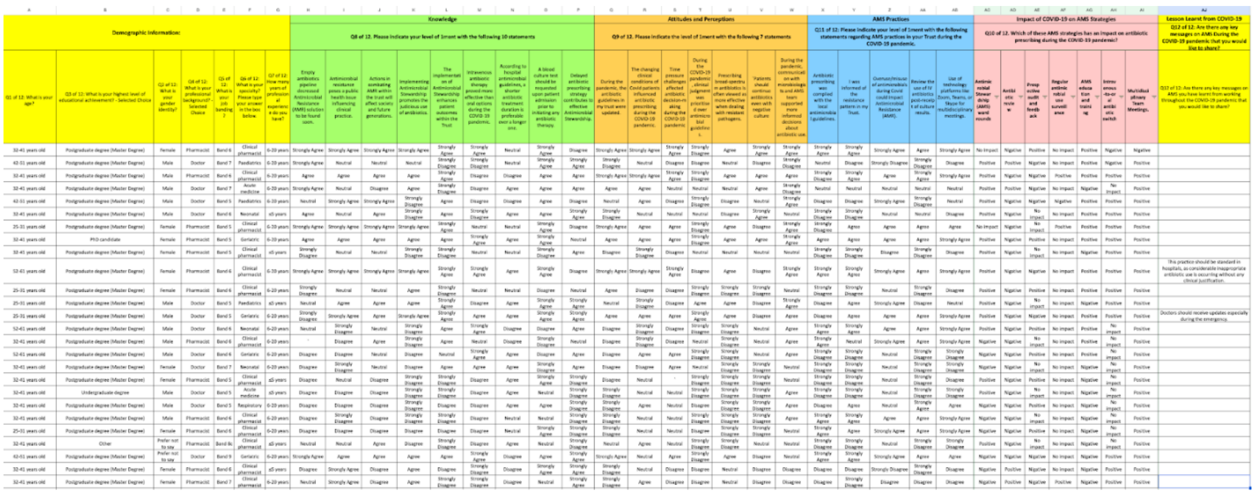


References

1. Public Health England. (2015, February 18). Antibiotic prescribing and behaviour change in healthcare settings. GOV.UK. https://www.gov.uk/government/publications/antibiotic-prescribing-and-behaviour-change-in-healthcare-settings

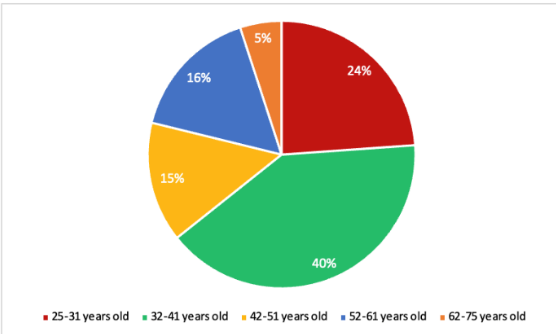
2. Antimicrobial stewardship: Start smart - then focus. (n.d.). GOV.UK. https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

**Appendix 53:** responses or raw data from the survey study. [Access data from this link]

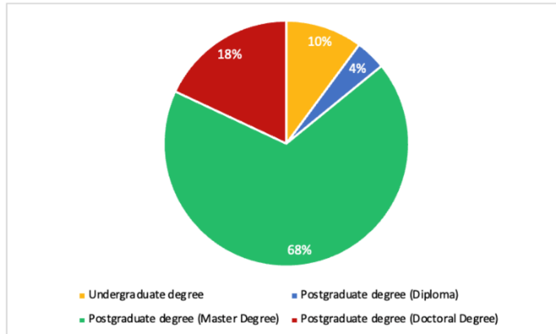


**Appendix 54.** Pie charts of the demographic characteristics of the survey respondents of health professionals

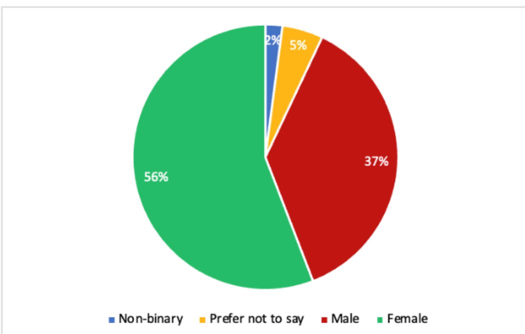
**Age**



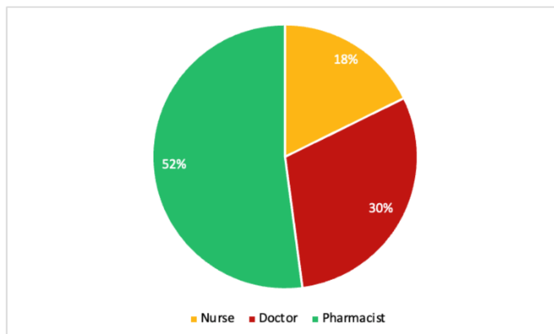

**Educational achievement**



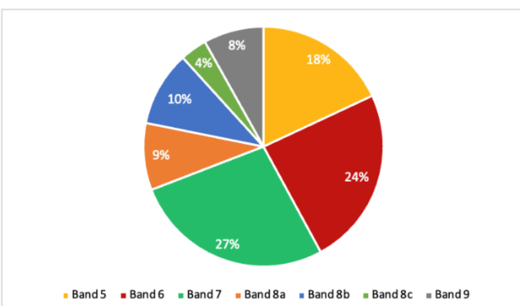

**Gender**



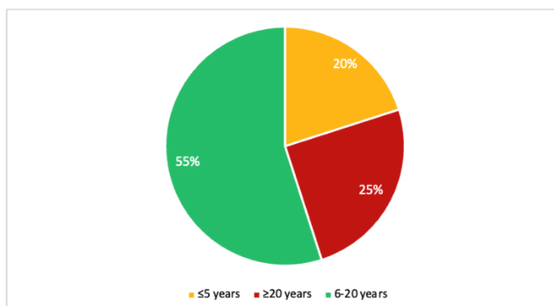

**Professional background**




**Job handling**




**Years of experience**



**Appendix 55:** Pharmacists KAP towards antibiotic prescribing. Access data analysis from this link

https://docs.google.com/document/d/1Jq__1JN-Z3W0vZObNX4PdiB0hto0ztKP/edit?usp=drive_link&ouid=108667268560233258048&rtpof=true&sd=true

| | | Count | Column N % |
|---|---|---|---|
| Empty antibiotics pipeline decreased Antimicrobial Resistance (AMR) solution to be found soon. | Strongly Agree | 19 | 15.2% |
| | Agree | 11 | 8.8% |
| | Neutral | 65 | 52.0% |
| | Disagree | 22 | 17.6% |
| | Strongly Disagree | 8 | 6.4% |
| Antimicrobial resistance poses a public health issue influencing clinical practice. | Strongly Agree | 106 | 84.8% |
| | Agree | 1 | 0.8% |
| | Neutral | 17 | 13.6% |
| | Disagree | 1 | 0.8% |
| | Strongly disagree | 0 | 0.0 |
| Actions in combating AMR within the trust will affect society and future generations. | Strongly Agree | 96 | 76.8% |
| | Agree | 18 | 14.4% |
| | Neutral | 10 | 8.0% |
| | Disagree | 1 | 0.8% |
| | Strongly disagree | 0 | 0.0 |
| Implementing Antimicrobial Stewardship promotes the judicious use of antibiotics. | Strongly Agree | 77 | 61.6% |
| | Agree | 30 | 24.0% |
| | Neutral | 16 | 12.8% |
| | Disagree | 2 | 1.6% |
| | Strongly disagree | 0 | 0.0 |
| The implementation of Antimicrobial Stewardship enhances patient outcomes within the Trust | Strongly Agree | 61 | 48.8% |
| | Agree | 45 | 36.0% |
| | Neutral | 18 | 14.4% |
| | Disagree | 1 | 0.8% |
| | Strongly disagree | 0 | 0.0 |
| Intravenous antibiotic therapy proved more effective than oral options during the COVID-19 pandemic. | Strongly Agree | 5 | 4.0% |
| | Agree | 31 | 24.8% |
| | Neutral | 50 | 40.0% |
| | Disagree | 24 | 19.2% |
| | Strongly Disagree | 15 | 12.0% |
| According to hospital antimicrobial guidelines, a shorter antibiotic treatment duration is preferable over a longer one. | Strongly Agree | 34 | 27.2% |
| | Agree | 53 | 42.4% |
| | Neutral | 37 | 29.6% |
| | Disagree | 1 | 0.8% |
| | Strongly disagree | 0 | 0.0 |
| A blood culture test should be requested upon patient admission prior to initiating any antibiotic therapy. | Strongly Agree | 42 | 33.6% |
| | Agree | 38 | 30.4% |
| | Neutral | 15 | 12.0% |
| | Disagree | 22 | 17.6% |
| | Strongly Disagree | 8 | 6.4% |
| Delayed antibiotic prescribing strategy contributes to effective Antimicrobial Stewardship. | Strongly Agree | 12 | 9.6% |
| | Agree | 55 | 44.0% |
| | Neutral | 22 | 17.6% |

**Appendix 56.** The demonstration of the AMS Dashboard. Access from this link.

# Antimicrobial Stewardship Dashboard

This Dashboard is based on Start Smart, Then Focus Public Health England Toolkit and the PhD Research Project of Investigating Antimicrobial Stewardship at One English NHS Foundation Trust

**Key for Antimicrobial Stewardship Dashboard**

**Introduction:**
Importance of measuring prescribing performance in AMS
Historical quote emphasising measurement for improvement
Need for metrics/measures for KPIs, quality assurance/improvement, benchmarking
Necessity for a measurable dashboard for antibiotic prescribing & AMS monitoring

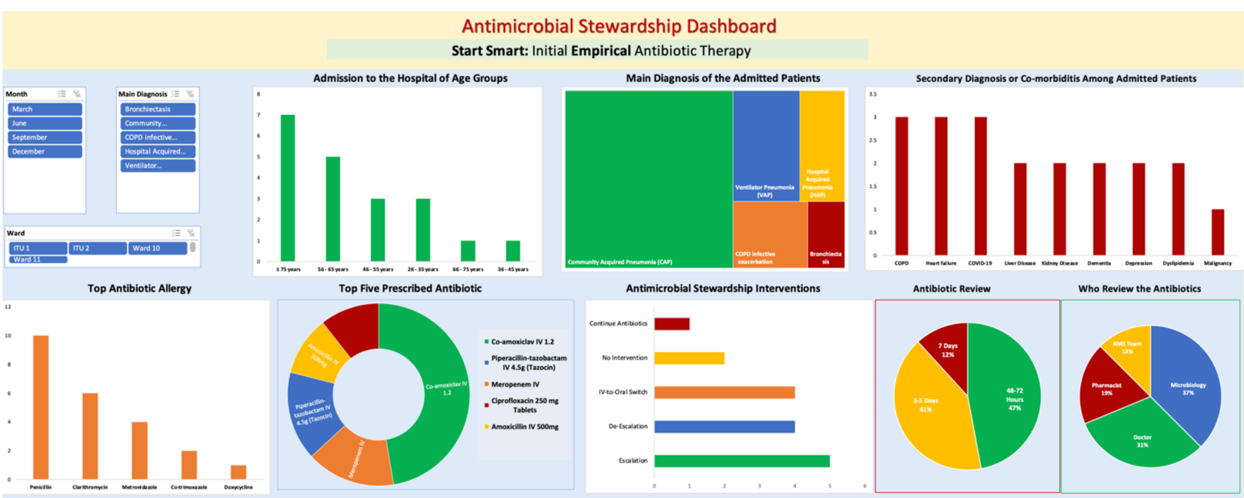
**Background:**
- Use of 'Data Extraction Form' from Study 2, Chapter 4
- Impact of COVID-19 on AMS from Study 3, Chapter 5

**Purpose of the Dashboard:**
Real-time visualization for AMS actions
Tool for hospital leaders for decision-making
Emphasis on starting with broad-spectrum agents & then focusing on evidence-based treatment
Challenges posed by antibiotic resistance & COVID-19 pandemic

**Dashboard Content - "Start Smart": Initial Empirical Antibiotic Therapy (Figure 1):**
1. Selection Filters:
   - Month: March, June, September, December
   - Main Diagnosis: Bronchiectasis, CAP, COPD, HAP, VAP
   - Wards: Ward 10, Ward 11, ITU 1, ITU 2
2. Admission by Age Groups: Bar graph with age groups 26-35, 66-75, 46-55
3. Main Diagnosis: Bar graph with CAP, VAP, HAP, COPD, Bronchiectasis
4. Secondary Diagnosis/Co-morbidities: Bar graph with COVID-19, COPD, Kidney Disease, Dyslipidemia
5. Top Antibiotic Allergy: Bar graph with Penicillin, Clarithromycin, Metronidazole, etc.
6. Top Prescribed Antibiotics: Pie chart with co-amoxiclav, piperacillin-tazobactam, meropenem, etc.
7. AMS Interventions: Bar graph with Continue Antibiotics, No Intervention, IV-to-Oral Switch, etc.
8. Antibiotic Review: Pie chart with durations 3-5 Days, 48-72 Hours, 7 Days
9. Who Reviews the Antibiotics: Pie chart with roles AMS Team, Microbiology, Pharmacist, Doctor

**Dashboard Content - "Then Focus": Targeted Antibiotic Therapy (Figure 2):**

| # | Patient Nam | Hospital Nu | Ward | Date of Birt | Date of Adr | Month | Year | Age | Age Group | Main Diagnosis | Secondry diagno | Signs and Sympton | Allergy | Antibiotic on Admission | CRP (Normal |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Test 1 | 1 | ITU 1 | 01/09/1945 | 01/03/2023 | March | 2023 | 78 | ≥ 75 years | Community Acquired Pneumonia (CAP) | COPD | Fever | Penicillin | Co-amoxiclav IV 1.2 | 257 |
| 2 | Test 2 | 2 | ITU 2 | 18/12/1927 | 02/03/2023 | March | 2023 | 96 | ≥ 75 years | Community Acquired Pneumonia (CAP) | Heart failure | Fever | Penicillin | Co-amoxiclav IV 1.2 | 66 |
| 3 | Test 3 | 3 | Ward 11 | 12/11/1930 | 03/03/2023 | March | 2023 | 93 | ≥ 75 years | Community Acquired Pneumonia (CAP) | Dementia | Fever | Clarithromycin | Co-amoxiclav IV 1.2 | 10 |
| 4 | Test 4 | 4 | Ward 10 | 06/03/1940 | 04/03/2023 | March | 2023 | 83 | ≥ 75 years | Community Acquired Pneumonia (CAP) | Dementia | Shortness of breath | Doxycycline | Co-amoxiclav IV 1.2 | 9 |
| 5 | Test 5 | 5 | ITU 2 | 01/09/1945 | 05/03/2023 | March | 2023 | 64 | 56 - 65 years | Community Acquired Pneumonia (CAP) | Dyslipidemia | Dysnea | Penicillin | Meropenem IV | 25 |
| 6 | Test 6 | 6 | ITU 2 | 18/12/1927 | 01/06/2023 | June | 2023 | 63 | 56 - 65 years | COPD infective exacerbation | Liver Disease | Cough | Penicillin | Meropenem IV | 68 |
| 7 | Test 7 | 7 | ITU 2 | 12/11/1930 | 02/06/2023 | June | 2023 | 78 | ≥ 75 years | Community Acquired Pneumonia (CAP) | Malignancy | Shortness of breath | Clarithromycin | Piperacillin-tazobactam IV 4.5g (T | 11 |
| 8 | Test 8 | 8 | ITU 2 | 06/03/1940 | 03/06/2023 | June | 2023 | 96 | ≥ 75 years | Community Acquired Pneumonia (CAP) | COPD | Dysnea | Metronidazole | Co-amoxiclav IV 1.2 | 113 |
| 9 | Test 9 | 9 | ITU 1 | 01/09/1945 | 04/06/2023 | June | 2023 | 53 | 46 - 55 years | Ventilator Pneumonia (VAP) | Liver Disease | Fever | Metronidazole | Piperacillin-tazobactam IV 4.5g (T | 11 |
| 10 | Test 10 | 10 | ITU 1 | 18/12/1927 | 05/06/2023 | June | 2023 | 59 | 56 - 65 years | Ventilator Pneumonia (VAP) | Heart failure | Shortness of breath | Penicillin | Co-amoxiclav IV 1.2 | 33 |
| 11 | Test 11 | 11 | ITU 1 | 12/11/1930 | 01/09/2023 | September | 2023 | 78 | ≥ 75 years | Ventilator Pneumonia (VAP) | Depression | Shortness of breath | Clarithromycin | Co-amoxiclav IV 1.2 | 110 |
| 12 | Test 12 | 12 | ITU 1 | 06/03/1940 | 02/09/2023 | September | 2023 | 65 | 56 - 65 years | Community Acquired Pneumonia (CAP) | Depression | Cough | Metronidazole | Co-amoxiclav IV 1.2 | 66 |
| 13 | Test 13 | 13 | ITU 1 | 01/09/1945 | 03/09/2023 | September | 2023 | 50 | 46 - 55 years | Community Acquired Pneumonia (CAP) | Heart failure | Cough | Penicillin | Clarithromycin 500 mg tablets | 10 |
| 14 | Test 14 | 14 | Ward 11 | 18/12/1927 | 04/09/2023 | September | 2023 | 45 | 36 - 45 years | Hospital Acquired Pneumonia (HAP) | Kidney Disease | Cough | Co-trimoxazole | Ciprofloxacin 250 mg Tablets | 9 |
| 15 | Test 15 | 15 | Ward 11 | 12/11/1930 | 05/09/2023 | September | 2023 | 56 | 56 - 65 years | Hospital Acquired Pneumonia (HAP) | COVID-19 | Shortness of breath | Penicillin | Ciprofloxacin 250 mg Tablets | 25 |
| 16 | Test 16 | 16 | Ward 11 | 06/03/1940 | 01/12/2023 | December | 2023 | 34 | 26 - 35 years | Community Acquired Pneumonia (CAP) | Dyslipidemia | Fever | Penicillin | Meropenem IV | 68 |
| 17 | Test 17 | 17 | Ward 10 | 01/09/1945 | 02/12/2023 | December | 2023 | 29 | 26 - 35 years | Community Acquired Pneumonia (CAP) | Kidney Disease | Fever | Co-trimoxazole | Piperacillin-tazobactam IV 4.5g (T | 11 |
| 18 | Test 18 | 18 | Ward 10 | 18/12/1927 | 03/12/2023 | December | 2023 | 70 | 66 - 75 years | Community Acquired Pneumonia (CAP) | COPD | Fever | Co-trimoxazole | Amoxicillin IV 500mg | 113 |
| 19 | Test 19 | 19 | Ward 10 | 12/11/1930 | 04/12/2023 | December | 2023 | 50 | 46 - 55 years | COPD infective exacerbation | COVID-19 | Fever | Penicillin | Amoxicillin IV 500mg | 11 |
| 20 | Test 20 | 20 | Ward 10 | 06/03/1940 | 05/12/2023 | December | 2023 | 39 | 26 - 35 years | Bronchiectasis | COVID-19 | Fever | Penicillin | Co-amoxiclav IV 1.2 | 33 |



**Appendix 57.** Five Rights of Antibiotic Safety: Antimicrobial Stewardship at One NHS Foundation Trust in England Before and During the COVID-19 Pandemic. Access from this link.

## Abstracts

Abstract citation ID: riad074.001

### Five Rights of Antibiotic Safety: Antimicrobial Stewardship at One NHS Foundation Trust in England Before and During the COVID-19 Pandemic

R. Abdelsalam Elshenawy, N. Umaru and Z. Aslanpour

Department of Clinical, Pharmaceutical and Biological Sciences, University of Hertfordshire School of Life and Medical Sciences

*Introduction:* The study highlights the urgency of combating rising multi-drug-resistant infections, projecting 10 million deaths annually by 2050. With over 1.2 million deaths in 2019, Antimicrobial Resistance (AMR) has become a significant public health issue. Antimicrobial Stewardship (AMS) promotes judicious antibiotic use[1]. 'The Five Rights of Antibiotic Safety' ensure appropriate usage. It encompasses the right patient, drug, dose, time, and duration[2]. The COVID-19 pandemic, causing around 6 million deaths by 2023, has intensified AMR challenges. The Royal Pharmaceutical Society's AMS policy advocates for maximising the use of pharmacists' expertise to promote prudent antibiotic use, strengthen stewardship, and reduce AMR[3].
*Aim:* This study aimed to evaluate AMS and adherence to the 'Five Rights of Antibiotic Safety' in antibiotic prescribing at an NHS Foundation Trust during 2019 and 2020 amidst the COVID-19 pandemic.
*Methods:* This research study was conducted using a cross-sectional retrospective design and undertook an in-depth analysis of 640 patient records in 2019 and 2020. The study included adult patients aged 25 and above, immunocompromised and pregnant individuals, and those prescribed antibiotics for respiratory tract infections or pneumonia during 2019 and 2020. A validated data extraction tool facilitated data collection. This study was registered under ISRCTN number 14825813, receiving ethical approval from the University of Hertfordshire Ethics and Health Research Authority (HRA) (REC Reference number 22/EM/0161). The Citizens Senate reviewed the study protocol, ensuring public and patient involvement.
*Results:* The study evaluated inappropriate antibiotic prescribing, identifying a rise in inappropriate antibiotic prescribing with no indication from 16% in 2019 to 20% in 2020. Inappropriate routes of administration also increased from 33% to 36%. While inappropriate drug choice remained steady around 63-64%, inappropriate dosing rose from 13% to 18%. Interestingly, inappropriate duration reduced slightly from 70% to 66%. The study assessed AMS champions, pharmacists' participation increased from 19% to 21%, and doctors decreased from 19% to 12%. However, combined collaboration jumped from 58% to 71%.
*Discussion/Conclusion:* This study highlights the surge in incorrect antibiotic prescribing during the 2020 COVID-19 pandemic, stressing the necessity of the 'Five Rights of Antibiotic Safety.' Strict guideline adherence and increased professional education are pivotal. Progress in reducing improper duration was seen, indicating the significance of refining prescribing practices. This research highlights the critical role of pharmacists and doctors as AMS champions. It demonstrates that their collaborative efforts during the pandemic positively impacted patient outcomes, thus reaffirming the Royal Pharmaceutical Society's AMS policy on the importance of a multidisciplinary team in ensuring appropriate antibiotic use.

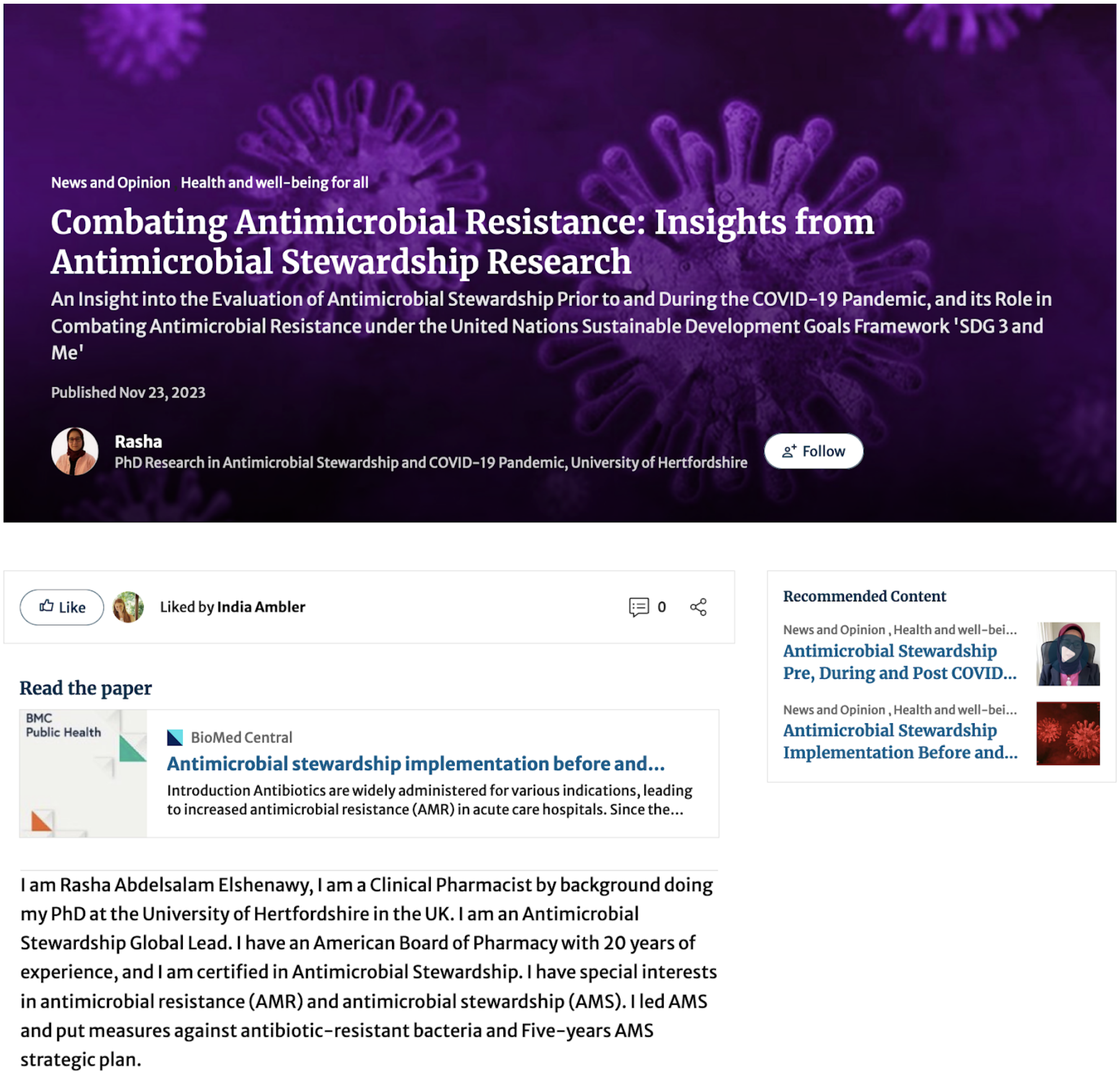
This study reveals a worrying increase in incorrect antibiotic use during 2020, calling for stricter compliance with the five safety rules and enhancing professional education. Reduced inappropriate duration of use suggests improvements in prescribing practices. The critical role of pharmacists and doctors in AMS, with heightened collaboration yielding prudent antibiotic use and better patient outcomes. Despite these insights, limitations like potential reporting bias, not exploring the causes of inappropriate prescribing in-depth, and a limited focus on doctors and pharmacists in AMS need future research.

Keywords: Five Rights of Antibiotic Safety; Inappropriate antibiotic prescribing; Antimicrobial Stewardship; COVID-19 Pandemic; and Multidisciplinary Collaboration

### References

1. Murray CJ. Global Burden of Bacterial Antimicrobial Resistance in 2019: a Systematic Analysis. The Lancet. 2022 Jan 19;399(10325):629–55.
2. Federico F. The Five Rights of Medication Administration | IHI - Institute for Healthcare Improvement [Internet]. www.ihi.org. 2007. Available from: https://www.ihi.org/resources/Pages/ImprovementStories/FiveRightsofMedicationAdministration.aspx
3. The pharmacy contribution to antimicrobial stewardship [Internet]. Available from: https://www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Policy/AMS%20policy.pdf.

**Appendix 58:** Combating Antimicrobial Resistance: Insights from Antimicrobial Stewardship Research. Access from this link: https://sustainabilitycommunity.springernature.com/posts/combating-antimicrobial-resistance-insights-from-antimicrobial-stewardship-research



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## Combating Antimicrobial Resistance: Insights from Antimicrobial Stewardship Research

An Insight into the Evaluation of Antimicrobial Stewardship Prior to and During the COVID-19 Pandemic, and its Role in Combating Antimicrobial Resistance under the United Nations Sustainable Development Goals Framework 'SDG 3 and Me'

Published Nov 23, 2023

Rasha
PhD Research in Antimicrobial Stewardship and COVID-19 Pandemic, University of Hertfordshire

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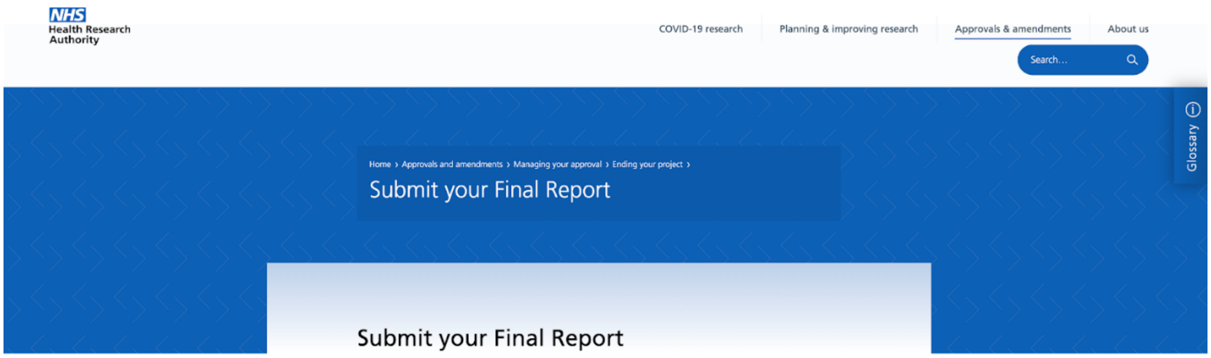
Introduction Antibiotics are widely administered for various indications, leading to increased antimicrobial resistance (AMR) in acute care hospitals. Since the...

I am Rasha Abdelsalam Elshenawy, I am a Clinical Pharmacist by background doing my PhD at the University of Hertfordshire in the UK. I am an Antimicrobial Stewardship Global Lead. I have an American Board of Pharmacy with 20 years of experience, and I am certified in Antimicrobial Stewardship. I have special interests in antimicrobial resistance (AMR) and antimicrobial stewardship (AMS). I led AMS and put measures against antibiotic-resistant bacteria and Five-years AMS strategic plan.

**Appendix 59.** The final Report of this PhD Research Project has been successfully submitted to the HRA website.

https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/final-report-form/




Submit your Final Report

Your Submission

Name of Chief Investigator
Zoe Aslanpour

Telephone Number of Chief Investigator

Email address of Chief Investigator
z.aslanpour@herts.ac.uk

Chief Investigator ORCID ID
https://orcid.org/0000-0002-2567-0540

Email address of person submitting the Final Report
r.a.elshenawy@herts.ac.uk

Full Study Title
An investigation into factors affecting the implementation of Antimicrobial Stewardship (AMS) before and during the COVID-19 pandemic in two acute care settings.

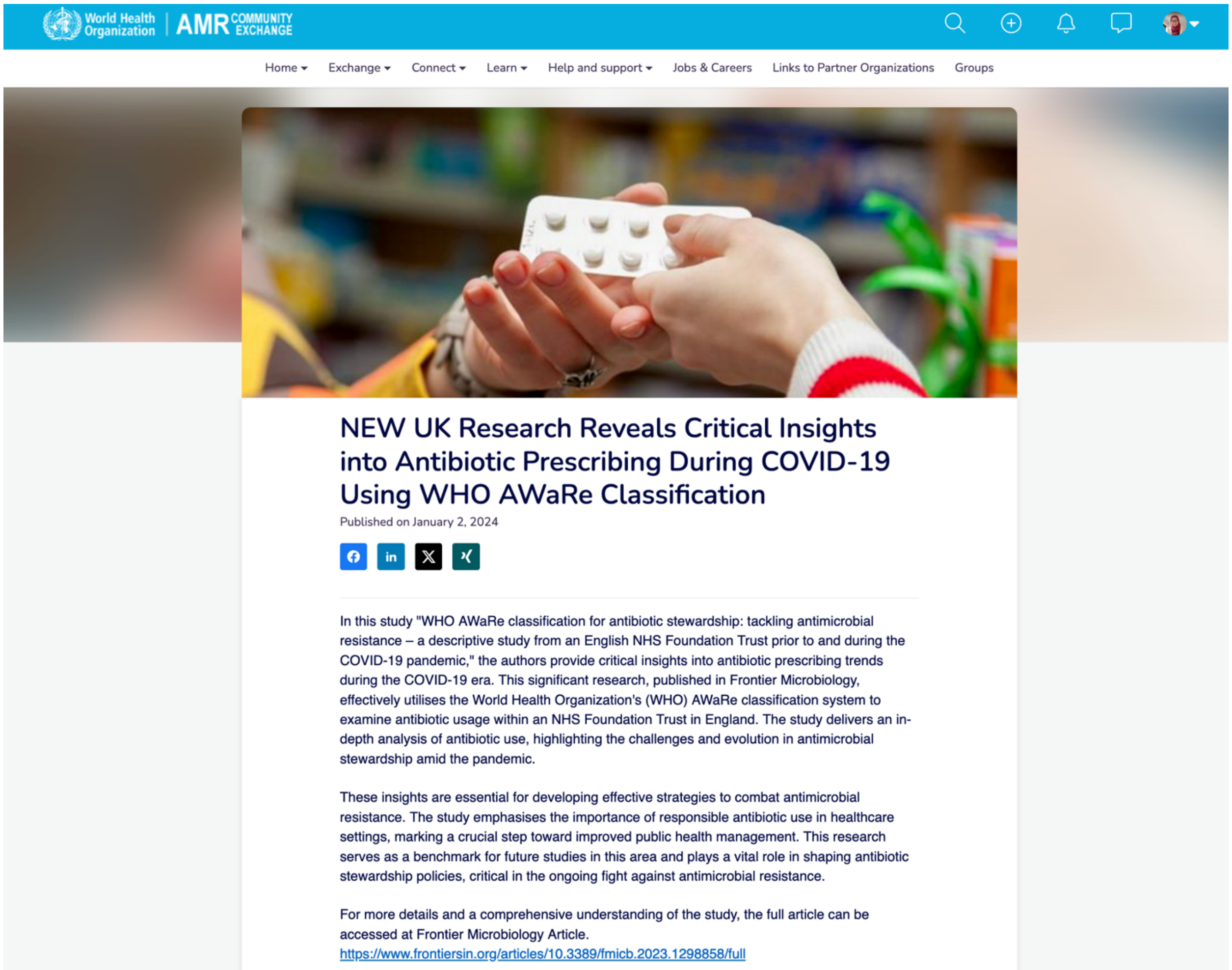
IRAS ID
314805

Name of the Research Ethics Committee that issued a Favourable Opinion for the study
East Midlands - Leicester South Research Ethics Committee

Sponsor Organisation Name
University of Hertfordshire

Study start date
2022-10-01

**Appendix 60.** NEW UK Research Reveals Critical Insights into Antibiotic Prescribing During COVID-19 Using WHO AWaRe Classification. [Access from this link](#) (Requires sign-in for only members of the WHO AMR community).



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## NEW UK Research Reveals Critical Insights into Antibiotic Prescribing During COVID-19 Using WHO AWaRe Classification

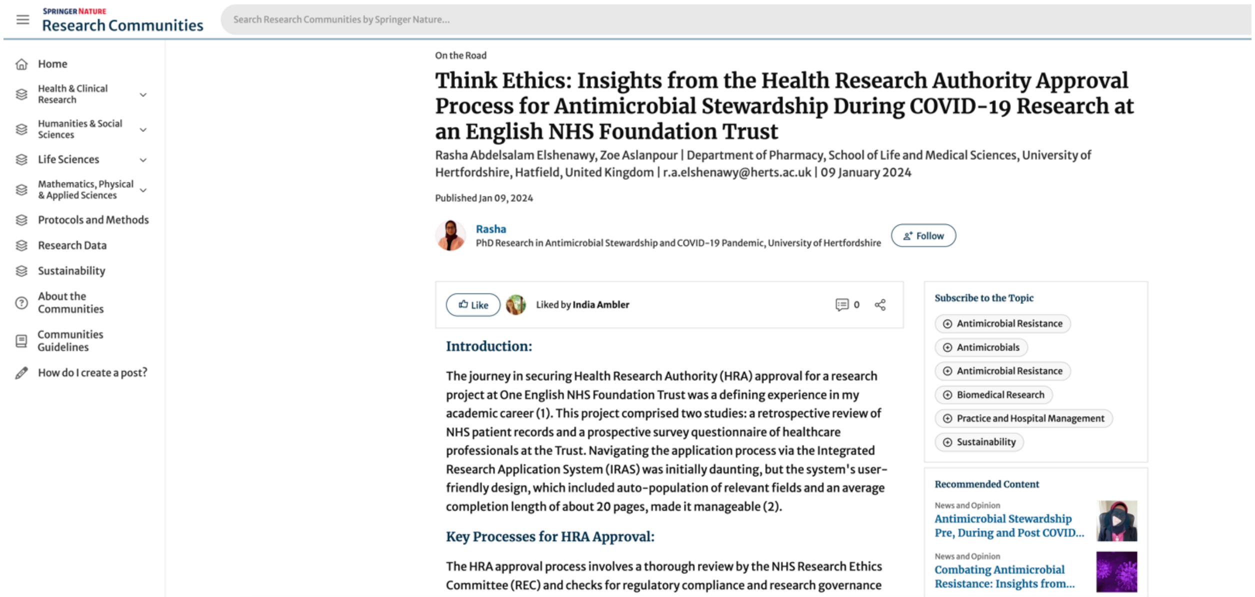
Published on January 2, 2024

In this study "WHO AWaRe classification for antibiotic stewardship: tackling antimicrobial resistance – a descriptive study from an English NHS Foundation Trust prior to and during the COVID-19 pandemic," the authors provide critical insights into antibiotic prescribing trends during the COVID-19 era. This significant research, published in Frontier Microbiology, effectively utilises the World Health Organization's (WHO) AWaRe classification system to examine antibiotic usage within an NHS Foundation Trust in England. The study delivers an in-depth analysis of antibiotic use, highlighting the challenges and evolution in antimicrobial stewardship amid the pandemic.

These insights are essential for developing effective strategies to combat antimicrobial resistance. The study emphasises the importance of responsible antibiotic use in healthcare settings, marking a crucial step toward improved public health management. This research serves as a benchmark for future studies in this area and plays a vital role in shaping antibiotic stewardship policies, critical in the ongoing fight against antimicrobial resistance.

For more details and a comprehensive understanding of the study, the full article can be accessed at Frontier Microbiology Article.
https://www.frontiersin.org/articles/10.3389/fmicb.2023.1298858/full

**Appendix 61.** Think Ethics: Insights from the Health Research Authority Approval Process for Antimicrobial Stewardship During COVID-19 Research at an English NHS Foundation Trust. Access from this link.



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On the Road

# Think Ethics: Insights from the Health Research Authority Approval Process for Antimicrobial Stewardship During COVID-19 Research at an English NHS Foundation Trust

Rasha Abdelsalam Elshenawy, Zoe Aslanpour | Department of Pharmacy, School of Life and Medical Sciences, University of Hertfordshire, Hatfield, United Kingdom | r.a.elshenawy@herts.ac.uk | 09 January 2024

Published Jan 09, 2024

Rasha
PhD Research in Antimicrobial Stewardship and COVID-19 Pandemic, University of Hertfordshire
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**Introduction:**

The journey in securing Health Research Authority (HRA) approval for a research project at One English NHS Foundation Trust was a defining experience in my academic career (1). This project comprised two studies: a retrospective review of NHS patient records and a prospective survey questionnaire of healthcare professionals at the Trust. Navigating the application process via the Integrated Research Application System (IRAS) was initially daunting, but the system's user-friendly design, which included auto-population of relevant fields and an average completion length of about 20 pages, made it manageable (2).

**Key Processes for HRA Approval:**

The HRA approval process involves a thorough review by the NHS Research Ethics Committee (REC) and checks for regulatory compliance and research governance

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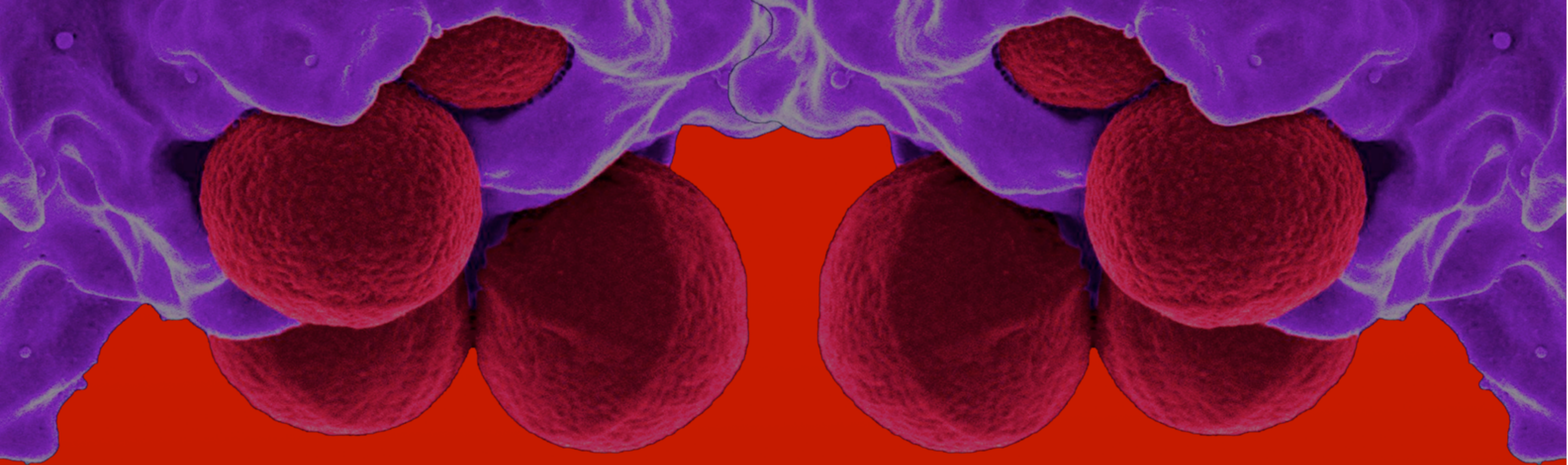
# Appendix 62.

COVID-19  Impact on Antimicrobial stewardship



# COVID-19

## Impact on Antimicrobial Stewardship

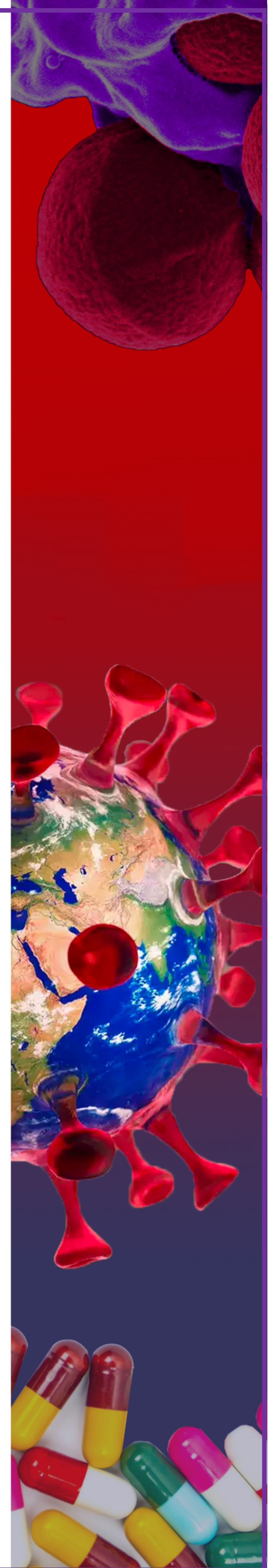
## 2023 Special Report

# COVID-19

**Impact on Antimicrobial Stewardship**

## Contents:





# Effective Antimicrobial stewardship During the COVID-19 Pandemic at Bedfordshire Hospitals NHS Foundation Trust

**COVID-19 Impact on Antimicrobial Stewardship Report: Research Project Outcome**

## Report Outline:

- This report highlights key findings from the research project, "Antimicrobial Stewardship (AMS) Implementation during the COVID-19 Pandemic in an Acute Care Setting."
- The document offers insights into the hospital's experiences with AMS during the pandemic, aiming to guide health professionals in refining their AMS practices during similar challenges.
- It also presents feedback from health professionals, highlighting the remarkable outcomes achieved through their concerted efforts in the survey response.
- There's a critical need to understanding how the COVID-19 pandemic influenced AMS practices. Learning lessons from these effects is vital for optimising AMS, refining antibiotic prescribing habits, and fighting antimicrobial resistance – a global challenge that healthcare professionals are central to combating.

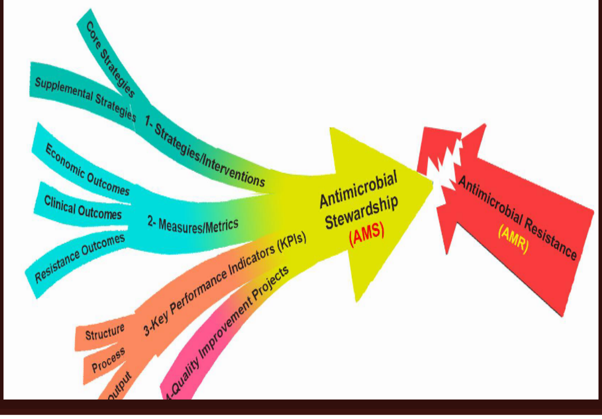
## Background

- Antimicrobial resistance (AMR) is a major global public health threat that can lead to treatment failures, deaths, and escalating healthcare costs (www.england.nhs.uk, 2020).
- Antimicrobial stewardship refers to coordinated efforts to promote appropriate antibiotic use to improve patient outcomes, reduce resistance, and decrease unnecessary costs (NICE, 2019) (Figure 1).

## Forward:

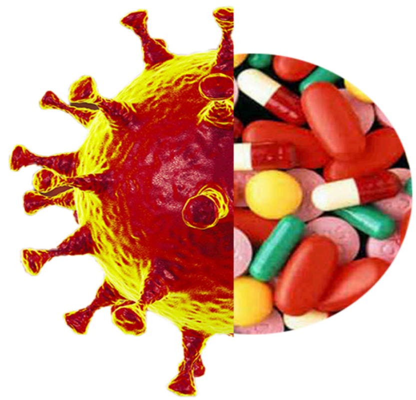
- As academic researchers and members of the healthcare community, with firsthand experience on the frontlines, we have a profound understanding of antimicrobial resistance—where bacteria become resistant to the antibiotics intended to kill them. Even before the COVID-19 outbreak, antimicrobial resistance stood as a paramount public health issue, and it remains so.

**Figure 1.** Antimicrobial Stewardship Implementation



- Both COVID-19 pandemic & antimicrobial resistance - silent pandemic are two sides of the same coin (ISRCTN., 2022) (Figure 2).

**Figure 2. COVID-19 Pandemic & Antimicrobial Resistance - Silent Pandemic: Two Sides of the Same Coin.**

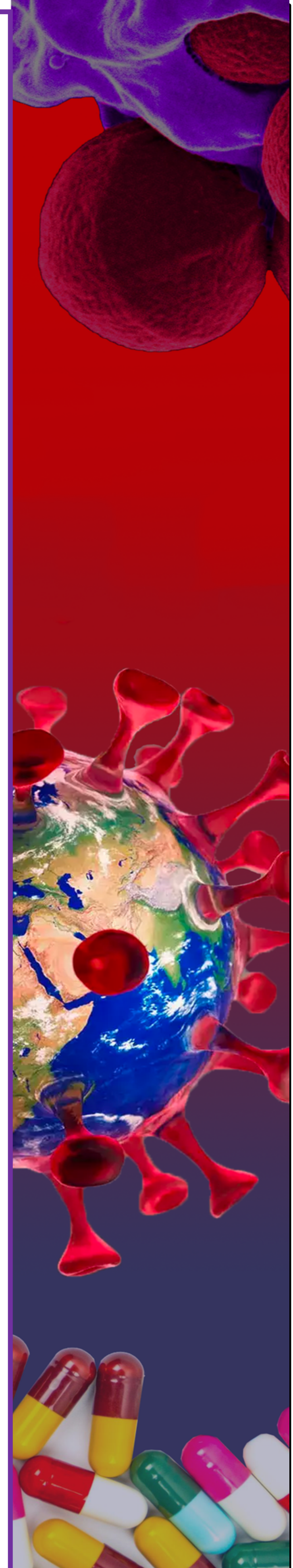


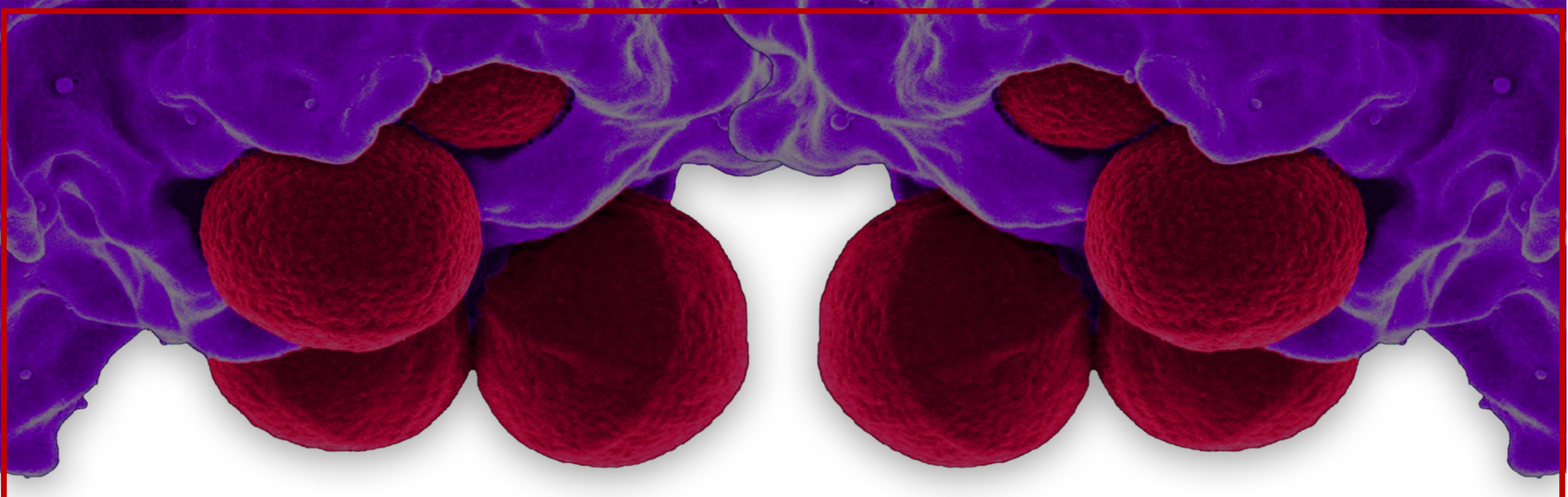
- Figure 3 below grabs our attention with a clear message: time is ticking on the fight against AMR. Imagine, by 2050, one person might die every **three seconds** if we don't act now. The bold countdown and standout purple shade emphasise how crucial and urgent this issue is. This isn't just a warning; it's a call to action (O'Neill, 2014).

**Figure 3. Antimicrobial Resistance: A Global Threat with Potential Devastating Consequences if NOT Tackled (O'Neill, 2016)**


# Objectives

- The primary aim of this research project was to investigate the implementation of antimicrobial stewardship and antibiotic prescribing practices prior to and during the COVID-19 pandemic at Bedfordshire Hospitals NHS Foundation Trust.
- Additionally, this research aimed to identify healthcare professionals' attitudes and perceptions towards antibiotic prescribing, AMR, and AMS practices to enhance antimicrobial stewardship.
- This research project was registered with ISRCTN in accordance with the WHO criteria (registration number 14825813) (www.isrctn.com, 2021).



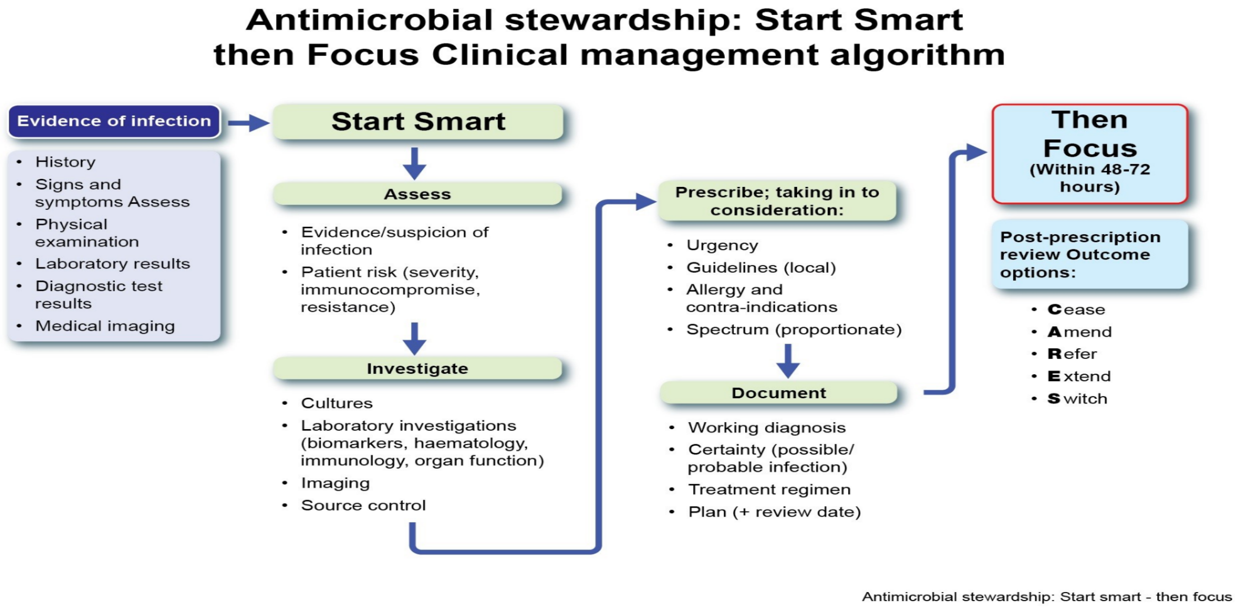


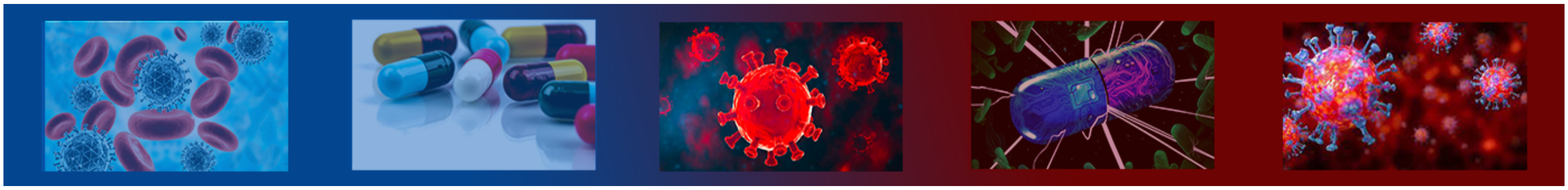
# Public Health England (PHE) 'Start Smart - Then Focus' Antimicrobial Stewardship Toolkit

The PHE **'Start Smart - Then Focus' antimicrobial stewardship toolkit'** provides guidance to facilitates judicious antibiotic use through timely initiation, review, and AMS implementation in acute care (GOV.UK, 2023) (Figure 4).

- **'Start Smart'** promotes responsible INITIAL antibiotic use with thorough assessment, appropriate prescribing per guidelines, and documentation.
- **'Then Focus'** involves actively reviewing and revising treatment after 24-72 hours based on new information.

**Figure 4.** AMS clinical management algorithm (GOV.UK, 2023).



The **'CARES'** framework guides **antibiotic review** outcomes:

- **C**ease treatment if no infection.
- **A**mend prescription with narrower spectrum agents.
- **R**efer to outpatient services like COPAT or virtual wards.
- **E**xtend treatment with clear future review dates.
- **S**witch from intravenous to oral agents where appropriate.

# Antimicrobial Stewardship Strategies in Hospitals

- Antimicrobial stewardship involves strategies and interventions aimed at improving appropriate antibiotic prescriptions in all healthcare settings. The literature provides tools, interventions, and activities collectively termed "strategies" to streamline and improve antimicrobial use and educate prescribers (Department of Health ESPAUR SSTF subcommittee, 2015). These strategies include "front-end" and "back-end" approaches. Front-end strategies require an approval process for antimicrobials, while back-end strategies involve reviewing therapy after initiation, often using prospective audit with intervention and feedback. Research indicates that back-end strategies are widely practiced, easily accepted by clinicians, and offer greater educational opportunities. Back-end strategies are likely to provide a more sustained impact in improving antimicrobial prescribing quality (Chung et al., 2013).
- Employed to encourage judicious antibiotic use and prescriber education (The British Society for Antimicrobial Chemotherapy, 2018) (Figure 5), all these strategies have been discussed in detail in the Systematic Literature Review (Rasha Abdelsalam Elshenawy et al., 2023). However, this chapter focuses on the retrospective study and will only evaluate the back-end strategies.

**Antimicrobial stewardship strategies** aim to improve appropriate antibiotic prescribing across healthcare settings. These strategies facilitate judicious antibiotic use through timely AMS initiation, review, and implementation. Strategies include:

- **"Front-end"** approaches requiring antibiotic approval and "back-end" approaches reviewing therapy after initiation.

- **"Back-end"** strategies, such as audit/feedback are more easily accepted, offer educational opportunities, and provide sustained impact. These strategies encourage judicious antibiotic use and prescriber education.

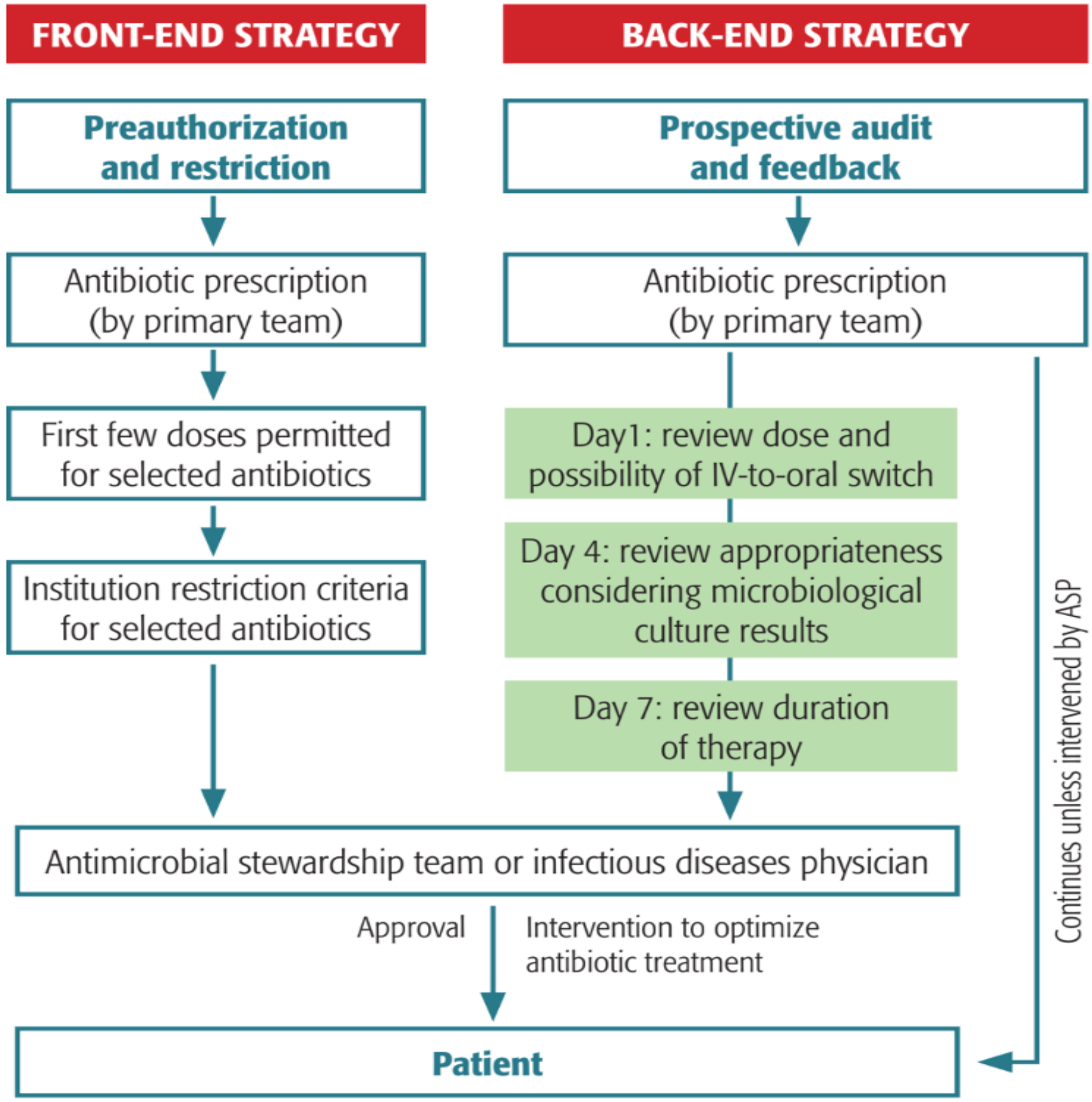
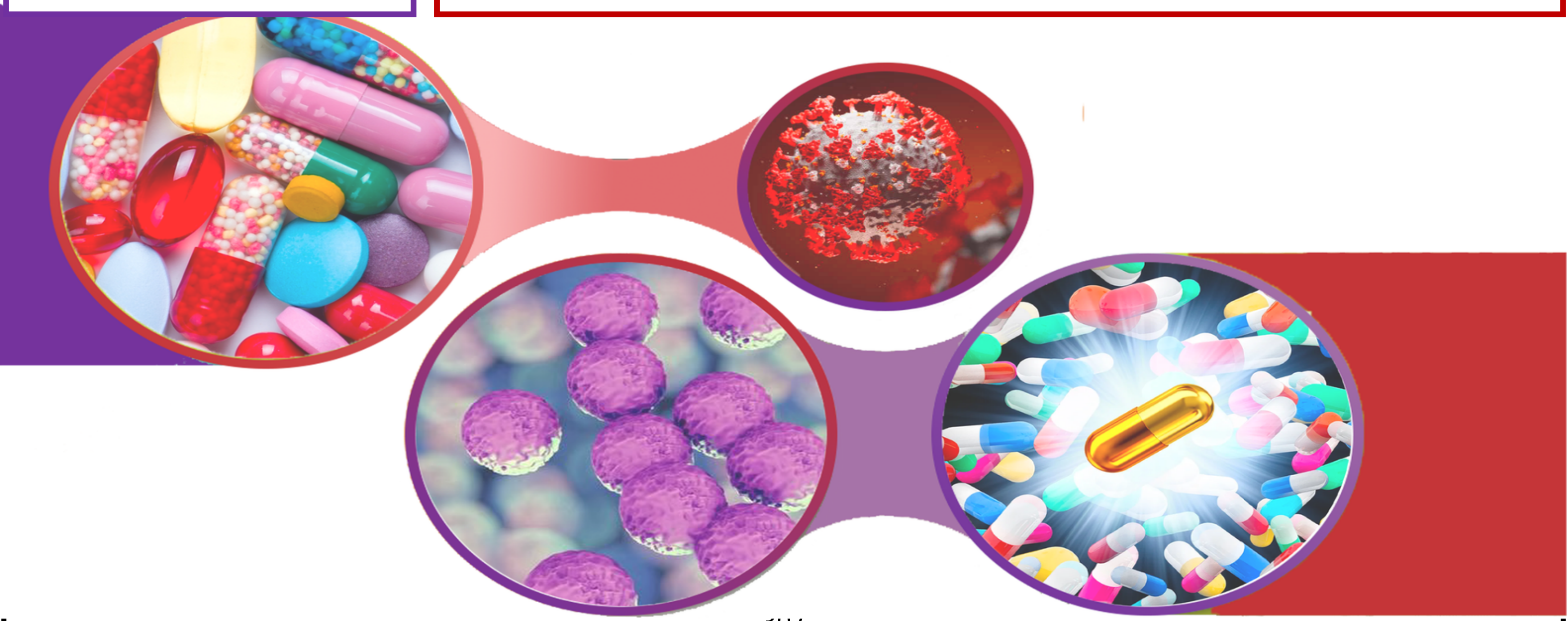



**Figure 5.** Front and Back-end Antimicrobial Strategy (Department of Health ESPAUR SSTF subcommittee, 2015).



# Registration

- This study has been registered in the ISRCTN registry, which is a primary registry recognized by WHO and ICMJE that accepts all clinical research studies. Additionally, this research is published in Octopus.

# Patient and public involvement

- Prior to conducting the study, the study protocol was sent to representatives of the Citizens Senate, a patient care organization with a good representation of many older people. They reviewed it and provided feedback. Study results will be shared through the communication team within the Trust.

# Public benefits:

- In 2019, over 1.2 million deaths were attributed to AMR. By October 2023, the COVID-19 pandemic had resulted in more than 6 million deaths. The pandemic exacerbated the AMR situation, amplifying the threat it posed. This research centered on the implementation of AMS both before and during the COVID-19 pandemic in acute care settings, offers pivotal insights for public health. It emphasizes the importance of optimizing antibiotic use to combat antibiotic resistance and ensure the sustained effectiveness of treatments. These insights not only advance better patient outcomes but also protect essential antibiotics for future generations and highlight lessons learned from the COVID-19 pandemic. The findings of this study will assist policymakers in their decision-making, guide healthcare professionals in responsible antibiotic prescribing, and enhance public awareness about AMR. Appropriate antibiotic use is pivotal in tackling the AMR challenge and safeguarding lives.

# Provenance and peer review

- Commissioned, internally and externally peer reviewed.

# Ethics approval

**Description of research methods, this research project consists of THREE sequential studies:**

**A Systematic literature review**

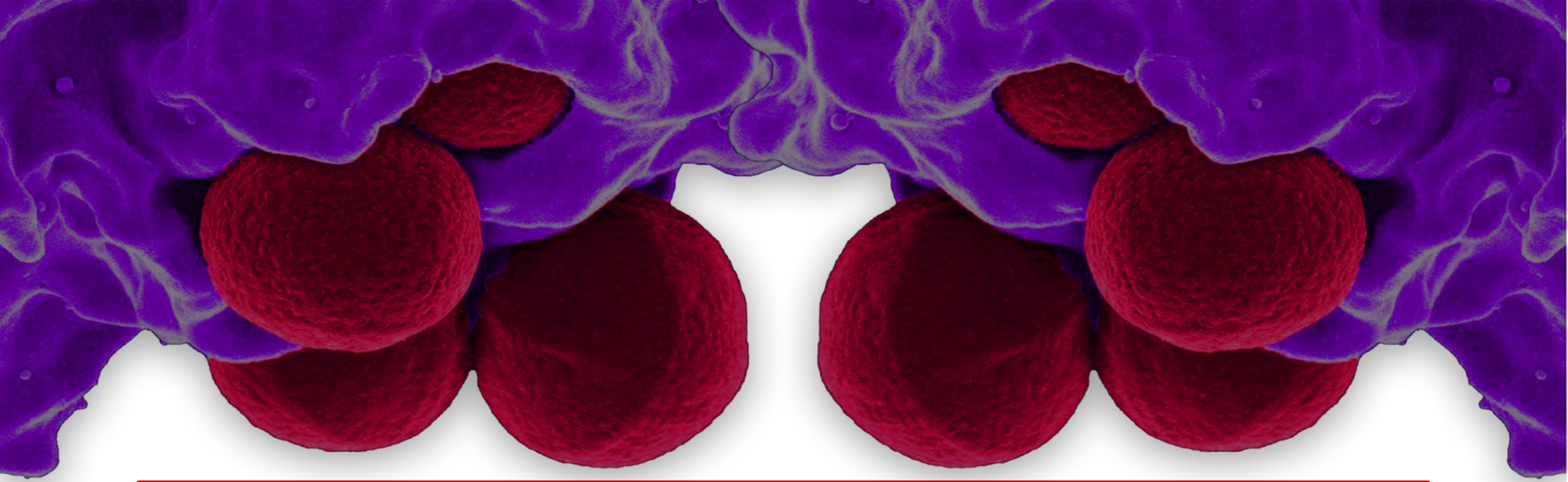
**A systematic literature review** of studies on antimicrobial stewardship (AMS) implementation has been conducted to investigate AMS strategies in acute care settings over the past 20 years. This review encompasses research conducted in acute care settings both prior to pandemic (PD) and during the COVID-19 pandemic (DP) on a global scale. The systematic literature review was registered with PROSPERO (registration number CRD42021242388) (York.ac.uk, 2022). The study has been successfully published in the PMC (PubMed Central) Journal.

**A retrospective study**

**A retrospective study** was undertaken at Bedfordshire Hospitals NHS Foundation Trust to assess antibiotic prescription patterns and AMS implementation before and during the COVID-19 pandemic. The study used medical records from adults aged 25+, pregnant women, and immunocompromised patients admitted in 2019 and 2020 with certain respiratory conditions. Exclusions included short A&E stays, non-prescription of antibiotics, and children. In total, 640 records (320 annually) were examined, each taking around 45 minutes. Data collection spanned 8 distinct periods, including four each from pre-pandemic and pandemic times. The review employed the PHE 'Start Smart - Then Focus' toolkit for validation.

**A prospective survey study**

**A prospective survey study** was conducted among healthcare professionals to gauge their understanding and perspectives on antibiotic prescription, AMR, and AMS during the COVID-19 era. The questionnaire was crafted from the PHE's report on secondary care hospital antibiotic prescriptions. The Royal Pharmaceutical Society and AMS pharmacists at the Trust validated the survey content. It targeted 240 healthcare professionals, specifically doctors, nurses, and pharmacists aged 25+. These professionals had to be registered with bodies like the GMC, GPhC, or NMC. Those lacking pandemic-era experience at the Trust were excluded. The chosen sample size ensured robust data collection for thorough analysis.



## Key Findings from the systematic literature review

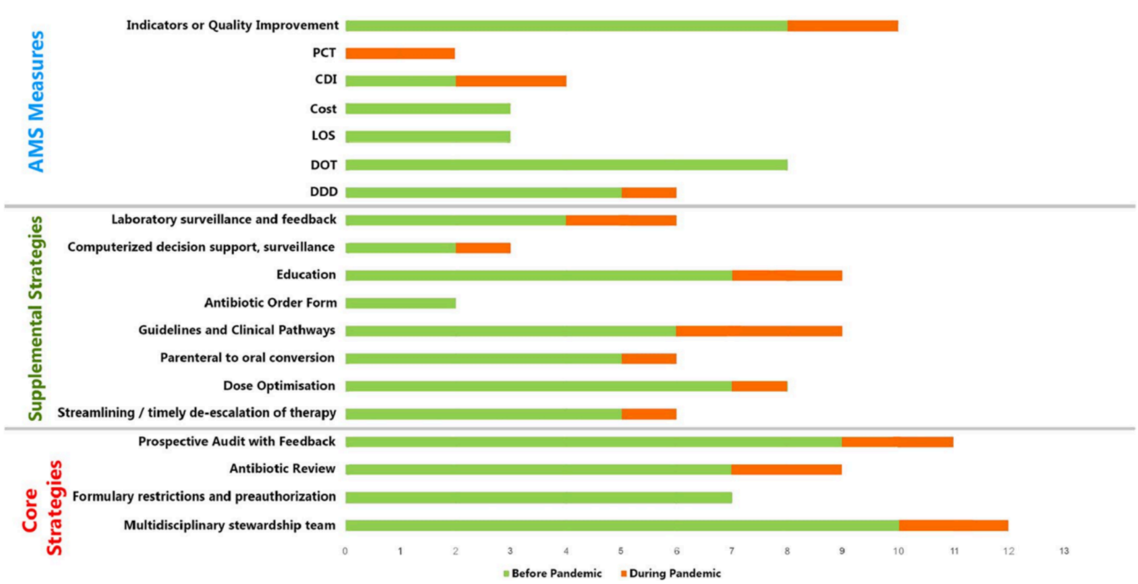
**Key findings from the systematic literature review** on impacts of COVID-19 on AMS implementation globally. The review analysed AMS strategies in acute care settings, comparing pre-pandemic and pandemic periods. The insights from the COVID-19 era emphasised the continued importance of AMS initiatives even post pandemic era. Key takeaways include:

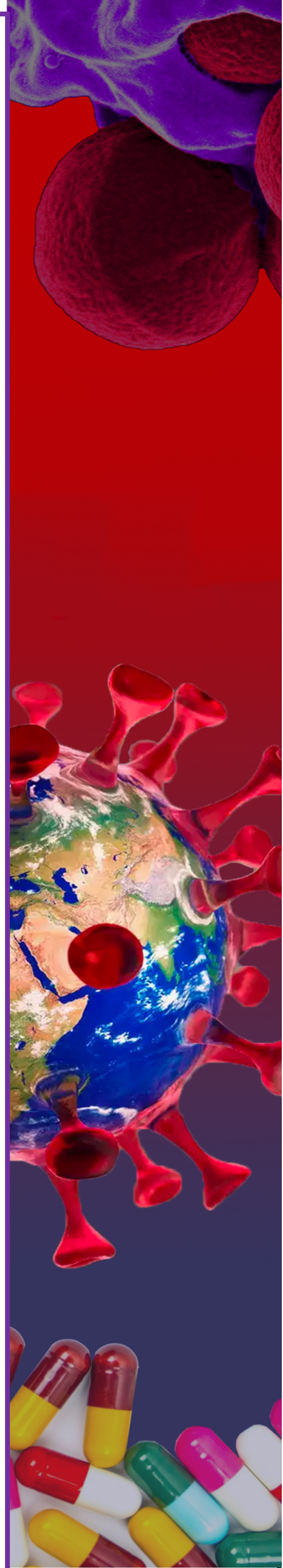
- A multidisciplinary team is essential for AMS structure and governance.
- For new stewardship programs, begin with core strategies and gradually incorporate supplemental ones.
- Hospitals should tailor AMS interventions based on local resources and expertise.
- Prospective audits and antibiotic reviews showed positive results in AMS implementation during the pandemic.
- Guidelines, clinical pathways, and education is vital for AMS success.
- National prescribing indicators, like the UK's National Action Plan, aim to reduce antibiotic use.
- New measures like Procalcitonin-guided antibiotic prescribing have proven effective.
- DDD and DOT are prevalent AMS measures, but standardization is required for comparative outcomes.
- Integrated tech support is crucial for sustained AMS and preparation for future emergencies.

### Summary of the Antimicrobial Stewardship Strategies and Measures from the Literature

- The Defined Daily Dose (DDD) is used globally to reflect antimicrobial usage, standardised by WHO as the average adult dose per day.
- DDD allows healthcare providers to calculate the total days of antimicrobial therapy by dividing the total used amount by the DDD for each drug.
- This standardisation enables comparison of antimicrobial usage across hospitals and countries.
- Hospitals should choose appropriate AMS metrics, considering the pros and cons of each, to ensure effective AMS implementation.
- Prior to the COVID-19 pandemic, DDD was referenced in five studies, Days of Therapy (DOT) in eight, Length of Stay (LOS) in three, costs in three, and Clostridioides difficile infection (CDI) in two.
- Quality Improvement indicators were noted in eight studies before the pandemic.
- During the pandemic, the use of DDD, CDI, Procalcitonin (PCT), and Quality Improvement indicators in studies dropped, with DDD featured in one study, CDI in two, PCT in one, and Quality Improvement indicators in two (Figure 6).

**Figure 6.** AMS before and during the COVID-19 pandemic in acute care settings (Total studies 13)



# 2- Key Findings from the Retrospective Medical Records Review Study

### Summary of Results

- Community-acquired pneumonia (CAP) remained a prevalent diagnosis.
- COVID-19 pneumonia showed a statistically significant increase in 2020.
- Comorbid conditions as hypercholesterolemia and heart failure presented significant odds ratios, but there was no significant change in the duration of antibiotic therapy.

### Increased Inappropriate Antibiotic Prescribing:

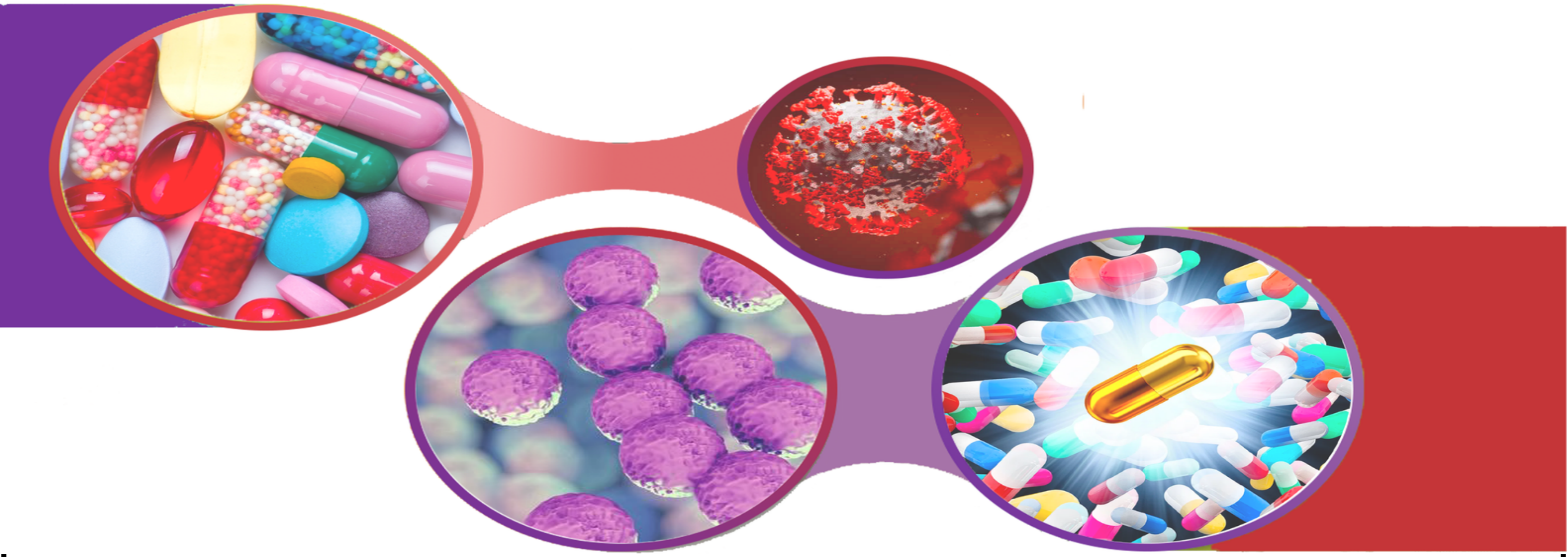
- Inappropriate antibiotic prescribing increased significantly during the COVID-19 pandemic compared to pre-pandemic for both pneumonia and upper respiratory tract infections.
- For pneumonia, inappropriate prescribing was 36.1% pre-pandemic and increased to 46.9% during the pandemic peak.
- Odds ratios indicated higher chances of 'Continue Antibiotics' and 'De-escalation' decisions during AMS interventions.

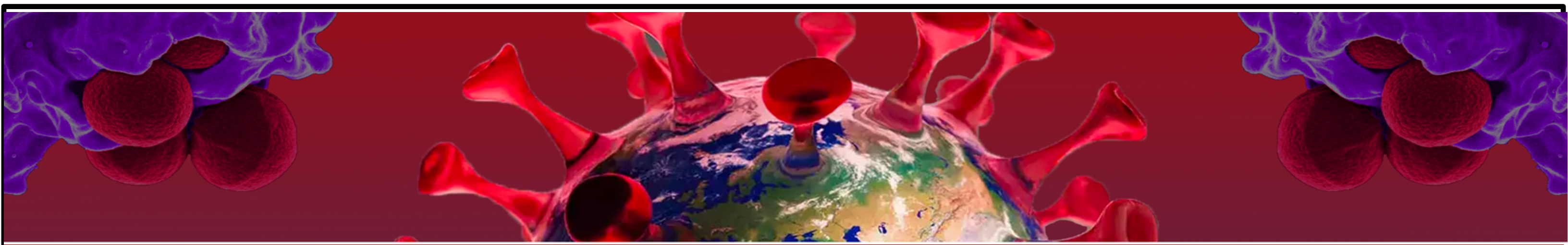
### Factors Affecting Antibiotic Prescribing

- Factors associated with inappropriate prescribing included older age, presence of comorbidities, ICU admission, and pneumonia diagnosis.
- Unclear diagnoses at admission affected appropriate antibiotic choice, but laboratory tests showed no significant differences except for Chest X-ray findings for pneumonia, which were more notable during the pandemic.
- During the pandemic, antibiotic therapy was commonly not aligned with culture and sensitivity report recommendations, which require further training and education.
- Antibiotic review after 48-72 hours is pivotal, to maintain AMS implementation and improve antibiotic prescribing.

### Generalisability of the Findings:

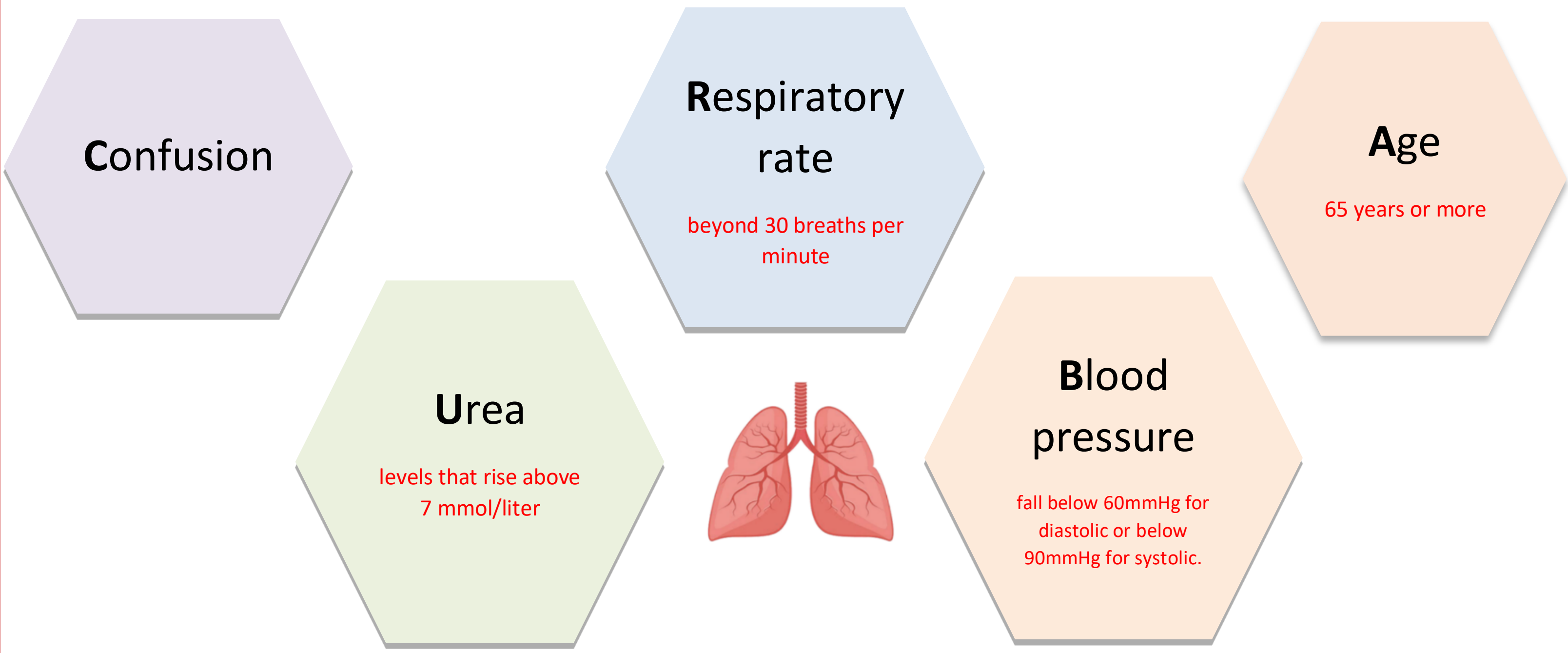
- The study setting, Bedfordshire Hospitals NHS Foundation Trust, suggests that the findings may be generalisable to other similar healthcare settings within the NHS system.





**Antimicrobial Prescribing in Community-acquired Pneumonia**

- The analysis revealed a tendency towards over-diagnosis of pneumonia. Community-acquired pneumonia (CAP) accounted for roughly 40% (128 out of 320) of prescribing indications in 2019, with a slight rise to 42% in 2020.
- The severity of CAP and the subsequent treatment approach is ascertained based on the **CURB65** score (Figures 7-8). Each of the ensuing prognostic indicators is allocated a **single point:**




In adult patients, the severity of CAP is appraised through clinical judgement, guided by mortality risk scores such as **CURB65 score:**

**Figure 7.** The CURB-65 Risk Assessment Framework for Community-Acquired Pneumonia

**A CURB-65 score of 0 or 1 signifies low severity.**

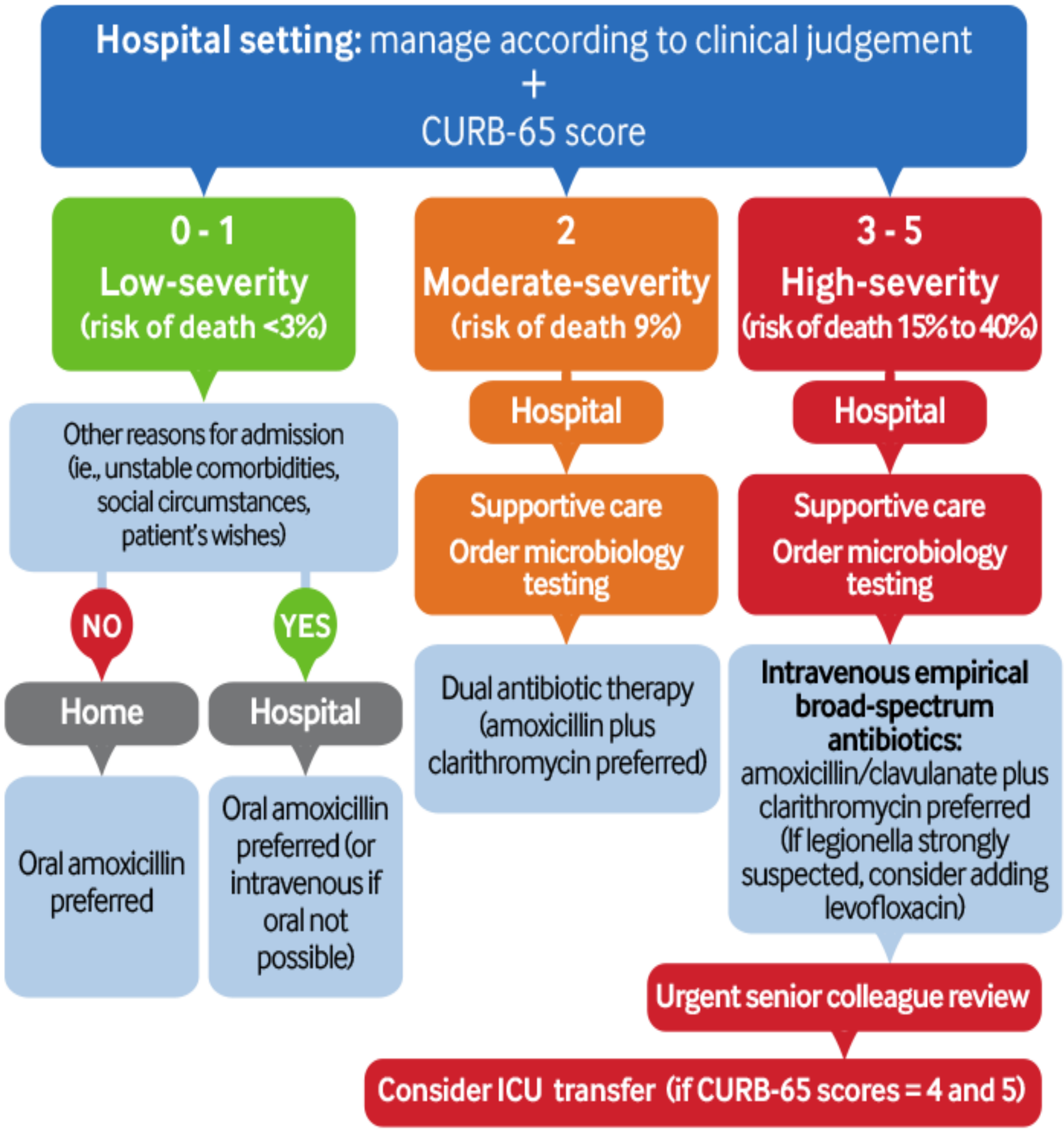
**Moderate severity is associated with a CURB-65 score of 2.**

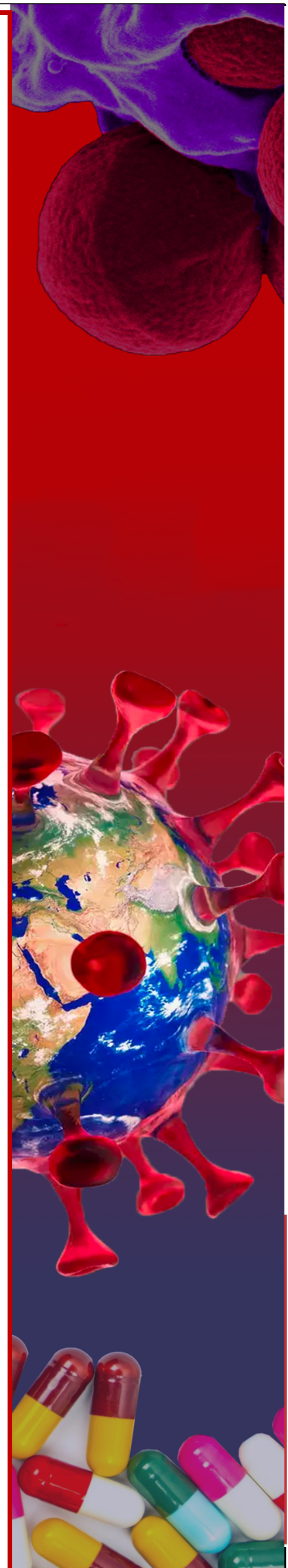
**High severity is denoted by a CURB-65 score ranging from 3 to 5.**

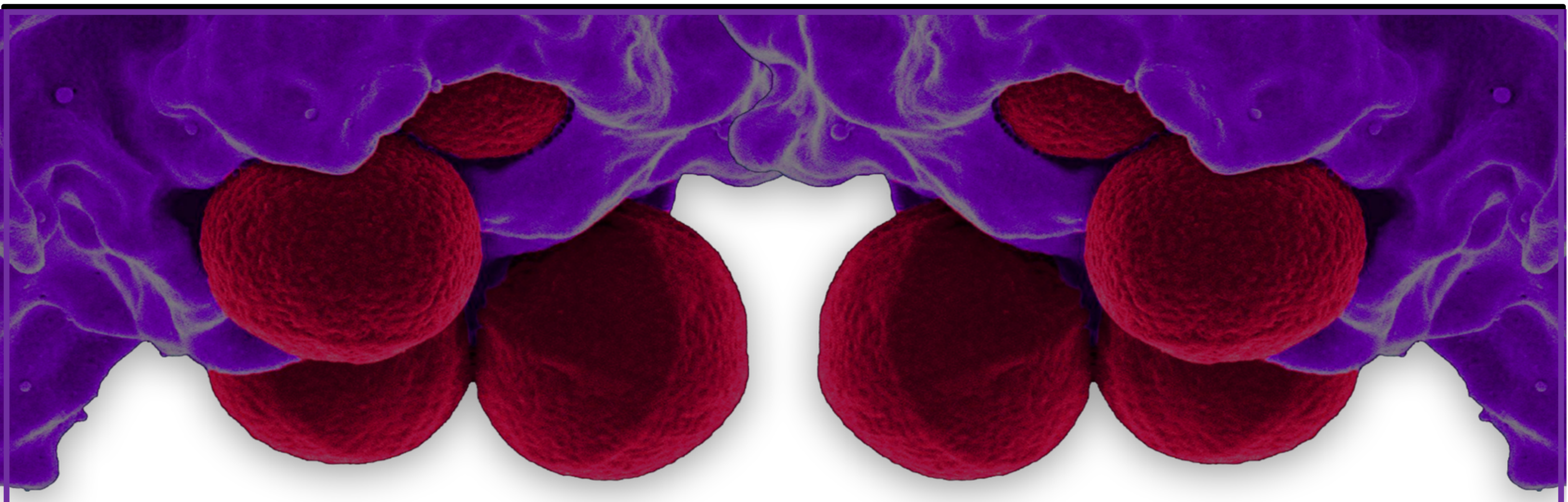
| CURB-65 | Clinical Feature | Points |
|---|---|---|
| C | Confusion | 1 |
| U | Urea>7 mmol/L | 1 |
| R | RR≥30 | 1 |
| B | SBP≤90 mm Hg OR DBP≤60 mm Hg | 1 |
| 65 | Age>65 | 1 |

- The local antimicrobial guidelines, in conjunction with the National Institute for Health and Care Excellence (NICE), dictate that antibiotic prescribing for CAP according to the CURB-65 score (Bedfordshire, 2019).
- As such, the selection of antibiotics is escalated concomitant with an increase in the CURB-65 score. However, within the data procured from the study population, the CURB-65 score was only reported in three instances. This scarcity of data may potentially influence the appropriateness of antibiotic prescribing for patients diagnosed with CAP (NICE, 2016).

**Figure 8.** Risk assessment and management of CAP in the first 4 hours of admission in an acute care setting (Bestpractice.bmj.com, 2020)

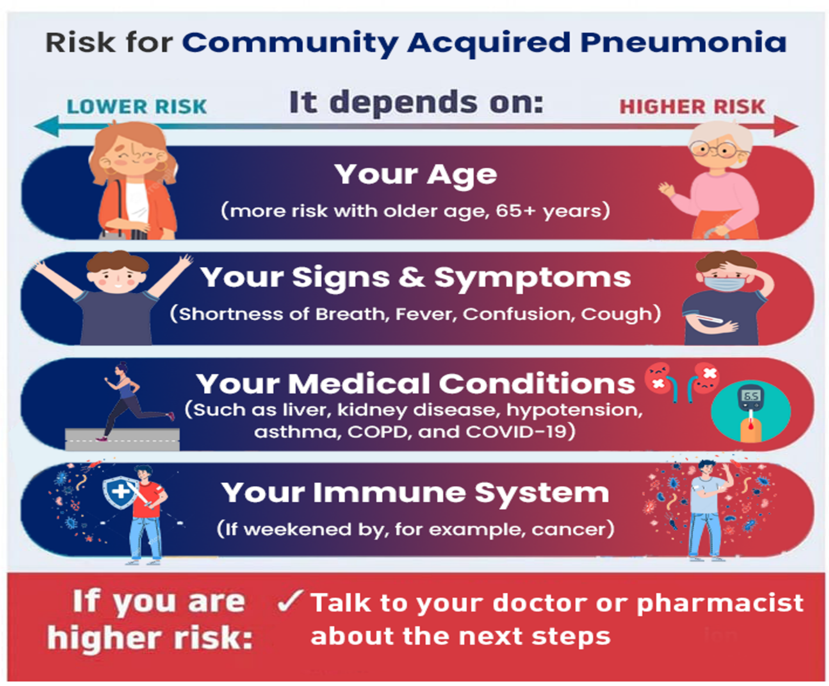




- Upon analysing the assembled data and the CURB-65 score, it was found that age of 65 or above, confusion, and hypotension were the most salient factors escalating the risk severity of CAP. Moreover, key symptoms upon admission, such as shortness of breath (SOB), fever, and cough, experienced an increase in 2020 compared to 2019. For instance, incidences of SOB rose to 33% (106 out of 320) in 2020, as opposed to the pre-pandemic level of 22.5% (72 out of 320) in 2019.
- Furthermore, the presence of other clinical conditions could influence the prescribing of antibiotics for CAP. Notably, respiratory conditions such as Chronic Obstructive Pulmonary Disease (COPD), Asthma, and COVID19 significantly impacted antibiotic prescribing patterns in 2020. Conditions that compromise the immune system, such as cancer, also play a pivotal role. Lastly, incidents such as accidental falls can exacerbate the severity of illness and consequently affect the appropriateness of antibiotic prescribing. However, it's essential to note that these findings necessitate further investigation to fully understand this complex issue.
- Public and Patient Involvement in promoting awareness and education regarding the risk of CAP is crucial. This poster is designed to help health professionals emphasize the importance of informing the public and patients about the risks and symptoms of CAP, with a particular focus on vulnerable populations (Figure 9)

**Figure 9.** Assessing Risk Factors for Community-Acquired Pneumonia: A Guide for Patients and Healthcare Providers



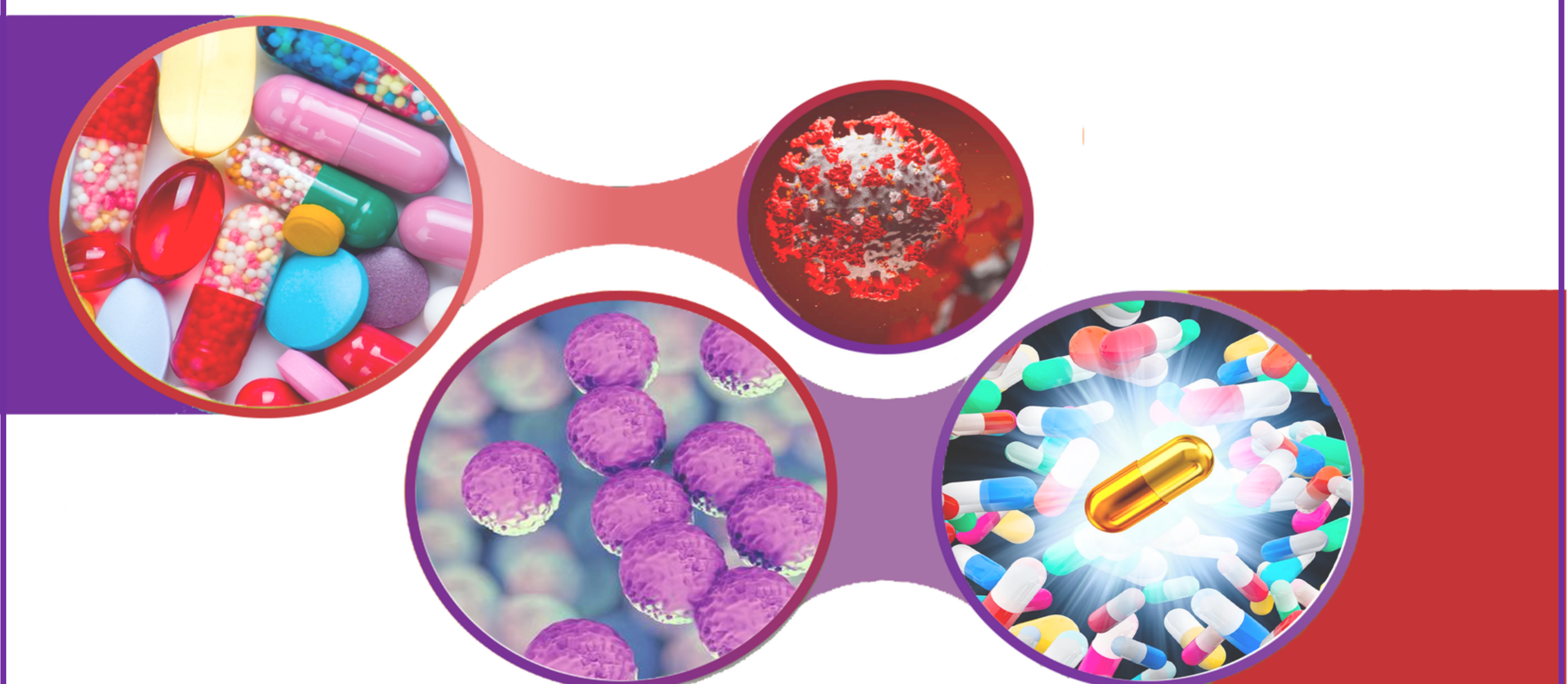
## Antimicrobial Prescribing in Hospital-Acquired Pneumonia

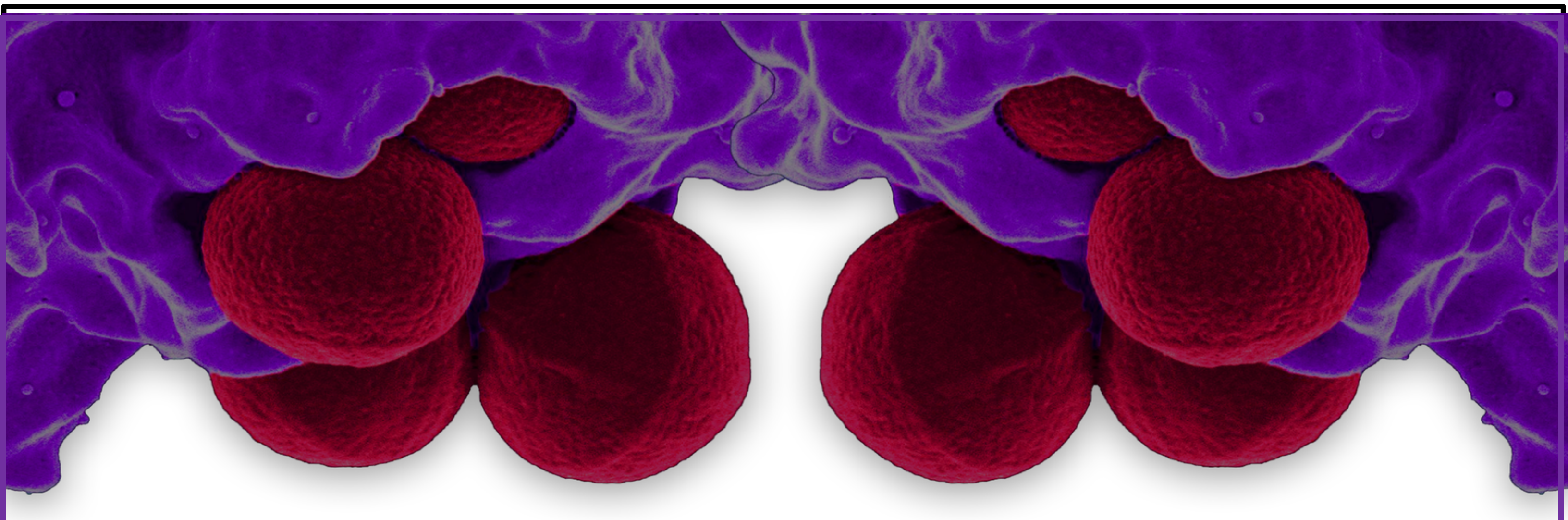
- Hospital-acquired pneumonia was the second most indication among the study population. It is a specific type of pneumonia that manifests 48 hours or more subsequent to hospital admission and was not in the incubation phase at the time of admission, background, prescribing considerations (NICE, 2019).
- According to local antimicrobial guidelines, **it is categorised into:**

1. **Early-onset** Hospital Acquired Pneumonia, which emerges **between 48 to 96 hours** from admission, with no prior antimicrobial treatment.

2. **Late-onset** Hospital Acquired Pneumonia, which appears **after 5 days** from admission or follows previous antimicrobial treatment.

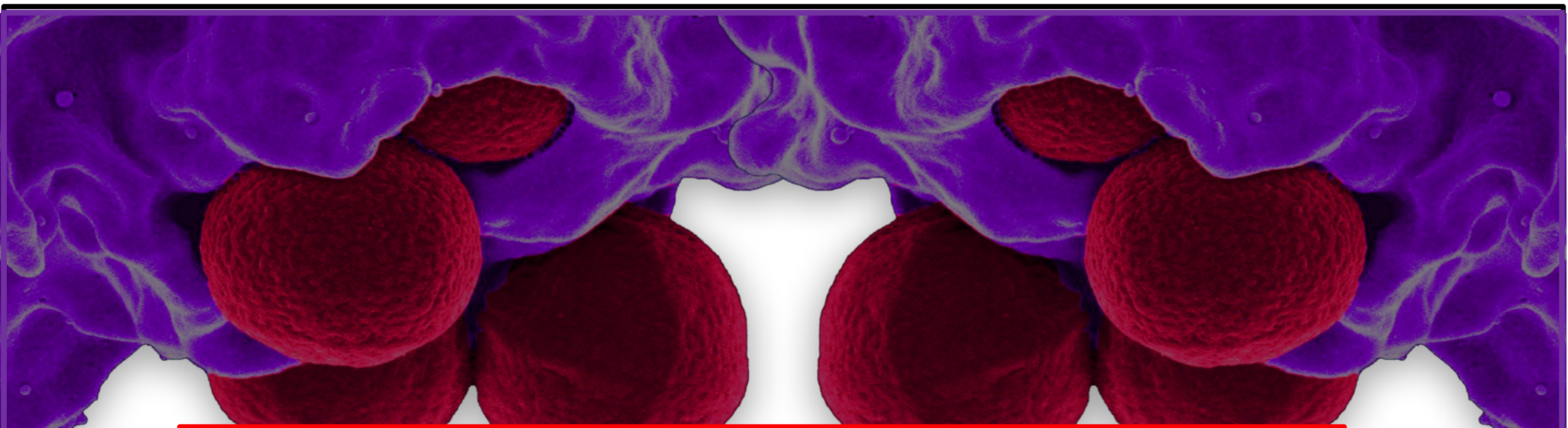
- The choice of antibiotics is contingent upon the classification of HAP. The antibiotics selection escalates with the increase in the patient's length of stay in the hospital.
- The analysis from this study has suggested that the incidence of Hospital-Acquired Pneumonia (HAP) saw a decline from 21% (equating to 67 out of 320 cases) to 16% (which represents 52 out of 320 cases) in the year 2020 (Table 4).
- Conversely, the prevalence of early-onset HAP was found to be 5% (equivalent to 5 out of 106 cases) among all the participants of the study. Nonetheless, the incidence of late-onset HAP was significantly higher, standing at 95%.





**Further results** have been evolved from the retrospective medical record review will be published soon, including:

- Prevalence of inappropriate antibiotic prescribing by indication.
- Prevalence of Healthcare-Associated Infections (HCAI).
- The Challenge and Risk of Interpreting Uncertain Diagnoses.
- Descriptive analysis of the prescribed antibiotics in 2019 and 2020.
- AWaRe Classification and Antibiotic Trends during the COVID-19 Pandemic.
- Defined Daily Dose (DDD) and trends of antibiotic prescribing in 2019 and 2020.
- The Seven Most Commonly Prescribed Antibiotics Before and During the Pandemic.
- Prevalence of Inappropriate Antibiotic Prescribing and the Impact of COVID-19.
- Factors Affecting Inappropriate Antibiotic Prescribing, such as IV-to-Oral Switch, Antibiotic allergy.



# 3- Key Findings from the Prospective Survey Questionnaire Study

**1. Awareness and Education on AMS:** There's a critical need for enhanced awareness and education on AMS interventions, especially concerning the use of 'IVOS', 'De-escalation', and 'Stop' strategies in antibiotic use. Healthcare professionals demonstrated good overall knowledge related to antimicrobial resistance, however, AMS attitudes and perceptions require further training and education.

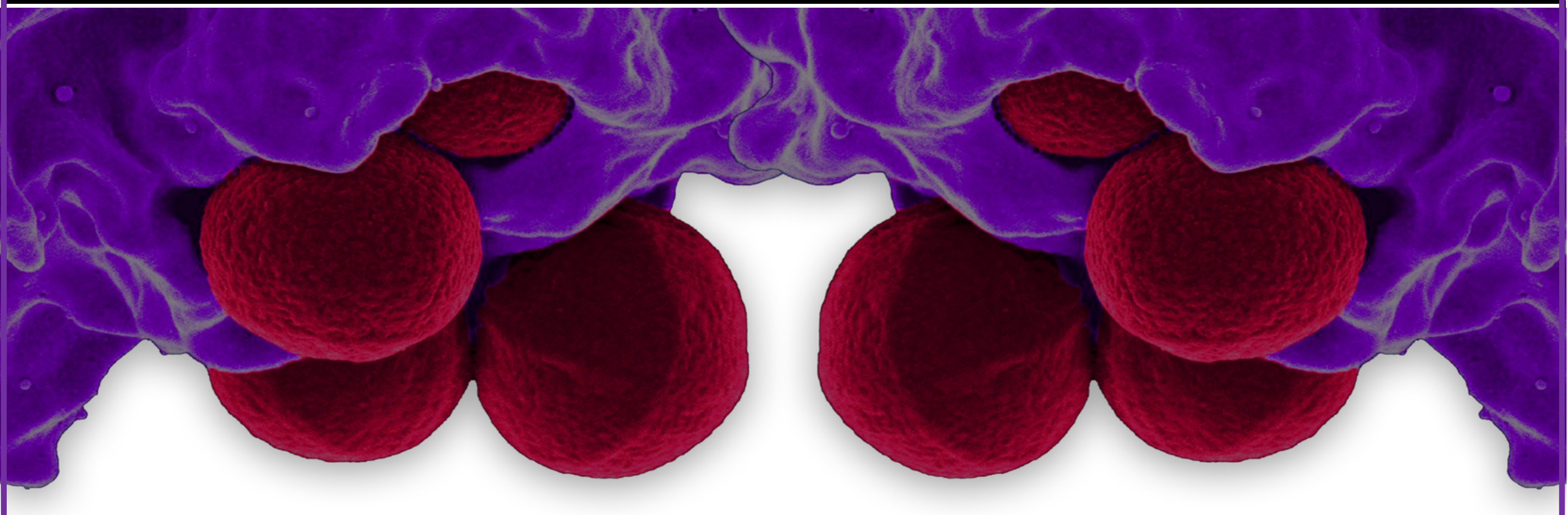
**2. The Pivotal Role of Pharmacists in AMS:** It is interesting to note that pharmacists possess a strong foundation of knowledge, as well as positive attitudes and perceptions toward antibiotic prescribing and AMS practices. This highlighted the essential role pharmacists play in co-leading AMS implementation alongside microbiology teams, thereby fostering interprofessional collaboration that facilitates appropriate antimicrobial use.

**3. Impact of COVID-19 on AMS:** AMS interventions, including ward rounds, education, guidelines, and auditing, experienced significant disruptions due to the negative impact of the COVID-19 pandemic.

**4. Barriers and Adaptations in AMS:** A profound understanding of healthcare professionals' perceptions and the factors affecting AMS implementation is necessary. Perceived barriers to optimal stewardship including workload % time constraints. COVID-19 impacted AMS activities, such as ward rounds, audits, and education, may have long-term effects on AMR trends.

**5. Educational Initiatives and Targeted Interventions:** The study identified a lack of robust educational programmes on AMS and a need for targeted interventions, especially for healthcare professionals lacking in specific AMS-related knowledge and practices. However, pharmacists showed the highest knowledge levels, for this reason, their role in maintaining AMS implementation is pivotal.

**6. The Future of AMS Post-Pandemic:** Innovations in educational resources, awareness, & collaborative efforts crucial to support AMS practices in the post-pandemic era. Additionally, supporting role of pharmacists in domain is essential, particularly in preparing for any future emergencies or crises, to sustain responsible antibiotic use & mitigate the threat of AMR, thereby safeguarding patient lives.



## INNOVATIVE Survey Dissemination at Bedfordshire Hospitals NHS Foundation Trust:

- Special thanks to the R&D department at Bedfordshire Trust for their recommendation to employ innovative methods in the survey distribution, which helped to boost participation among HCPs (Figure 10). Collaboration among the R&D team, AMS pharmacists, and the microbiology consultant was key in using a variety of distribution channels, such as:

**1. Email invitations sent to group lists of pharmacists, doctors, and nurses.**

**2. Survey posters placed strategically in wards, medicine trolleys, nurse stations, MDT rooms and notice boards.**

**3. Inclusion in the weekly newsletter circulating the survey link/package.**

**4. Select optimal distribution times - early morning, lunchtime, and after duty.**

**5. Participants could withdraw before submitting, but responses were anonymised after.**

**6. Efforts made to ensure confidentiality and consistently encourage participation.**

**7. Emails AMS pharmacists and newsletter reminders by “Communication Team’ before the survey closed.**

**8. WhatsApp, emails, and other channels are also used to disseminate the survey link among HCPs.**

**9. Multi-modal distribution strategies aimed to optimise survey participation.**

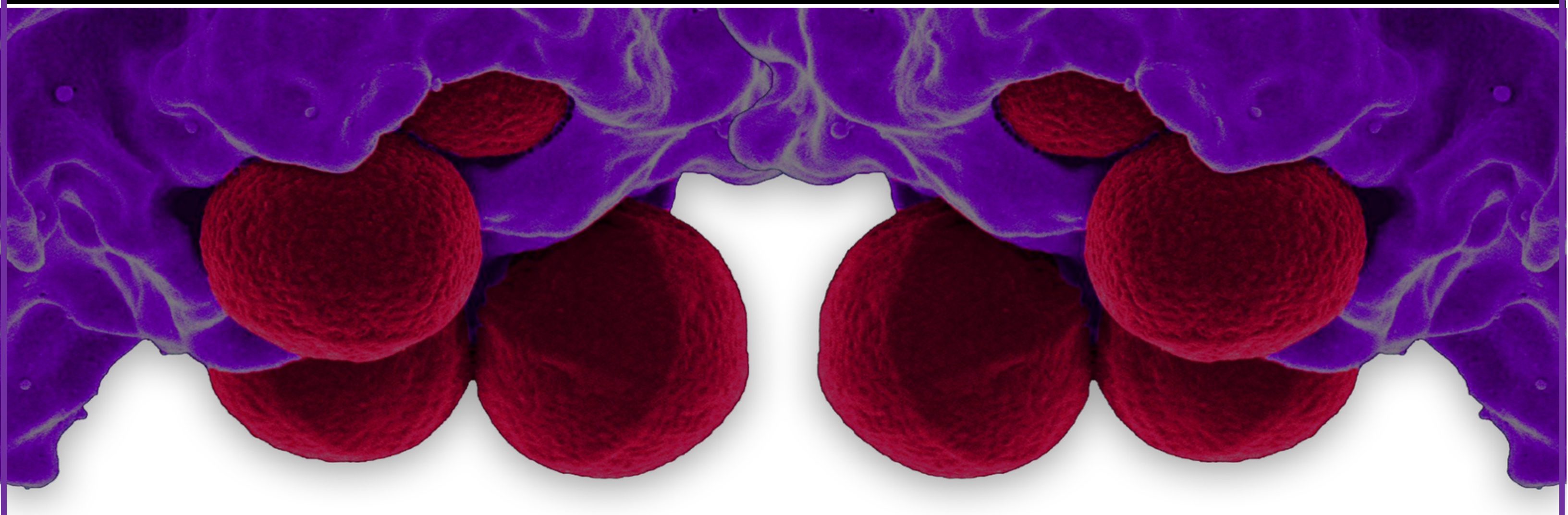
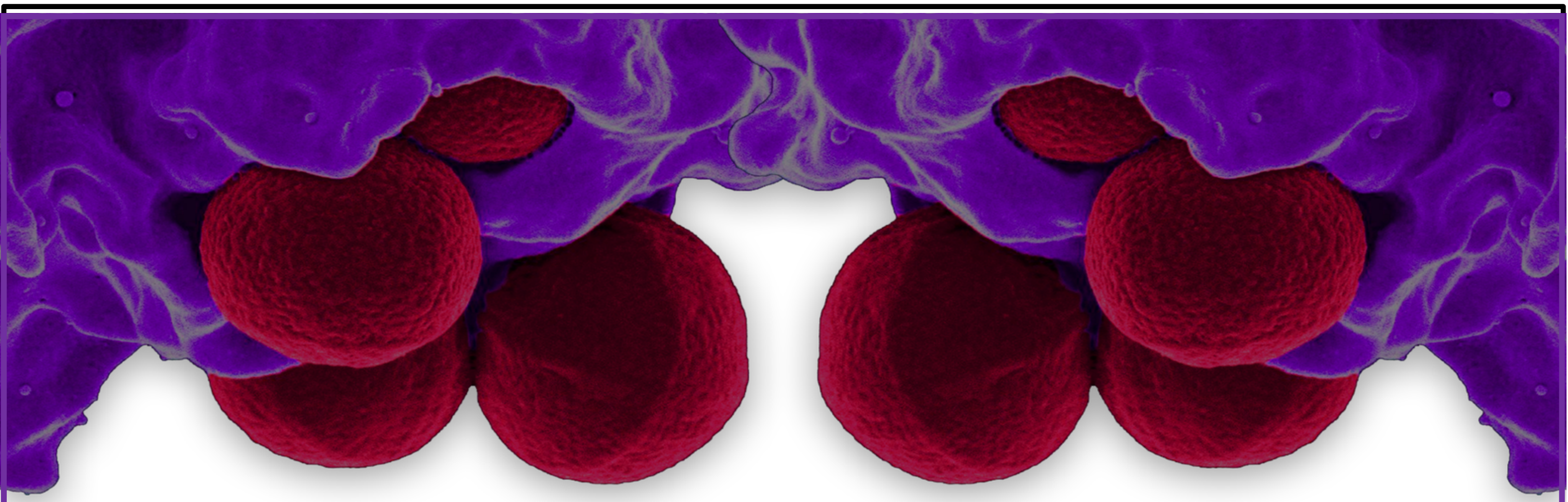


**Figure 10.** Innovative Distribution Strategies in Antimicrobial Resistance Survey Distribution in the Trust.

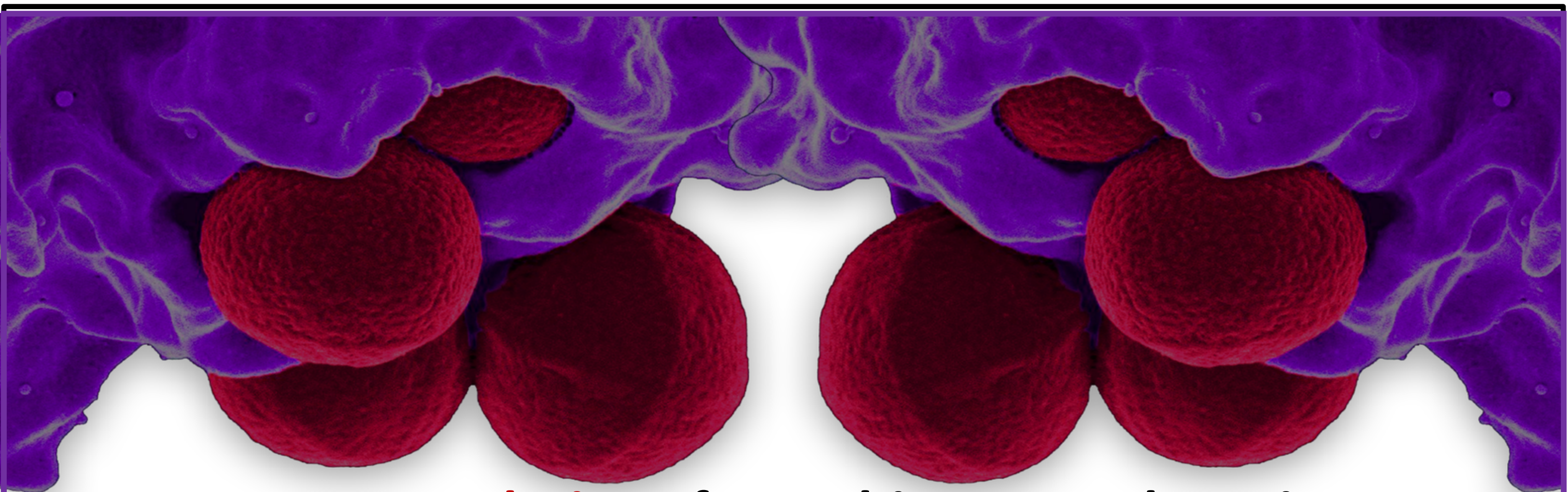


## Highlights of the survey questionnaire study results

1. The survey highlights the need to increase awareness and knowledge among healthcare HCPs towards antibiotic prescribing through positive attitudes and effective practices.
2. Factors such as age, gender, background, and experience influence knowledge, attitudes, and practices (KAP).
3. Lack of robust AMS education and training worsens AMR. Establishing impactful educational initiatives is critical.
4. The survey provides new insights into COVID-19's impacts on antibiotic prescribing, AMR, and AMS activities.
5. Significant disruptions occurred in AMS ward rounds, audits, and education during the pandemic.
6. Consequences of decreased AMS on rising AMR may become apparent in coming years, requiring vigilant monitoring.
7. The pandemic highlighted the importance of innovative tools, education, awareness, and collaboration to strengthen AMS and pharmacists' roles in the future.

**Overall**

The preceding **THREE** studies emphasised the critical need to tackle the rise in inappropriate antibiotic usage, highlighting the necessity for effective AMS strategies and education. This is particularly urgent given the COVID-19 pandemic's significant disruption of prescribing habits and AMS efforts.



# Recommendations from This Research Project

## Healthcare Policy

- Establish AMS multidisciplinary committees in each Trust.
- Regularly update local antibiotic guidelines based on antibiograms and surveillance.
- Conduct regular AMS ward rounds with effectiveness measures.
- Provide training to enhance AMS skills of healthcare professionals.
- Promote research into AMS interventions.
- Develop connections between secondary and primary settings.
- Incorporate AMS measures into electronic prescribing systems.
- Promote AMS auditing tools as the Start Smart Then Focus.

## Academic

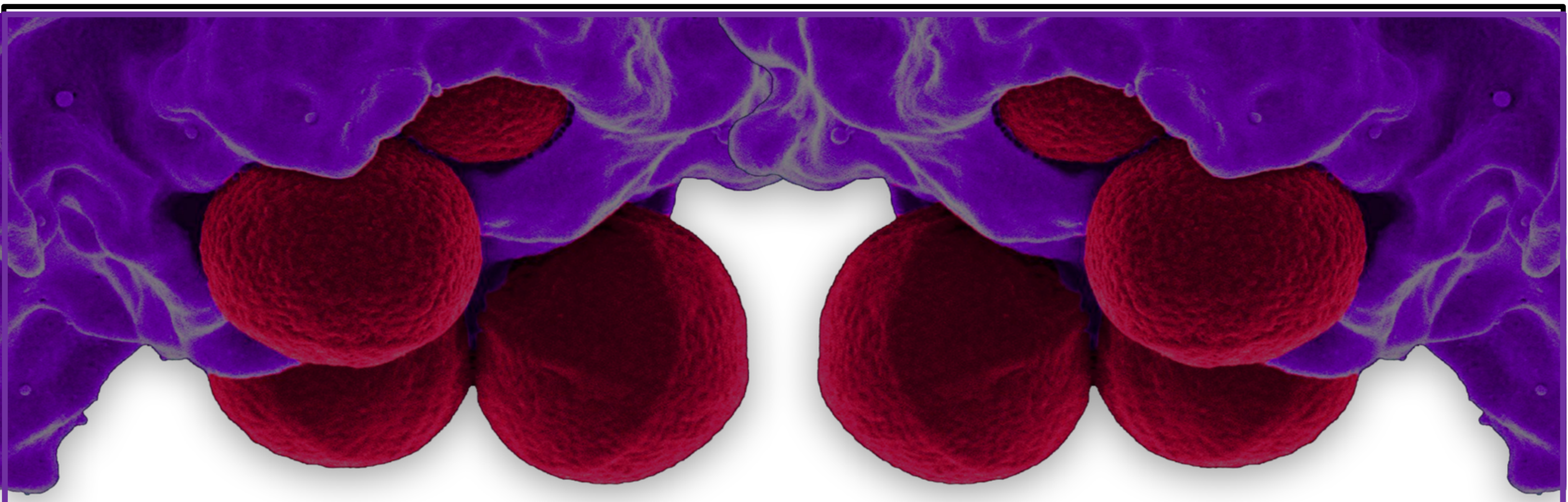
- Incorporate AMS into undergraduate curricula for medicine, pharmacy, nursing.
- Promote interprofessional AMS education at the undergraduate level.
- Develop AMS curricula for postgraduate and continuing education.
- Establish AMS-focused registration programs.
- Encourage AMS professional development and use of metrics.

## Clinical Practice

- Designate AMS leads/teams and identify barriers.
- Conduct regular antibiotic reviews and AMS ward rounds.
- Promote antibiotic reviews at 48-72 hours and 5-7 days post admission.
- Improve documentation of AMS interventions and diagnosis.
- Develop local antibiotic policies aligned with guidelines and antibiograms.
- Make local antibiotic guidelines easily accessible through digital methods.
- Note prior antibiotic use from primary care in hospital systems - Emphasise patient empowerment and public involvement.

## Public Health

- Conduct public campaigns to increase AMS/AMR awareness year-round.
- Cultivate patient/public advocacy and involvement in AMS.
- Provide AMS/AMR educational materials in healthcare facilities and waiting areas.
- Incorporate AMS information and updates on hospital websites.

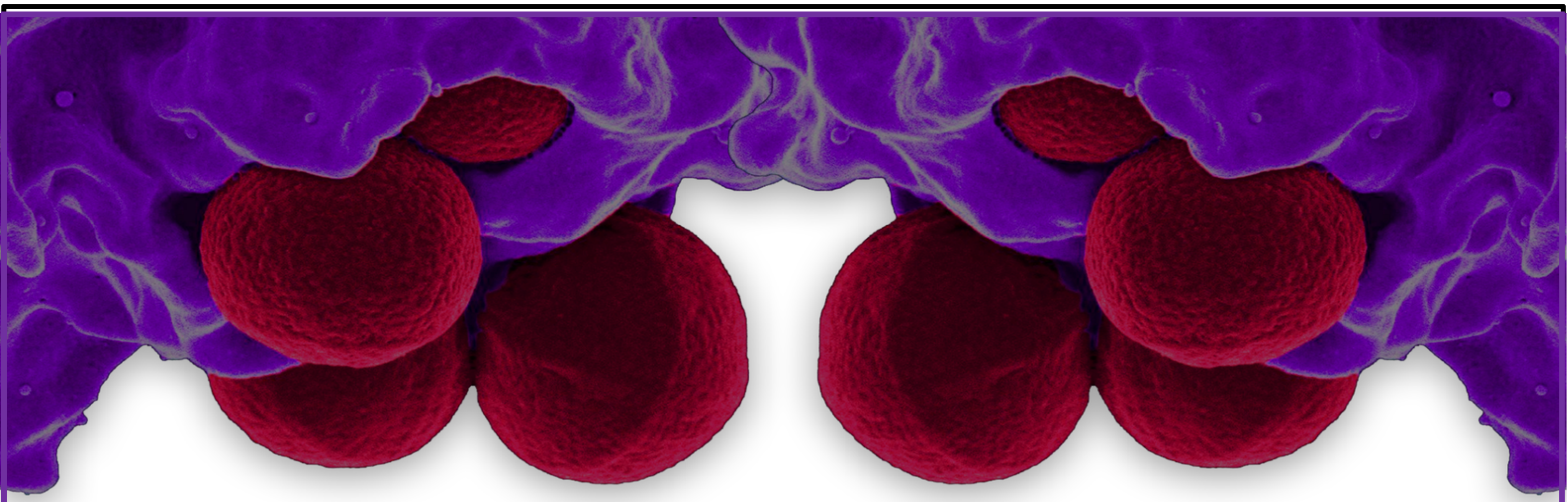


## Research Project Outputs

### 1- Antimicrobial Stewardship Roadmap

- **AMS Gap Analysis Tool**: Identifies strengths and weaknesses in current antimicrobial practices to target areas for improvement.
- **AMS Strategic Plan**: Develops a comprehensive vision and objectives for stewardship based on gap analysis findings.
- **Action Plan**: Translates strategic vision into concrete initiatives and steps, supported by scientific evidence.
- **AMS Toolkit:** Provides resources and tools to support the implementation of the action plan, promoting judicious antibiotic use.

- **AMS Implementation:** Executes the action plan, applying interventions to promote optimal antibiotic prescribing practices.
- **AMS Measures:** Utilises dashboards, metrics, and KPIs to evaluate the effectiveness and sustainability of AMS interventions.
- **Continuous Improvement Cycle:** Allows for reassessment and re-evaluation to maintain the relevance and effectiveness of AMS implementation.
- **AMS Training Program**: Proposes ongoing education and training for healthcare professionals to sustain and improve AMS practices.
- **Challenges and Adaptation:** Acknowledges the impact of crises as COVID-19 pandemic on AMS and the need for adaptive strategies.
- **Communication and Education:** Highlights the importance of sharing AMS progress and education with both healthcare professionals and the public for broader awareness.



## Research Project Outputs

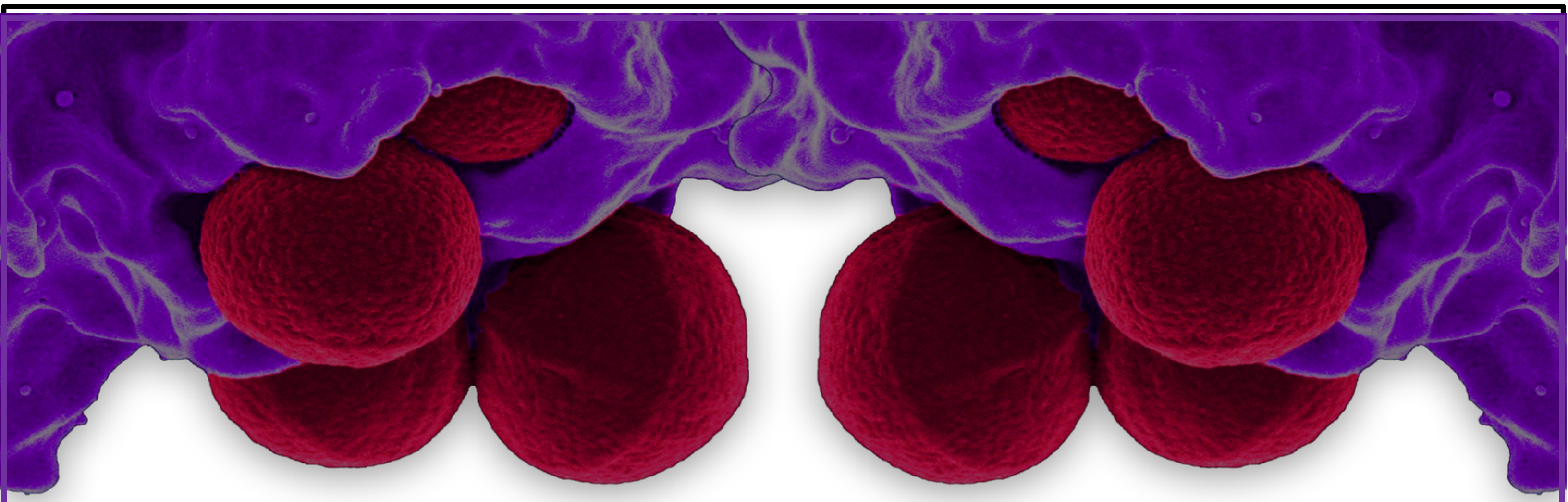
### 2- Antimicrobial Stewardship Dynamic Dashboard:

- **AMS and Antibiotic Prescribing:** Essential for assessing AMS impact and benefits for patients. Measurements serve as KPIs, quality assurance, and improvement tools.
- **Data Extraction and Dashboard Utility:** AMS Dashboard supports consistent assessment and identifies improvement areas.
- **Impact of COVID-19 on AMS:** The pandemic affected AMS education and audit feedback negatively. Rise in broad-spectrum antibiotics use, HCIs and resistance concerns.
- **Importance of the Dashboard:** Facilitates smart starting with broad-spectrum antibiotics when necessary. Supports targeted treatment based on clinical evidence.
- **Dashboard Contents:**

1. Selection Filters: Interactive controls for data segregation (by month, main diagnosis, wards).
2. Hospital Admissions: Bar graphs for age groups and diagnoses.
3. Antibiotic Allergies and Prescriptions: Graphs and charts for allergies and prescription frequency.
4. AMS Interventions: Visuals on interventions and antibiotic review frequency.
5. Professional Reviews: Pie charts roles in antibiotic reviews

- **Features of the AMS Dashboard:** Real-time visualization for immediate action and promotes informed decision-making by hospital leadership.
- **Targeted Therapy and Length of Stay:** Details interventions and antibiotic use during hospital stay and upon discharge and provides insights into patient hospital stay duration.
- **Persistence of AMS Principles:** Necessary across hospital sectors during and post-pandemic, and aids in maintaining AMS practices during emergencies.

**The description provided offers a comprehensive overview of the functionalities and the significance of the Antimicrobial Stewardship Dynamic Dashboard, underpinning its role in enhancing antimicrobial usage, supporting AMS initiatives, and addressing challenges in antibiotic prescribing practices, especially in the context of the COVID-19 pandemic.**



# Research Project Outputs

## 3. Antimicrobial Stewardship Comprehensive Training Program

**Background and need for AMS Education:**

- Recent studies indicate challenges in AMS education during the COVID-19 pandemic.
- There is a noted rise in inappropriate antibiotic dosing and a decline in adherence to prescribing guidelines.
- The course is designed to address educational gaps and improve stewardship practices.

**Course Structure:**

- Integrates insights from key studies on AMS practices during the pandemic.
- Provides a step-by-step guide through the AMS Roadmap for strategy implementation.

**Educational Framework:**

- Based on the "Start Smart, Then Focus" toolkit and the UK AMR 5-year action plan.
- Aimed at comprehensive understanding and application of AMS strategies.

**Course Aims:** To develop AMS knowledge applicable across health systems. To empower learners to lead AMS interventions. To promote systematic patient management approaches.

**Proposed Outcomes**:

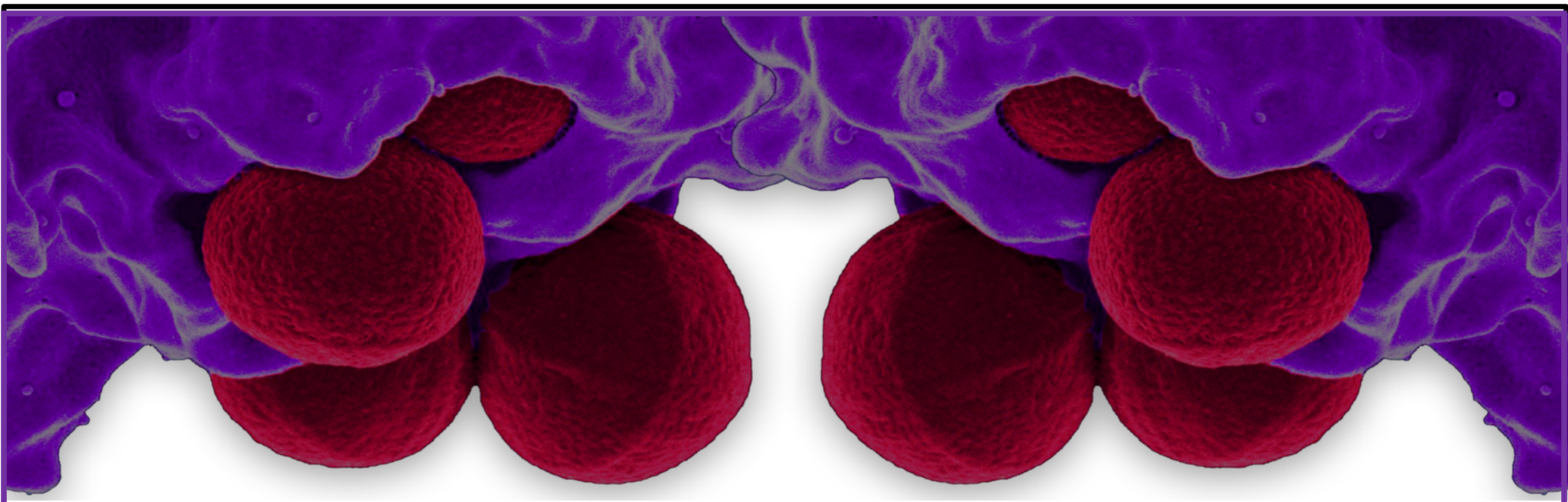
- Ability to apply AMS strategies against AMR.
- Skill to assess and improve AMS practices.
- Competence in managing infectious conditions using current guidelines.
- Capability to use AMS tools for stewardship and quality improvement.

**Learning Topics:** 20 'Essential' topics covering a comprehensive AMS framework. Learning topics are detailed in the course material.

**Target Audience:** Healthcare professionals, including pharmacists, doctors, nurses, and AMS leads.

**Accreditation and Learning Methodology:** Proposed to be CPD accredited for practical workplace application. Project-based learning module for peer collaboration and engagement.

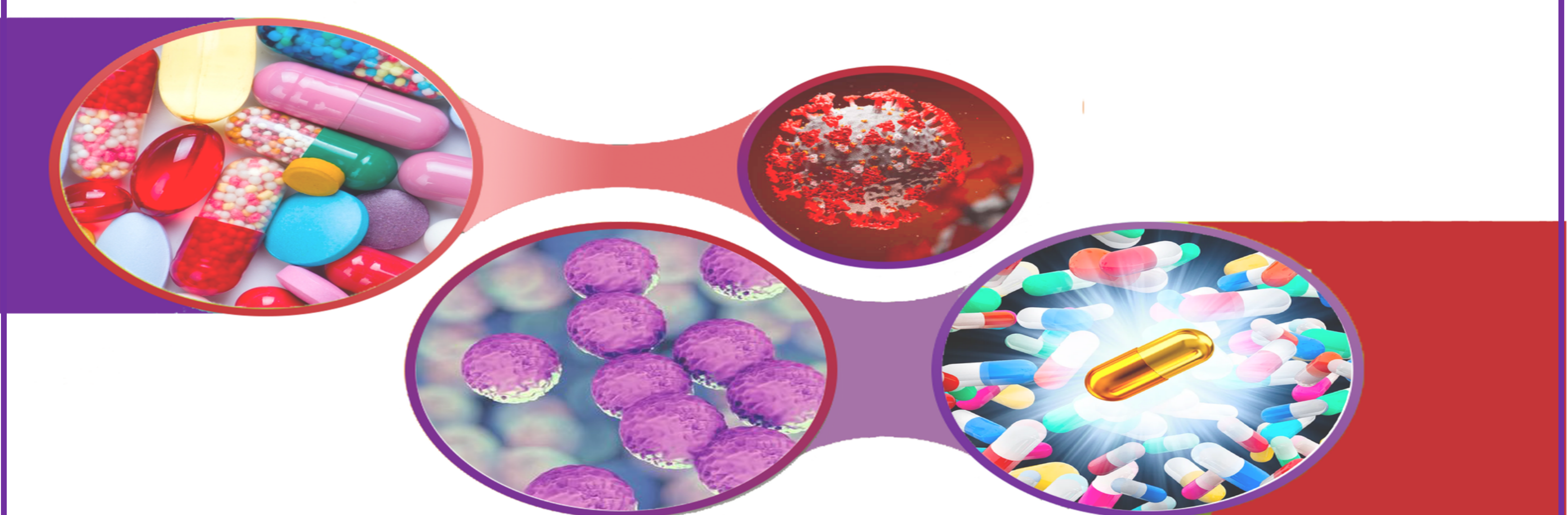
**Delivery and Support:** A blended learning approach with face-to-face and self-directed modules. Includes case-based discussions and learner support systems.

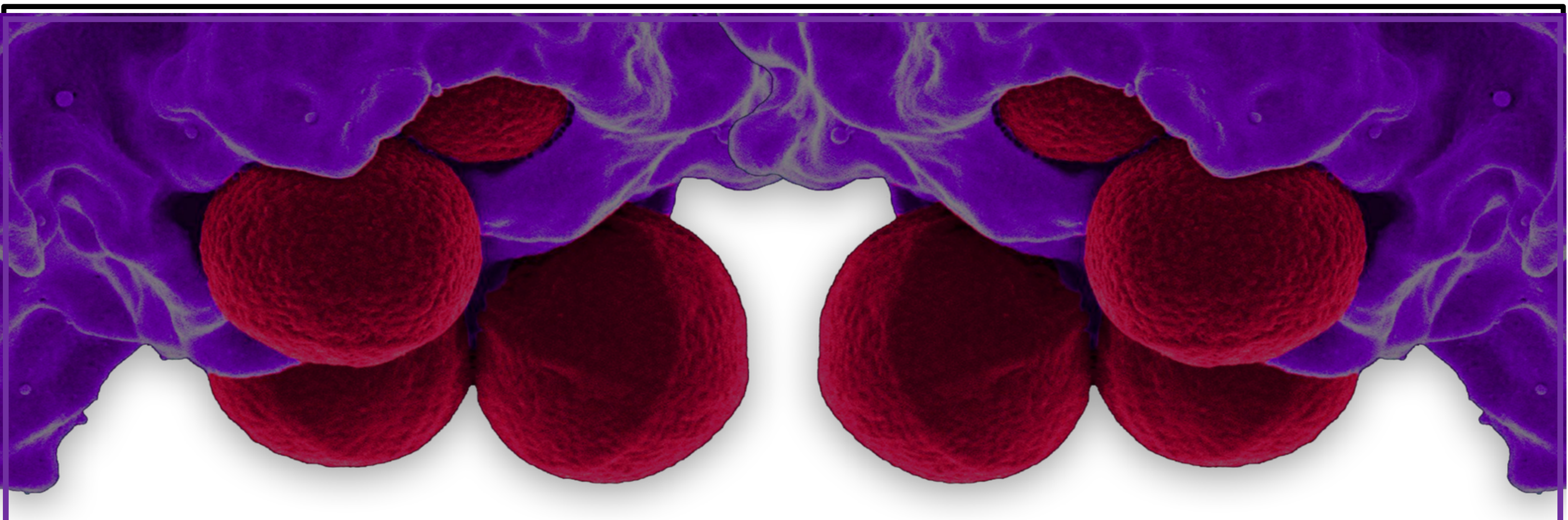


## Research Project Outputs

### 4. Antimicrobial Stewardship Card

- Utilisation of a QR code for the survey questionnaire study, prominently displayed for HCPs, as an essential contribution to the research project's success provide an impressive outcome.
- The presence of mobile tools, internet resources, and hospital systems notwithstanding. However, the high workload and numerous distractions call for an easily accessible AMS card as a potential practical solution.
- The AMS card could aid in enhancing antibiotic prescribing practices and streamline the implementation of AMS.





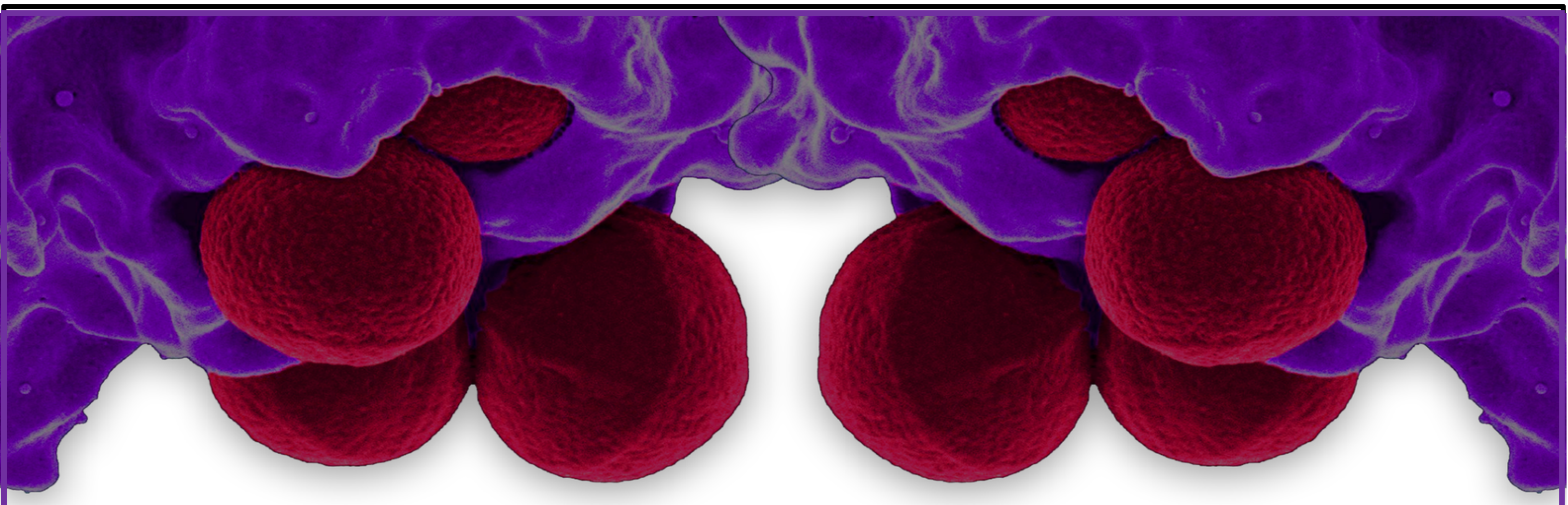
# Pharmacist Role in Antimicrobial Stewardship

### Pharmacists in AMS: Critical Contributions in Implementation

- Results from these three studies elucidate the role of pharmacists in AMS implementation and emphasise the importance of involving pharmacists in the AMS multidisciplinary team.
- Their role in co-leading AMS alongside microbiology and in AMS advisory committees is highlighted. Pharmacists also require an intensive and comprehensive AMS training program to prepare them to lead AMS implementation, share results with health professionals, and effectively utilise the AMS dynamic dashboard. This will enable them to visualise AMS practices on a frequent basis, share results with hospital leaders, and contribute to the national AMR action plan. Pharmacists need a toolkit, education, and skills that equip them to spearhead AMS implementation.
- The tools produced from this research project could enable pharmacists to excel in their workplace.
- This includes a roadmap for AMS implementation tailored for HCPs and health systems, guidance on using the dynamic dashboard, a comprehensive training program, and the AMS Card. The findings from these three studies highlight the pivotal role of pharmacists in co-leading AMS implementation, especially during the pandemic.

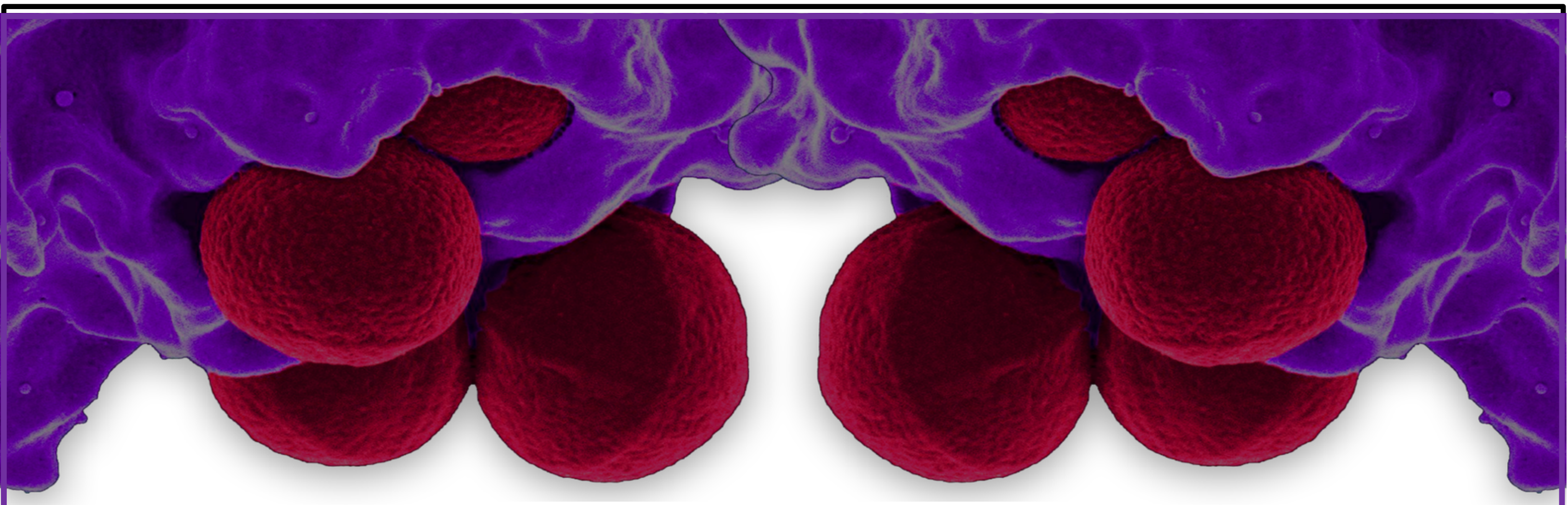
### Pharmacists' Role in AMS Implementation in the Post-COVID-19 Era

- Certainly, the indispensable roles of pharmacists will continue even after the COVID-19 world. They will follow the gradual return to everyday life carefully and continue improving global health so the world can rebuild trust and return to interconnectedness as before.
- In the post-COVID-19 world, pharmacists play an increasingly vital role in AMS implementation. Their contributions have become even more essential given the pandemic's emphasis on effective antimicrobial use and the dangers of AMR.
- As the world transitions back to normal, pharmacists collaborate more with multidisciplinary teams to enhance AMS practices, maintain appropriate antibiotic prescribing, and judicious antibiotic use. AMS efforts in the future.



## Future Research

- Future research is required to investigate practically the effect of AMS implementation post pandemic, to make sure of preparedness for any future or upcoming crisis.
- Future survey is also required to explore HCPs attitudes and perceptions after comprehensive training and education and AMS implementation.
- Investigate the long-term and short-term impacts of AMS globally, especially on clinical and non-clinical outcomes, as well as its efficacy in mitigating AMR and protecting patients.
- Regularly review and update antimicrobial medicine guidelines in line with national guidelines, surveillance reports, and local antibiograms.
- Explore the suitability of AMS implementation across different healthcare settings.
- In the UK, focus AMS research on interventional aspects such as evaluating pre- and post-implementation impact and designing AMS dashboards.
- Assess AMS impact on economic, clinical, and resistance outcomes like reduced hospital stays, decreased infections, and lower antibiotic-resistant bacteria.
- Expand AMS surveys to hospitalized children and their caregivers to understand perspectives on post-discharge antibiotic use.
- Measure AMS program effectiveness through further surveys on AMS practices and prescribing patterns after implementation.
- Conduct discussions on AMS implementation to foster acceptance into national action plans, and continually evaluate AMS interventions like IV-to-oral switches.
- Identify the most effective AMS education methods to increase engagement and mitigate AMR.



# CONCLUSION

- This research provided an in-depth understanding of antimicrobial stewardship and factors affecting inappropriate antibiotic prescribing in acute care settings, including understand the impact of COVID-19 pandemic on antibiotic prescribing, and lessons learnt from the COVID-19 pandemic, in order to improve antibiotic prescribing and mitigate the antimicrobial resistance challenge, and be prepared for any future or upcoming emergency or crisis.
- This research project stressed on the effectiveness of audits, feedback, and antibiotic reviews. Despite disruptions, maintaining guidelines and education proved critical for AMS continuity. Emphasis on computerised systems, AMS champions, and addressing prescribing influences was highlighted.
- Findings reveal a knowledge gap in AMS among healthcare professionals, particularly doctors and nurses, and the need for enhanced educational programs.
- Additionally, this research showed the pivotal role of pharmacist in AMS implementation and education.
- The study advocates for strengthened AMS through regular measures, and a strategic roadmap.
- It calls for collaborative efforts across the healthcare spectrum to combat antimicrobial resistance, ensure responsible antibiotic use, and sustain AMS amidst future challenges.

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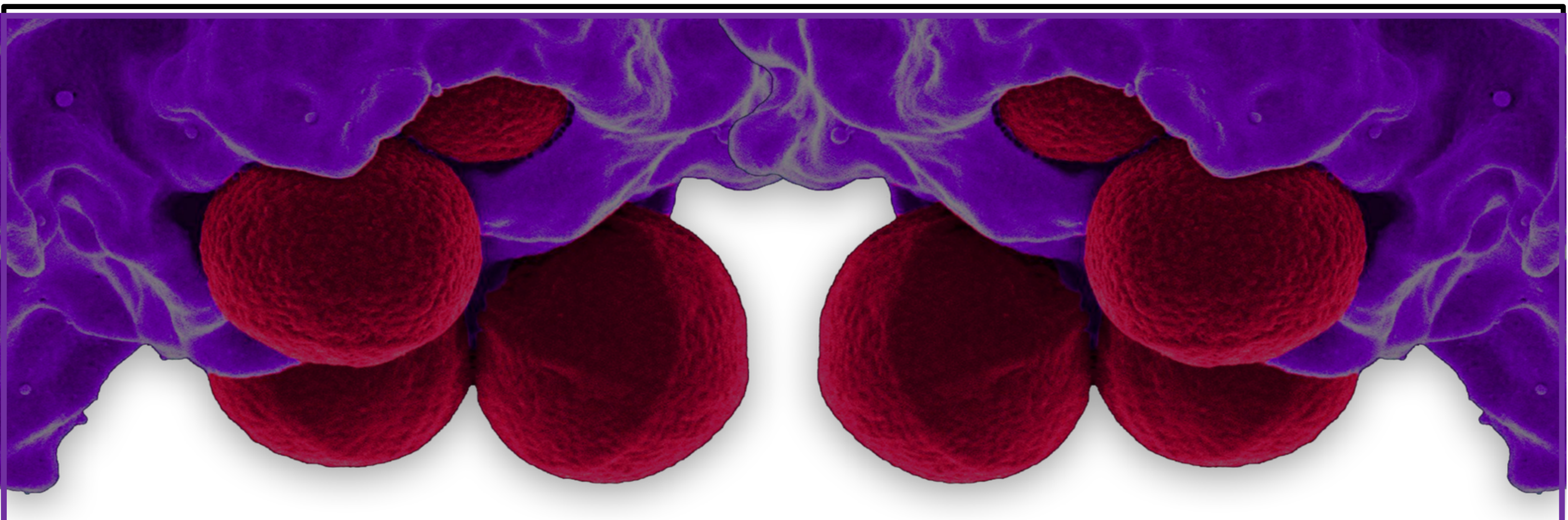
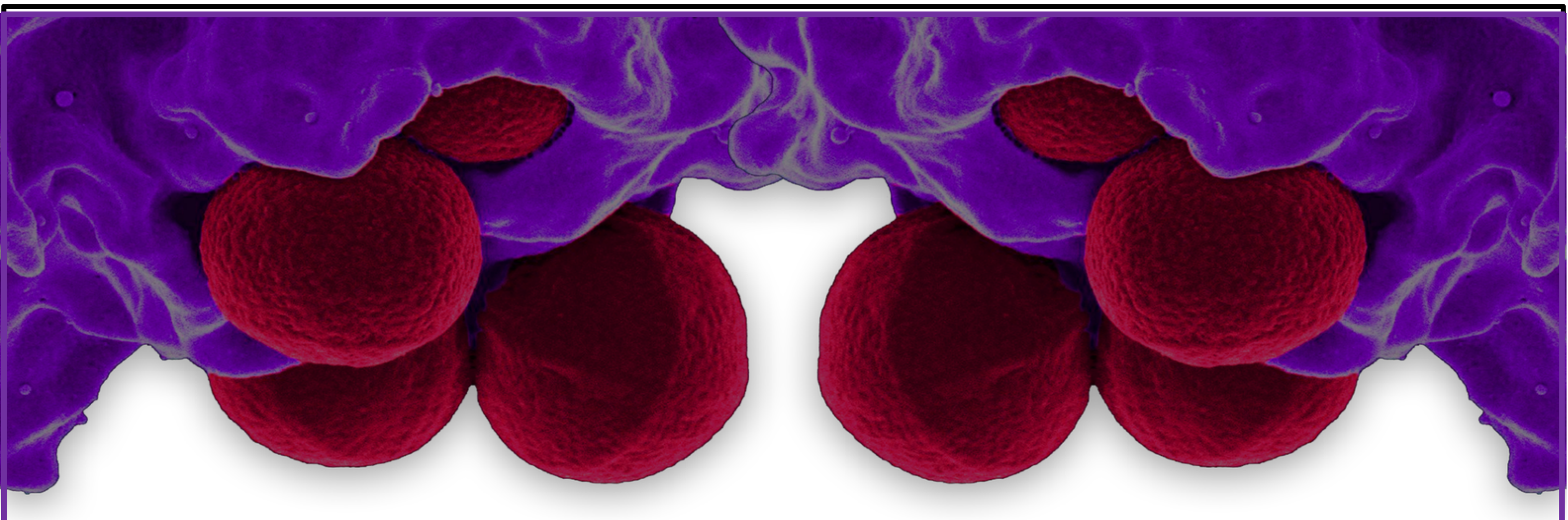
# Dissemination of this Research Project

- An investigation into the effectiveness of antimicrobial stewardship during a pandemic- COVID-19 in acute care setting: Published in Prospero.
- Antimicrobial stewardship before and during the COVID-19 pandemic: Published ISRCTN Medicine Blog.
- Antimicrobial stewardship implementation before and during the COVID-19 pandemic in the acute care settings: A systematic literature review.
- Antimicrobial Stewardship Implementation Before and During the COVID-19 Pandemic in Acute-care settings: Published in Springer Community related to the United Nations sustainable goals.
- Antimicrobial stewardship implementation before and during the COVID-19 pandemic: Published in WHO AMR Exchange on Antimicrobial Stewardship & COVID-19.
- How did the COVID-19 pandemic impact antibiotic prescribing and antimicrobial stewardship in acute care settings?: Published in Octopus.
- An investigation into factors affecting antibiotic use during the COVID-19 pandemic in two hospitals: Published in ISRCTN related to WHO criteria.



## Future Dissemination of the research findings

- Essential dissemination of research findings on AMS to amplify study impact.
- Publication of insights and data across academic and clinical platforms for wide accessibility.
- Presentation of results at national and international conferences for professional dialogue.
- Engagement with networks and interest groups to extend the reach of our findings.
- Open invitation for further engagement with the research team for discussions and collaborations.
- Aim to inspire action and continued research into AMS optimisation amidst global healthcare challenges.



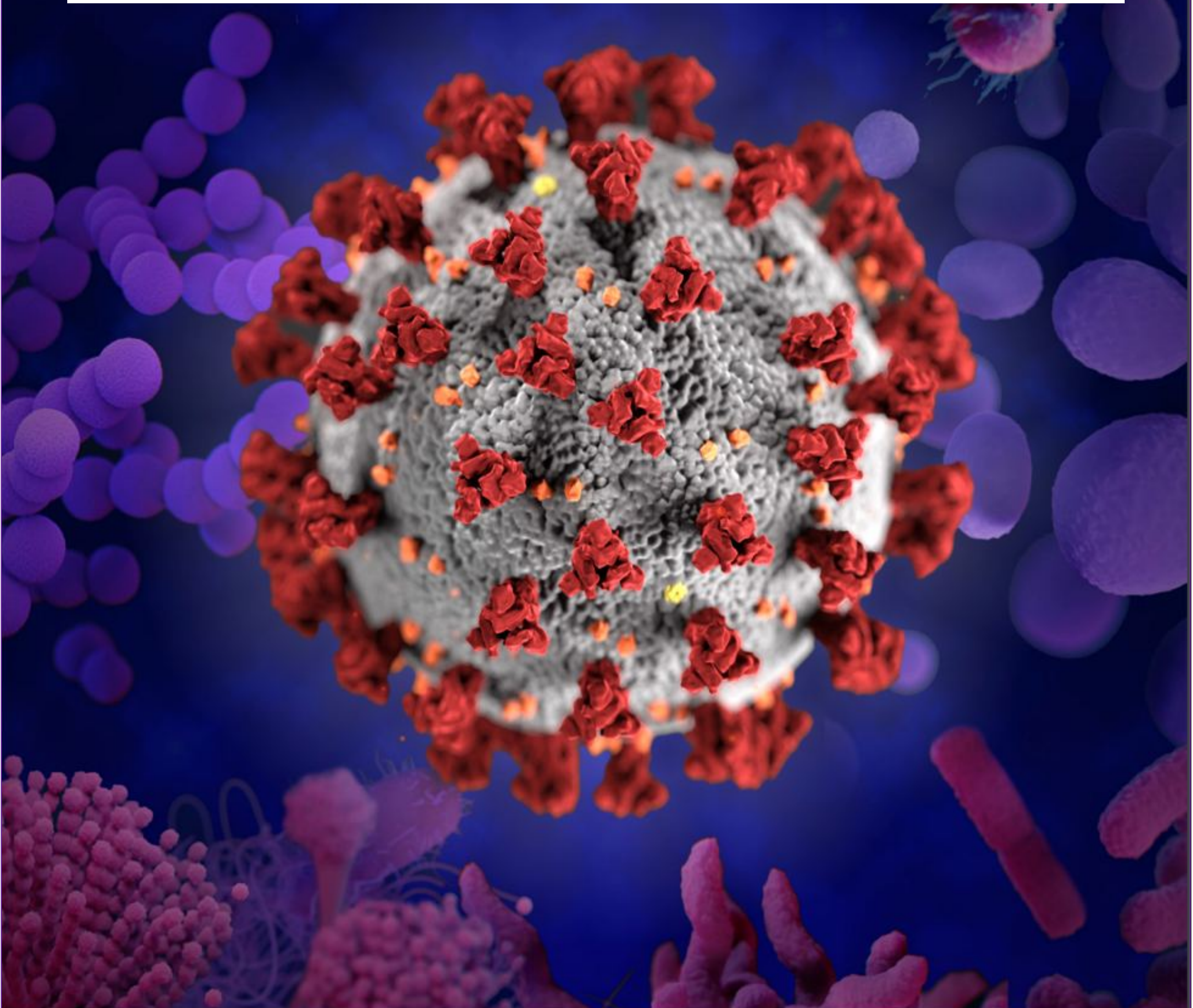
This report is dedicated to the healthcare professionals working at Bedfordshire, who gave tirelessly of themselves and risked their lives during the COVID-19 pandemic.

These individuals give selflessly of their time and safety to protect patients from emerging disease threats.

Thank you for your sacrifices and willingness to serve.

University of Hertfordshire UH

NHS
Bedfordshire Hospitals
NHS Foundation Trust

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Publication Date: November 2023


## Appendix 63.

Antimicrobial stewardship implementation  before and during the COVID-19 pandemic  in the acute care settings: a systematic review.

Access from this link:
https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-023-15072-5#:~:text=There%20are%20many%20lessons%20learnt,during%20the%20COVID%2D19%20pandemic.

Elshenawy *et al. BMC Public Health (2023) 23:309*
https://doi.org/10.1186/s12889-023-15072-5

BMC Public Health

RESEARCH

Open Access

# Antimicrobial stewardship implementation before and during the COVID-19 pandemic in the acute care settings: a systematic review

Rasha Abdelsalam Elshenawy*, Nkiruka Umaru, Amal Bandar Alharbi and Zoe Aslanpour

**Abstract**

**Introduction** Antibiotics are widely administered for various indications, leading to increased antimicrobial resistance (AMR) in acute care hospitals. Since the onset of the COVID-19 pandemic, Antimicrobial Stewardship (AMS) effective strategies should be used to maintain the rational use of antibiotics and decrease the threat of Antimicrobial Resistance (AMR).

**Aim** This systematic literature review aims to investigate the AMS intervention Before-the-pandemic (BP) and During-the-pandemic (DP) from the literature.

**Design and setting** Systematic literature review of primary studies on AMS implementation in acute care settings.

**Methods** Relevant studies published between 2000 and March 2021 were obtained from Medline (via PubMed), OVID, CINAHL, International Pharmaceutical Abstracts, Psych Info, Scopus, Web of Science, Cochrane Library, OpenGrey, and Google Scholar, using a comprehensive list of search terms. Public Health England (PHE) toolkit was agreed upon as a gold standard for the AMS implementation.

**Results** There were 8763 articles retrieved from the databases. Out of these, 13 full-text articles met the inclusion criteria for the review. The AMS implementation was identified in the included studies into AMS strategies (Core strategies & Supplemental strategies), and AMS measures BP and DP.

**Conclusion** This Systematic literature review summarises AMS implementation strategies and measures all over the previous 20 years of research. There are many lessons learnt from COVID-19 pandemic. The proper selection of the AMS implementation strategies and measures appeared to be effective in maintaining the appropriate use of antibiotics and decreasing the AMR threat, especially during the COVID-19 pandemic. Further studies are required to provide empirical data to evaluate the AMS implementation and identify which of these strategies and measures were effective BP and DP. In order to be prepared for any emergency/crisis or future pandemics.

**Keywords** Antimicrobial stewardship strategies, Antimicrobial stewardship measures, Antimicrobial resistance, Coronavirus, COVID-19 pandemic, Acute care settings

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## Introduction

Sir Alexander Fleming mentioned the concept of Antimicrobial Resistance (AMR) during his Nobel Prize lecture [1]. The rise in multi-drug-resistant infections threatens global health through significant morbidity, mortality, and economic loss. Following the O'Neill review and findings in 2016, the number of deaths from AMR infections was estimated to reach 10 million annually due to the AMR crisis [2]. AMR is a silent pandemic and one of the biggest threats to global health [3]. In 2019, it was estimated that more than 1.2 million people died worldwide from AMR [4].

Public Health England (PHE) has also emphasised the need for AMS implementation to maintain the appropriate use of antibiotics [5]. Antimicrobial Stewardship (AMS) is a coherent set of actions that promotes the effective use of antibiotics. It aims to maintain the optimal selection, dosage, route, and duration of antibiotic treatment [6]. For more definitions of Antimicrobial Stewardship, see Supplementary Table S1. Many AMS strategies are used to maintain the judicious use of antibiotics and educate prescribers. Furthermore, the AMS implementation should be measured in order to evaluate the outcomes of AMS implementation [7, 8].

The outbreak of infection caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2; COVID-19) from Wuhan, China, in December 2019 escalated rapidly to become a global pandemic [9]. In June 2022, the global estimate for people who tested positive for COVID-19 was approximately 544 million. Additionally, the estimated number of total deaths is 6 million, 10% of the worldwide deaths of 60 million [10]. Recent evidence suggests that, as a consequence of the COVID-19 pandemic, increasing numbers of patients admitted to hospitals have been prescribed empirical antimicrobial therapy, which may not always be appropriate, potentially increasing the number of resistant infections globally [11, 12]. While consideration for AMR and AMS focused on supporting the selection of optimal empirical therapies and appropriate de-escalation or discontinuation of antimicrobials when bacterial co-infection is present or absent is essential [13].

Indeed, results from one of the previously published systematic reviews suggested that co-infection prevalence with resistant bacterial organisms was 24%. Sadly, of the 1959 unique isolates identified within the included studies, 569 (29%) were deemed resistant [11]. Another systematic review and meta-analysis also found an overall high antimicrobial consumption among COVID-19 patients [14]. However, the AMS intervention during the COVID-19 pandemic within a systematic review has not been published to date. A critical knowledge gap exists regarding the AMS implementation strategies DP in acute care settings. This systematic review addressed the research question: "What are the AMS implementation strategies and measures?" The objectives were to (1) review AMS before and during the COVID-19 pandemic; (2) assess the acute care settings and geography; (3) document AMS strategies and measures if available, and (4) estimate the proportion of each strategy and measures reported in the literature.

## Materials and methods

### Registration

Prior to the initial search, the review was registered at PROSPERO (registration number CRD42021242388) [15]. The scope of the review was defined by applying the acronym PICOS (Population, Intervention, Comparison, Outcome, Setting), as shown in Table 1. A systematic search of databases was conducted using the following keywords and their synonyms (for more details, see Supplementary Tables S2 and S3). After this, follow the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines for reporting. The PRISMA 2020 was drawn up and approved by the research team before the commencement of the systematic review [16]. The plan was employed as a guidance document to systematically review relevant primary studies published between 2000 and 2021. It described the review's scope, intended purpose, and methodological and analytical approach. Ethical approval was not required before the commencement of the review as the use of patients' identifiable data was not intended.

### Eligibility screening

The articles retrieved from the databases were exported into CSV and Excel sheets for screening and identification of the eligible articles by RAE. Titles and abstracts were screened for relevance; duplicates were removed, followed by a screening of the complete articles for possible inclusion by one reviewer (RAE). Another reviewer (ZA) independently reviewed the titles, abstracts, and full studies, confirmed the relevance of studies in meeting the inclusion criteria and excluded studies deemed irrelevant. Three reviewers (ZOA and NU) screened the first 60 records to establish the quality of screening at this stage and ascertain that the level of agreement and discrepancies were addressed through mutual consensus among the reviewers. Additional suggestions and amendments to the search teams and relevant keywords were made. There was complete agreement on the relevance of selected studies by RAE, ZA and NU.

### Inclusion criteria

Selected studies were assessed against the following inclusion criteria: (i) Peer-reviewed English articles; (ii) Population of patients prescribed antibiotics aged 18 years and over; (iii) Studies describing the AMS intervention in acute care settings; (iv) Outcomes of AMS strategies, measures, metrics before and during the COVID-19 pandemic; (v) Primary studies; and (vi) Published between 2000 and 2021. The included study designs were observational (retrospective

**Table 1** Inclusion and exclusion criteria

| | Inclusion criteria | Exclusion criteria |
|---|---|---|
| **Participants** | Studies targeting the public/patients' use of antibiotics Healthcare Professionals (HCPs) who are responsible for prescribing, dispensing, or administering antibiotics (doctors, pharmacists) | Non-HCPs (patient family or community or nursing or long-term care patients) |
| **Intervention** | Studies describe an intervention to improve antibiotic prescribing or AMS or any other intervention as the use of the parenteral-to-oral switch and the duration of IV and oral antibiotics | Studies that do not describe an AMS intervention |
| **Comparison** | Comparison with a control group/a group that carried out usual care without an AMS intervention; comparison between two or more AMS interventions | |
| **Context** | Interventions carried out in adult inpatient settings in acute care hospitals | Interventions carried out in nursing homes, care homes or long-term healthcare facilities; community settings; paediatric setting/hospital; and animals/ veterinary practice |
| **Outcomes** | Primary outcomes: reviewing the AMS implementation before and during the COVID-19 pandemic | |
| | Secondary outcomes: other AMS measures, metrics, and quality improvement before and during the COVID-19 pandemic | |
| **Study design** | Randomized Controlled Trials (RCTs), non-randomized trials, Controlled Before-After (CBA) studies, interrupted time series designs, case–control and cohort studies, cross-sectional studies, and qualitative studies | Literature reviews, systematic reviews, meta-analyses, single case studies, case reports, and conference abstracts |

(a) *HCPs* Healthcare Professionals, *AMS* Antimicrobial Stewardship, *COVID-19* Coronavirus

(b) *RCTs* Randomized Controlled Trials, *CBA* Controlled Before-After

or prospective case–control, case series non-interventional, cross-sectional, cohort) and interventional (quasi-experimental, randomised controlled trials) studies (Table 1).

### Exclusion criteria

Any study that did not fulfil the criteria for inclusion, studies unrelated to review objectives, abstract-only papers, non-human subject studies, literature and systematic review studies were excluded from this study.

### Data sources and search methods

An electronic search of International Pharmaceutical Abstracts, MEDLINE (via PubMed), CINAHL, PsychINFO, SCOPUS, Cochrane Library, Web of Science and Google Scholar [17]. Choices of databases to be searched were based on insights from the method's section-related reviews. The search was restricted to articles published from January 2000 to March 2021 (For more details, see Supplementary Table S3). The AMS strategies and metrics identified within the MEDLINE database through the MeSH term "antimicrobial stewardship" was employed as search terms for AMS intervention. Antibiotic use before and during the COVID-19 pandemic was employed as the search term. Settings were specified as acute care settings, AND/OR were used to combine search terms (Table 2). The "snowballing" strategy, going through the reference list of all included studies to obtain further relevant studies, was also employed.

### Quality assessment of included studies

The latest version of the Mixed Method Appraisal Tool (MMAT) was used to evaluate the quality of the included studies. Version 2018 of the MMAT was subject to content validity and usefulness [18]. Following a

**Table 2** The systematic literature review of search strategies

| Search Strategy |
|---|
| 1. Antimicrobial resistance OR antibiotic management OR acute care settings OR hospitals |
| 2. Antimicrobial stewardship OR antimicrobial utilisation OR antimicrobial use OR antimicrobial stewardship strategies OR antibiotic metrics OR antimicrobial stewardship intervention OR antimicrobial stewardship outcomes OR antibiotic use |
| 3. COVID19 OR coronavirus OR SARS CoV2 OR severe acute respiratory infection OR pandemic |
| 4. 1 AND 2 AND 3 |
| 5. Limit 18–65 to yr. = '2000–2021' = lang: 'English' |

(a) *COVID-19* Coronavirus

(b) *SARS CoV2* Severe Acute Respiratory Syndrome Coronavirus 2 literature search of the databases and eligibility screening, the final included studies were independently reviewed to ensure the quality assessment's accuracy, validity and reliability. The three authors (RAE, NA and ZA) critically appraised all the included studies independently, and then the results were discussed (for more details about the quality of studies, see Supplementary Table S4).

#### Data extraction and analysis/synthesis

Data extraction forms were created by the primary reviewer (RAE). It included the author's last name, year of study, country, study design, the AMS intervention strategies, AMS outcome measures, and quality of study analysis (Supplementary Figure S1). Three studies were initially piloted to test the form. RAE extracted the data from these three studies into the data extraction tool, and any discrepancies in the extracted data were discussed with the other authors. Data obtained were grouped and summarised using narrative synthesis into two groups: BP and DP (Table 3). RAE extracted the data for the included studies. In order to maintain the reliability and validity of the data extraction, another author (ABA) independently extracted the data from the included studies into data extraction form. Discrepancies in the extracted data were documented and resolved by discussion or adjudication with a third author (ZA). Meta-analysis could not be performed because of the heterogeneity of the included studies.

The following data were extracted for all included articles (Table 3):

- author of study;
- year of study (before or during the COVID-19 pandemic);
- country of study;
- study design;
- antimicrobial stewardship strategies;
- antimicrobial stewardship metrics/measures and quality improvements;

### Results

The search yielded a total of 8,763 Abstracts, which were potentially eligible for inclusion: MEDLINE ($n$=3,640), all OVID journals ($n$=44), CINHAL PLUS ($n$=4,708), PsycINFO ($n$=10), SCOPUS ($n$=101), Web of Science ($n$=12), Cochrane ($n$=75), and an additional 173 records through Google Scholar. After removing duplicates, 4,566 articles remained for the title and abstract screening. One hundred and one published articles were eligible for full-text screening, of which 79 met the inclusion criteria (Fig. 1). Sixty-six articles were excluded as they had not fulfilled the inclusion criteria for the following reasons: lack of AMS intervention reported ($n$=36), inappropriate study settings ($n$=22), and inappropriate outcomes such as infection control precautions ($n$=8). The final included studies were 13 (Fig. 1).

The geographical origin of the 13 studies was as follows: United States ($n$=4) [19, 21, 23, 24], United Kingdom ($n$=2) [30, 31], India ($n$=2) [26, 27], Germany ($n$=1) [22], Netherlands ($n$=1) [20], Jordan ($n$=1) [28], Japan ($n$=1) [25], Greece ($n$=1) [29]. 10 of 13 (77%) studies were conducted before the pandemic. However, only 3 of 10 (23%) studies were conducted during the COVID-19 pandemic [29–31]. The following study designs were identified: retrospective cohort ($n$=2) [22, 31], cross-sectional ($n$=6) [19, 23, 25, 28–30], prospective cohort ($n$=2) [21, 26], Quasi-experimental study ($n$=2) [24, 27], and 1 Randomized clinical trial [20]. In this review, the PHE toolkit of AMS was used as a gold standard for analysing AMS implementation. AMS strategies were categorised into AMS core & supplemental strategies according to the AMS toolkit into core and supplemental strategies [5]. Additionally, the practical guide for AMS implementation and measures was used in the analysis [8] (Table 3).

#### AMS strategies before and during the COVID-19 pandemic

Strategies and interventions aimed at improving appropriate prescription of antibiotics in all acute care settings. They are considered an essential part of "antimicrobial stewardship". According to the literature, there are many antimicrobial stewardship tools, interventions and activities (collectively termed "strategies") that can be used to streamline and improve antimicrobial use and educate prescribers [7]. For more details about AMS strategies, see Supplementary Tables S5 and S6. In this systematic literature review, a range of AMS strategies has been classified according to the AMS implementation guidelines of the United States Infectious Disease Society of America (IDSA) and UK Public Health England AMS toolkit into core and supplemental strategies [5, 7].

Before the pandemic, regarding the core strategies, AMS Multidisciplinary Team was found in ten studies [19–28], and Prospective Audit & Feedback strategy was found in nine studies [19, 20, 22–28]. However, Antibiotic Review was noticed in seven studies [19, 21, 23, 24, 26–28]. For AMS supplemental strategies, Formulary Restriction & pre-authorisation was found in seven studies [19, 20, 22–26], Dose Optimisation strategy was found in seven studies [19, 22–24, 26–28], Streamlining/timely de-escalation of therapy strategy was found in five studies [19, 22, 23, 26, 27], Parenteral to oral conversion was found in five studies [19–21, 23, 26], and Guidelines and Clinical were found in six

**Table 3** Characteristics of Included studies before and during the COVID-19 pandemic

| Study | Country | Study type | AMS strategies | AMS Measures/Metrics |
|---|---|---|---|---|
| Trivedi (2013) [19] | United States | Cross-sectional study | - AMS core strategies included formulary restriction, antibiotic review, automatic stop orders, preauthorisation, and prospective review with feedback<br>- AMS supplemental strategies included education, dose optimisation, dose adjustments, guidelines and clinical pathways, parenteral-to-oral switch, streamlining de-escalation, and antimicrobial order forms | - Outcomes measured included antimicrobial resistance patterns (39%), antimicrobial utilisation (36%), antimicrobial costs (35%), Clostridium Difficile infection rates (32%), adverse effects (22%), 17% reported monitoring DDD and 13% reported monitoring DOT<br>- For a positive trend in outcomes data since the initiation of the ASP, including improved antimicrobial use (74%), decreased antimicrobial costs (63%), improved antimicrobial susceptibility patterns (47%), and 38% used computer software to interface with electronic records facilitated AMS |
| Kallen (2017) [20] | Netherlands | Randomised clinical trial | - Data extraction and feedback on the overall antibiotic use<br>- Point Prevalence Study of the European Centre for Disease Prevention and Control (PPS-ECDC) was conducted to provide feedback on validated Quality Indicators (QIs) for appropriate antibiotic use (PPS-QI), such as IV-to-oral switch projects (43%) and projects focusing on appropriate treatment for patients with pneumonia (21%) or the appropriate use of restricted antibiotics (19%) | Primary outcome<br>The geometric mean LOS was 9.5 days (95% CI 8.9–10.1, $N=4245$ patients) at baseline versus 8.7 days (95% CI 8.1–9.2, $N=4195$ patients) after intervention while adjusting for dependencies within clusters and potential confounders. After adjusting for the secular trend, the estimated decrease in geometric mean LOS was 0.5 days: 9.5 days (95% CI 8.9–10.1, $N=4245$ patients) at baseline versus 9.0 days after intervention (95% CI 8.5–9.6); $P<0.001$, $N=4195$ patients<br><br>Secondary outcomes<br>DOT per 100 admissions decreased from 1320 (95% CI 1253–1387, $N=4245$ patients) at baseline to 1185 (95% CI 1119–1252, $N=4195$ patients) after the intervention ($P<0.001$). Similar trends were found for days of IV antibiotics. A larger decrease was found for restricted DOT per 100 admissions ($P<0.001$). The percentage of patients admitted to the ICU was lower after the intervention (4.8%, $N=201$ patients) compared with a baseline (5.9%, $N=251$ patients) |
| Tamma (2021) [21] | United States | Prospective study | Implementation webinars of AMS, antibiotic guidelines, antibiotic time-out, clinical rounds, and antibiotic user guides, identify antibiotic safety and adverse events, antibiotic review, use innovative strategy of the four moments of antibiotic decision-making framework including: make the diagnosis, cultures, and empiric therapy, stop, narrow, change to oral antibiotics and duration | Primary outcome (Unit-Level Antibiotic Use Data):<br>- Comparing January–February with November–December 2018, antibiotic use decreased from 900.7 to 870.4 DOT per 1000 PD (− 30.3 DOTs; 95%CI, − 52.6 to − 8.0 DOT; $P=.008$)<br>- Fluoroquinolone use decreased from 105.0 to 84.6 DOT per 1000 PD across all units between January–February and November–December (− 20.4 DOT; 95%CI, − 25.4 to − 15.5 DOT; $P=.009$)<br><br>Secondary outcome (C difficile identification):<br>- The number of hospital-onset C difficile Laboratory-identified events per 10 000 PD across the Safety Program cohort was 6.3 for quarter 1, 5.3 for quarter 2, 6.0 for quarter 3, and 5.1 for quarter 4 in the 2018 calendar year in the participating units. The incidence rate of hospital-onset C difficile Laboratory-identified events decreased from quarter 1 to quarter 4 by 19.5% (95%CI, − 33.5%to − 2.4%, $P=.03$) |

**Table 3** (continued)

| Study | Country | Study type | AMS strategies | AMS Measures/Metrics |
|---|---|---|---|---|
| Surat (2021) [22] | Germany | Retrospective study | - AMS multidisciplinary committee and regular ward rounds<br>- Formulary restriction of specific antibiotics (e.g., tigecycline and colistin)<br>- Creation of selective antibiotic resistogram profiles<br>- Electronic access to antimicrobial prescribing guidelines, and mobile applications<br>- Introduction of both surveillance data on AMR and antibiotic consumption rate<br>- In accordance with the current effective clinical practice guidelines for antimicrobial prophylaxis, the standard prophylactic regime changed from cefuroxime to cefazolin (depending on the procedure, it may differ)<br>- Further targets involved following antibiotic groups: meropenem, which AMS strived to reduce its usage, and fluoroquinolones, which involved drastic change in hospital's general antibiotic policy | Primary outcome (The primary endpoint was defined as the total DOT for intraabdominal infections): An overall reduction in the total days on antibiotic therapy (ABT) from a mean of 6.1 days to 4.8 days ($p = 0.02$) was noted in the antimicrobial stewardship program (ASP) period, decreasing the days of therapy per 100 patient days (DOT/100PD) from 47.0 to 42.2 ($p = 0.035$)<br>Secondary outcome (The secondary endpoints included the appropriateness (indication and documentation) of the postoperative antibiotic therapy (PAT), the empiric selection of antibiotics and the frequency of antibiotic changes):<br>- The rate of patients receiving postoperative antibiotic therapy decreased from 56.8% to 45.2% ($p = 0.002$) in the ASP period<br>- A trend of change in the duration of postoperative antibiotic therapy from 8.1 to 7.2 days ($p = 0.08$) was observed<br>- The individual assessments of postoperative therapy revealed significantly less inappropriate (no indication) postoperative antibiotic therapy, shortened treatment durations (not significant) and an influence on the choice of antibiotics, with the use of more narrow-spectrum antibiotics |
| Weston (2012) [23] | United States | Cross-sectional study | - Antibiotic restriction, by using new restriction methods, such as front-end back end, automatic stop orders, ID consult required, verbal approval required<br>- Antibiotic guidelines and clinical pathways, antimicrobial order forms, streamlining or de-escalation, dose optimisation, parenteral-to-oral switch, and closed formulary | - Combining the results of both surveys, 31 out of 44 (70%) institutions had formal ASP in place. 13 institutions indicated on either survey that they did not have a formal ASP program. 25/38 institutions who responded to the second survey, had had an existing ASP |

**Table 3** (continued)

| Study | Country | Study type | AMS strategies | AMS Measures/Metrics |
|---|---|---|---|---|
| Mehta (2014) [24] | United States | Quasi-experimental study | Prior authorization and prospective audit with feedback | - The change from prior authorization to prospective audit with feedback was associated with a significant increase both in use of the affected antimicrobials and in overall use of all antimicrobial agents<br>- Broad-spectrum anti-gram-negative agents that still required prior authorization during both time periods continued to decline in use after the change in ASP<br>- The overall change in stewardship approach was associated with a significant increase in hospital LOS<br>- During the pre-intervention period, use of broad-spectrum anti-gram-negative antibiotics was declining at a rate of − 4.00 DOT/1,000-PD per month. However, during the post-intervention period, use increased by 0.80 DOT/1,000-PD per month, indicating that the change in ASP was associated with a slope change of 4.80 DOT/1,000-PD per month ($P < .001$)<br>- After decreasing during the 2 years before the ASP change, use of cefepime and piperacillin/tazobactam significantly increased following the transition to prospective audit with feedback by 3.21 DOT/1,000-PD per month ($P = .003$)<br>- Overall use of all systemic antimicrobial agents significantly increased after the change in ASP method ($P < .001$)<br>- Vancomycin use declined before the intervention but significantly increased after the intervention ($P = .005$). The use of non-audited antimicrobials significantly increased after the change in ASP methods ($P < .001$), the slope during the postintervention period continued to decline at − 1.87 DOT/1,000-PD per month<br>- The LOT of all systemic antimicrobials declined before the intervention by − 2.30 LOT/1,000-PD per month, and, despite a significant increase in slope ($P = .029$), use continued to decrease after the intervention by − 0.33 LOT/1,000-PD per month |

**Table 3** (continued)

| Study | Country | Study type | AMS strategies | AMS Measures/Metrics |
|---|---|---|---|---|
| Moriyama, (2021) [25] | Japan | cross-sectional study | - Prospective audit and feedback protocol were observed in 23 (59.0%) hospitals when using broad-spectrum antimicrobials<br>- Preauthorization was observed in 4 (10.3%) hospitals for using broad-spectrum antimicrobials.—Notification protocols support form was present in 37 (94.9%) for use of broad-spectrum antimicrobials | - The number of hospitals with preauthorization and notification protocols, respectively, using the investigated antibiotics were as follows: broad-spectrum antimicrobials overall 4 (10.3%) and 37 (94.9%); carbapenem 2 (5.1%) and 34 (87.2%); 3rd generation cephalosporin 0 (0%) and 0 (0%); 4th generation cephalosporin 0 (0%) and 10 (25.6%); piperacillin/tazobactam 0 (0%) and 17 (43.6%); and intravenous quinolone 3 (7.7%), and 18 (46.2%)<br>- Regarding preauthorization and notification protocols, there were no significant differences between small/middle-sized hospitals and large hospitals<br>- The numbers for hospitals that had intervention procedures within 7 d and 28 d, respectively, for each investigated antibiotic were as follows: broad-spectrum antimicrobials overall 17 (43.6%) and 34 (87.2%); carbapenem 16 (41.0%) and 34 (87.2%); 3rd generation cephalosporin 1 (2.6%) and 11 (28.2%); 4th generation cephalosporin 7n(17.9%) and 20 (51.3%); piperacillin/tazobactam 12 (30.8%) and 23 (59.0%); and intravenous quinolone 13 (30.8%) and 22 (56.4%). Intervention procedures to use broad-spectrum antimicrobials within 7 d were statistically more frequent in small/middle-sized hospitals than in large hospitals with findings as follows: overall, OR = 5.7, 95% CI = 1.4–23.5, $p = 0.023$; carbapenem, OR = 4.7, 95% CI = 1.1–19.1, $p = 0.049$; piperacillin/tazobactam, OR = 7.3, 95% CI = 1.3–39.9, $p = 0.018$; and intravenous quinolone, OR = 8.8, 95% CI = 1.6–48.2, $p = 0.008$ |
| Thakkar (2021) [26] | India | Prospective study | - The pre-existing components of the hospital antimicrobial stewardship program included generation of antibiogram, formulation/ education and dissemination of antibiotic policies for surgical prophylaxis, community and hospital acquired infections and auditing antibiotics for surgical prophylaxis<br>- Prospective audit and feedback for the restricted antimicrobials<br>- Antibiotic restriction using the justification form | - Around 1.4% of admitted patients were put on restricted antimicrobials. The total days of therapy (DOT) were 41.5/1000 inpatient days<br>- Unjustified use of antimicrobials was reported in 13% and recommendation of the AMS for de-escalation were accepted in 89% by the treatment team<br>- There was no significant difference between antimicrobial DOT of the restricted antimicrobials between 2018 and 2019<br>- The colistin susceptibility rates remained stable compared to the previous years |

**Table 3** (continued)

| Study | Country | Study type | AMS strategies | AMS Measures/Metrics |
|---|---|---|---|---|
| Panditrao (2021) [27] | India | Quasi-experimental study | - Baseline Phase: from April–June 2017<br>Routine prospective audit and feedback was undertaken<br>- Intervention Phase: from July–December 2017<br>The following interventions were added:<br>Timeout, Correction of doses, continued education for rational use of antimicrobials, Care bundle approach for prevention of hospital-acquired infections (HAIs) | - There was a reduction in the cumulative DDD/1000 PD for all antimicrobials in the intervention phase compared with baseline (baseline phase 1326.3 DDD/1000PD vs. intervention phase 1313.5 DDD/1000PD)<br>- There was no change in the average number of antimicrobials per individual patient stay in the hospital between the baseline and intervention phases; $P = 0.59$)<br>- DOT/1000PD declined from 1112.3 in the baseline phase to 1048.6 days in the intervention phase, while LOT/1000 PD changed from 956.0 in the baseline phase to 936.3 during the intervention phase<br>- There was a decrease in DDD/1000 PD for antimicrobials such as piperacillin/tazobactam, imipenem, meropenem, clindamycin, levofloxacin, and amikacin, while there was an increase in DDD/1000 PD of vancomycin, colistin, cefoperazone/sulbactam, metronidazole and teicoplanin<br>- There was a decrease in percentage of carbapenem use in the intervention phase compared with the baseline phase (26.3% vs. 20.9%), whereas there was an increase in the use of polymyxins, particularly colistin (11.1% vs. 6.2%) and glycopeptides (vancomycin and teicoplanin) (12.3% vs 11.0%) |
| Ababneh (2020) [28] | Jordan | Cross-sectional study | This study quantified antimicrobial use in inpatient settings as part of antimicrobial stewardship program surveillance | - In terms of DDDs, carbapenems (ertapenem, meropenem, imipenem) were the most commonly used agents in a total of 28.0 DDD/100 admissions, followed by glycopeptides (vancomycin, teicoplanin) in a total of 26.8 DDD/100 admissions, piperacillin-tazobactam with 20.5 DDD/100 admissions and ceftriaxone with 14.2 DDD/100 admissions, fluoroquinolones (ciprofloxacin and levofloxacin) in a total of 11.2 DDD/100 admissions<br>- The highest prescription rate of antibiotics was in the internal medicine wards (49.8 DDD/100 admissions), followed by surgery wards (33.2 DDD/100 admissions), intensive care unit (20.6 DDD/100 admissions), paediatrics (10.5DDD/100 admissions), oncology (10.4DDD/100 admissions)<br>- Regarding DOTs, piperacillin-tazobactam was the most commonly used agent (27.6 DOT/100 admissions), followed by carbapenems (27.2 DOT/100 admissions), glycopeptides (24.7 DOT/100 admissions), fluoroquinolones (12.4 DOT.100 admissions), and cefazolin (11.4 DOT/100 admissions) |

**Table 3** (continued)

| Study | Country | Study type | AMS strategies | AMS Measures/Metrics |
|---|---|---|---|---|
| Spernovasilis (2021) [29] | Greece | Cross-sectional study | - Prospective audit and feedback strategy, along with a case-based education of treating doctors<br>- Antibiotic review after 24 h, 72 h and 7 days | - Doctors believed that the prospective audit and feedback ASP strategy is more effective and educational than the preauthorization ASP strategy (70.3% and 77.7%, respectively)<br>- Most respondents (90.6%) agreed that the implementation of an ASP improves the patients' outcome compared to the absence of such a programme<br>- Less than 25% of participants agreed that the prospective audit and feedback strategy of the current ASP should change<br>- More than 80% of respondents agreed that in-person consultation is the preferred practice for the ASP and education |
| Ashiru-Oredope (2021) [30] | United Kingdom | Cross sectional study | - Audits and Regular surveillance of antimicrobial use/<br>- Point Prevalence Surveys<br>- Quality improvement initiatives<br>- Education, AMS meetings, multidisciplinary team and ward rounds<br>- Writing non-COVID-19 guidelines<br>- IV to oral switches<br>- AMS surveillance activities<br>- Technology (virtual meetings, virtual platforms, remote working and ward rounds)<br>- Introduction of novel biomarkers (e.g., Procalcitonin) for differentiating viral and bacterial infections<br>- The use of hospital electronic prescribing systems facilitated<br>- AMS activities by antimicrobial pharmacists; allowing them to target their activities, for example, identification of patients receiving excessive durations of antibiotics<br>- Infection prevention control<br>- Clinics/out-patient consults and Outpatient parenteral antibiotic therapy (OPAT)<br>- Changing current inpatient processes such as COVID-19 patients receiving a senior review more quickly<br>- Prescribing indicators/targets reporting, and Antibiotic Review Kit (ARK)<br>- AMS committee meeting (formal or informal) | - From qualitative open questions: respondents highlighted core AMS work e.g., reviewing and writing non-COVID-19 guidelines as being the most affected<br>- Respondents were concerned about increased antibiotic use, delayed IV to oral switches (IVOST), and prolonged antibiotic durations<br>- The respondents also were concerned that cases of Clostridioides difficile Infection (CDI) were rising in some hospitals<br>- Stock shortages were also identified as difficult to manage due to overwhelmed supply chains for antibiotics, antivirals and in some cases personal protective equipment (PPE)<br>- Positive COVID-19 outcomes included: technology being increasingly used as a tool to facilitate stewardship, e.g., virtual meetings and ward rounds<br>- Another positive outcome was the increased introduction of novel biomarkers (e.g., procalcitonin) for differentiating viral and bacterial infections<br>- The use of hospital electronic prescribing systems facilitated AMS activities by antimicrobial pharmacists<br>- There has also been a positive increase in the multidisciplinary team<br>- Increased awareness of antimicrobial guidelines and improvements seen in infection prevention |

**Table 3** (continued)

| Study | Country | Study type | AMS strategies | AMS Measures/Metrics |
|---|---|---|---|---|
| Williams (2021) [31] | United Kingdom | Retrospective study | - Seventy-three (33%) patients in the negative PCT group were on antibiotics 48 h following diagnosis of COVID-19 compared with 126 (84%) patients in the positive PCT group (*P* < 0.001), suggesting good compliance with the guideline | Primary outcome:<br>- Patients in the negative PCT group received significantly fewer DDDs of antibiotics (both total and per alive day) compared with patients in the positive PCT group (median DDD 3.0 vs 6.8; *P* < 0.001)<br>- A significant relationship between PCT and total DDDs remained after accounting for confounders; on average, a patient with PCT > 0.25 ng/mL had almost three-fold more DDDs of antibiotics compared with patients with PCT 0.25 ng/mL [coefficient 2.72, 95% confidence interval (CI) 2.03e3.62; *P* < 0.001]<br><br>Secondary outcomes:<br>- Sixty-two (28%) patients in the negative PCT group died compared with 54 (36%) patients in the positive PCT group (P.0.021), and 19 (9%) patients in the negative PCT group were admitted to the ICU compared with 28 (19%) patients in the positive PCT group (P.0.007)<br>- Meropenem was the only carbapenem used in the study population. With specific reference to meropenem consumption, positive PCT was associated with a three-fold increase in the odds of receiving any meropenem during the course of hospital admission (odds ratio 3.16, 95% CI 1.50e6.65; *P* = 0.002) |

a) *AMS* Antimicrobial Stewardship, *DDD* Defined Daily Doses, *DOT* Days of Therapy, *ASP* Antimicrobial Stewardship Program, AMR Antimicrobial Resistance

b) *PPS-ECDC* Point Prevalence Study of the European Centre for Disease Prevention and Control, *QIs* Quality Indicators

c) *PPS-QI* Point Prevalence Surveys, *LOS* Length of Stay, *ICU* Intensive Care Unit, *ABT* Antibiotic Therapy

d) *PAT* Postoperative Antibiotic Therapy, *LOT* Length of Therapy, *HAIs* Hospital-Acquired Infections, *COVID-19* Coronavirus

e) *IVOST* IV to oral switches, *CDI* Clostridioides Difficile Infection, *PPE* Personal Protective Equipment

f) *OPAT* Outpatient Parenteral Antibiotic Therapy, *ARK* Antibiotic Review Kit, *PCT* Procalcitonin, *CI* Confidence Interval

[*] Though this study was published during the COVID-19 pandemic, it was conducted before the pandemic and the AMS was implemented BP

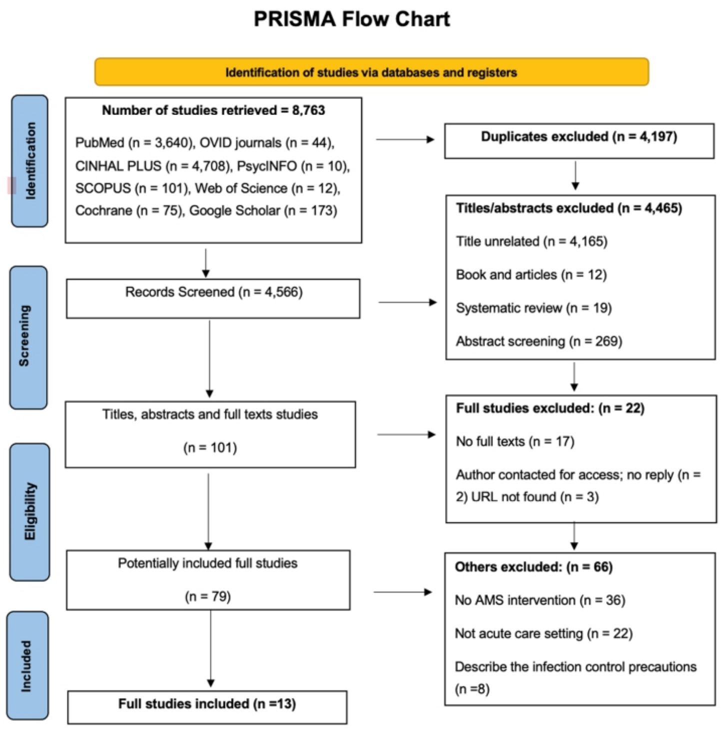


**Fig. 1** Flow chart showing the selection of eligible studies for inclusion in the systematic review

studies [19, 21–23, 27, 28], Antibiotic Order Form was found in two studies [19, 23], Education was found in six studies [19–23, 26, 27], Computerized Decision Support, surveillance was found in two studies [19, 23], and Laboratory Surveillance and Feedback was found in four studies [19, 22, 24, 26] (Table 4).

During the COVID-19 pandemic, concerning the core AMS strategies, each of AMS Multidisciplinary Team, Prospective Audit & Feedback strategy, and Antibiotic Review was found in two studies [29, 30]. For AMS supplemental strategies, Dose Optimisation strategy was found in only one study [29]. However, each Streamlining/timely de-escalation and Parenteral-to-Oral conversion was found in one study [30]. Additionally, Guidelines and Clinical Pathways were found in three studies [29–31], Education was found in two studies [29, 30], Computerized decision support and Surveillance were found in one study [31], and Laboratory surveillance and feedback found in two studies [29, 31] (Fig. 2).

### Identifying key AMS measures for improvement

Measurement of prescribing performance is essential to evaluate the impact of AMS implementation in clinical practice and its demonstrable benefits for patients. The British scientist mentioned in his Popular Lecture, "If you cannot measure it, you cannot improve it" Lord Kelvin 1824–1907 [32]. Improving antimicrobial use must be measured by Identifying the measurable elements/metrics that can be used to evaluate the outcomes of AMS. These metrics can be used for many purposes, such as quality assurance, improvement, and comparisons/benchmarking either intra-hospital or Inter-hospital. Establishing what to measure is one of the essential steps to maintain sustainability in AMS intervention [7, 33].

Measuring stewardship can be divided into four categories: antimicrobial consumption, process measures, outcome measures, and financial [34]. Before 2019, there were no reliable means for measuring antimicrobial usage or correlating usage to resistance until 2019, when the WHO promoted measurable tools that can be used

**Table 4** Summary of finding about antimicrobial stewardship implementation before and during the COVID-19 pandemic

| Study | | | Antimicrobial Stewardship (AMS) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | AMS Strategies | | | | | | | | |
| | | | AMS Core Strategies | | | | AMS Supplemental Strategies | | | | |
| | Before-the-pandemic | During-the-pandemic | Multidisciplinary stewardship team | Formulary restrictions and preauthorization | Antibiotic Review | Prospective Audit and Feedback | Streamlining/ timely de-escalation of therapy | Dose Optimisation | Parenteral to oral conversion | Guidelines and Clinical Pathways | Antibiotic Order Form |
| Trivedi (2013) [19] | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Kallen (2017) [20] | ✓ | | ✓ | ✓ | | ✓ | | | ✓ | | |
| Tamma (2021) [21] | ✓ | | ✓ | | ✓ | | | | ✓ | ✓ | |
| Surat (2021) [22] | ✓ | | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | |
| Weston (2012) [23] | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Mehta (2014) [24] | ✓ | | ✓ | ✓ | ✓ | ✓ | | ✓ | | | |
| Moriyama (2021) [25] | ✓ | | ✓ | ✓ | | ✓ | | | | | |
| Thakkar (2021) [26] | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | |
| Panditrao (2021) [27] | ✓ | | ✓ | | ✓ | ✓ | ✓ | ✓ | | ✓ | |
| Ababneh (2020) [28] | ✓ | | ✓ | | ✓ | ✓ | | ✓ | | ✓ | |
| Spernovasilis (2021) [29] | | ✓ | ✓ | | ✓ | ✓ | | ✓ | | ✓ | |
| Ashiru-Oredope (2021) [30] | | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | ✓ | |
| Williams (2021) [31] | | ✓ | | | | | | | | ✓ | |

**Table 4** (continued)

| Study | Antimicrobial Stewardship (AMS) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | AMS Measure | | | | | | | | | |
| | AMS Education | Computerized decision support, surveillance | Laboratory surveillance and feedback | Defined Daily Dose (DDD) | Days of Therapy (DOT) | Length of Stay (LOS) | Cost | Clostridioides Difficile Infection (CDI) | Procalcitonin (PCT) | Indicators or Quality Improvement Projects |
| Trivedi (2013) [19] | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ | | ✓ |
| Kallen (2017) [20] | ✓ | | | ✓ | ✓ | ✓ | | | | ✓ |
| Tamma (2021) [21] | ✓ | | | | ✓ | | | ✓ | | ✓ |
| Surat (2021) [22] | ✓ | | ✓ | ✓ | ✓ | ✓ | | | | ✓ |
| Weston (2012) [23] | ✓ | ✓ | | | | | | | | ✓ |
| Mehta (2014) [24] | | | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| Moriyama (2021) [25] | | | | | | | ✓ | | | |
| Thakkar (2021) [26] | ✓ | | ✓ | | ✓ | | | | | |
| Panditrao (2021) [27] | ✓ | | | ✓ | ✓ | | | | | ✓ |
| Ababneh (2020) [28] | | | | ✓ | ✓ | | | | | ✓ |
| Spernovasilis (2021) [29] | ✓ | | ✓ | | | | | | | |
| Ashiru-Oredope (2021) [30] | ✓ | | | | | | | ✓ | ✓ | ✓ |
| Williams (2021) [31] | | ✓ | ✓ | ✓ | | | | ✓ | ✓ | ✓ |

*DDD* Defined Daily Doses, DOT Days of Therapy, *CDI* Clostridioides Difficile Infection, *LOS* Length of Stay, PCT Procalcitonin

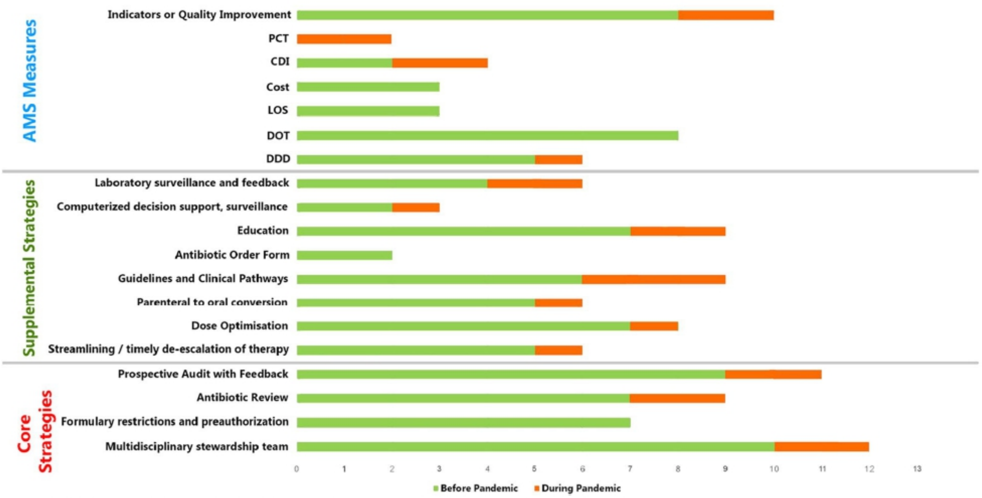


**Fig. 2** AMS before and during the COVID-19 pandemic in acute care settings (Total studies 13)

worldwide to accurately reflect antimicrobial usage, such as the Defined Daily Dose (DDD) [34]. WHO defined DDD as the assumed average maintenance dose per day for the antibiotic used for its main indication in adults. To estimate the total number of days of antimicrobial therapy, healthcare personnel divide the total grams of each antimicrobial used for a given period by the WHO-defined DDD for the individual antimicrobials. Because DDD is a standardised unit of measure, it allows comparisons with antimicrobial usage in other hospitals and countries [35]. Each hospital should select suitable measures/metrics that maintain the effective implementation of the AMS. It is important to be aware of each metrics' advantages and disadvantages to maintain a proper selection. For more details about AMS outcome measures and metrics, see Supplementary Tables S8 and S9.

Before the COVID-19 pandemic, DDD was noticed in five studies [19, 20, 22, 27, 28], Days of Therapy (DOT) was found in eight studies [19–22, 24, 26–28], and Length of Stay (LOS) was found in three studies [20, 22, 24], and Cost was found in three studies [19, 24, 25], and CDI was found in two studies [19, 21] However Indicators or Quality Improvement was found in eight studies [19–24, 27, 28].

During the COVID-19 pandemic, DDD was found in only one study [31], – Clostridioides Difficile Infection (CDI) was found in two studies [30, 31], and Procalcitonin (PCT) was found in one study [31]. Indicators or Quality Improvement was found in two studies [30, 31] (Table 4) (Fig. 2).

## Discussion

This systematic review analysed data from over 63,921 patients who received antibiotics in acute care settings between 2000 and 2021. The goal was to explore strategies and measures for implementing antimicrobial stewardship (AMS). It was found that overuse and irrational use of antimicrobials is a significant problem for healthcare, which can lead to negative impacts on patient safety, the emergence of antibiotic resistance, and increased economic burden [36, 37]. The majority of respiratory tract infections, particularly Upper Respiratory Tract Infections (URTIs), are caused by viruses but are often treated with antimicrobials [38]. There is a lack of strong evidence supporting AMS implementation, which has led to confusion and disagreement about their effectiveness. This high antimicrobial consumption in COVID-19 patients was initiated after early reports from China revealed that 50% of patients died from secondary bacterial infection [39, 40]. A range of stewardship interventions has been reviewed in the IDSA guidelines [7]. When establishing a new stewardship program, it is best to start with the core strategies and focus on achieving and maintaining them before adding some supplemental strategies. A list of the Antimicrobial Stewardship Toolkit is shown in Table 4 and Fig. 2. In the published literature, effective AMS strategies should be able to decrease antimicrobial exposure, decrease costs, and improve clinical outcomes [24].

**AMS core strategies**

Two core ASP strategies have emerged: front-end strategies, which involve an approval process for making antimicrobials available (formulary restrictions and pre-authorization), and back-end strategies, which involve reviewing antimicrobial use after therapy has been initiated (prospective audit with intervention and feedback). A review of these strategies found that back-end strategies, although more labour-intensive, are more widely practised, more easily accepted by clinicians, and provide more educational opportunities, leading to a more sustained impact on improving antimicrobial prescribing quality [8]. The front-end strategy used BP in 54% of studies, while the back-end strategy was used in 85% of all studies and two studies DP [29, 30].

**AMS multidisciplinary team**

A multidisciplinary AMS team was found in most of the included studies, 92%. It was considered one of the key components of the structure and governance of the AMS. It consists of a core membership of an infectious disease physician (or lead doctor or physician champion), a clinical microbiologist, and a clinical pharmacist with expertise in infection (Supplementary Figure S2). Other members could be specialist nurses, for example, infection prevention or stewardship nurses, quality improvement /risk management/patient safety managers, and clinicians interested in infection. The multidisciplinary AMS team should perform a gap analysis of antimicrobial use at the facility to identify priority areas for improvement and set up a plan for AMS implementation and measurement [8]. Before the pandemic, one of the studies conducted across the United States (US) hospitals found that proper communication with the multidisciplinary AMS team was key for successful AMS implementation. For example, provide a forum for participants to ask the AMS team questions about project logistics, implementation strategies, and clinical management strategies and to share local successes and challenges. Project email addresses and designated, external site-specific quality improvement experts are also available to all participants at each site [21]. Interestingly, in 2022, there was a study conducted in Lebanon. It was the first study in Lebanon to examine the impact of the implementation of the post-prescription review and feedback (PPRF) AMS program with an infectious disease (ID) physician-driven strategy of AMS. In the intervention period of this program, there was a significant reduction in DOT, type of illness treated, types of antimicrobials in use and an indirect decrease in the length of hospital stay. Though the acceptance of the AMS multidisciplinary team recommendations were 88%, which was higher than in prior studies that typically noted an acceptance rate of 60–70%, COVID-19 was one of the limitations of this study. This is due to shortages of providers, which affected the ease of education of the treatment teams DP [41]. During the COVID-19 pandemic, a study conducted in the United Kingdom (UK) aimed to measure the COVID-19 impact on national antimicrobial stewardship (AMS) activities. There has also been a positive increase in multidisciplinary work where pharmacist contributions have been welcomed. Increased awareness of antimicrobial guidelines and improvements seen in infection prevention [30].

A multidisciplinary AMS team was found in most of the included studies, 92%. It was considered the key components of the structure and governance of the AMS. The team typically consists of an infectious disease physician, clinical microbiologist, clinical pharmacist with expertise in infection, and other members such as specialist nurses and quality improvement/patient safety managers [8]. The multidisciplinary AMS team was responsible for analysing antimicrobial use at the facility and developing a plan for AMS implementation and measurement. Communication with the AMS team was found to be important for successful AMS implementation in one study conducted in the United States [19].

**Formulary restrictions and pre-authorization**

The study was conducted in Pennsylvania and compared the change from the pre-authorisation AMS strategy to the prospective audit with feedback. There was a significant increase in the use of the affected antimicrobials and the overall use of all antimicrobial agents. During the preintervention period, both total systemic antimicrobial use (− 9.75 DOT/1,000-PD per month) and broad-spectrum anti-gram-negative antimicrobial use (− 4.00 DOT/1,000-PD) declined [24]. Another study was conducted in Massachusetts. It aimed to study the new restriction methods, such as Front-End Back End, Automatic Stop Orders, ID Consult and Verbal Approval. It included a list of restricted antimicrobial agents (broad spectrum and later generation antimicrobials), such as New Specific Medication Restrictions: Anti-Pseudomonas, Carbapenems, Tigecycline, Vancomycin, Colistin, Daptomycin, Linezolid, Antifungals, Fluoroquinolones. The result from this study indicated that Daptomycin and Linezolid were the most frequently restricted antimicrobials [23]. An interesting study conducted in India evaluating the use of the justification form to prescribe restricted antimicrobials, such as colistin, polymyxin B, tigecycline, intravenous (IV) minocycline, IV fosfomycin, daptomycin & echinocandins (caspofungin, micafungin & anidulafungin) found that prescribing any of these antimicrobials necessitated filling an antimicrobial justification form, which was then sent to the AMS multidisciplinary committee. These forms were tallied with a daily indent list from the pharmacy of restricted antimicrobials, and any missing forms were requested to be submitted. At 48–72 h from the time of prescription, the AMS committee for review [26].

#### Antibiotic review

The antibiotic review was one of the effective AMS strategies BP and DP. It was found in 69% (9 of 13) of the included studies. Antibiotic review could be conducted after 24 h (Day 1) of prescribing the antibiotics. It included a review of the doses and the possibility of an IV-to-oral switch. It also could be conducted on Day 4 to review appropriateness considering microbiological culture results or on Day 7 to review the duration of therapy [8]. We found that the antibiotic review 48–72 Hours from the time of prescription was conducted by microbiology [22] or the AMS multidisciplinary committee [26]. Interestingly, the use of the Team Antibiotic Review Form (TARF) Document by frontline prescribers was significant in decreasing antibiotic use. It was used in conjunction with antibiotic stewards for patients actively receiving antibiotics to facilitate discussions about appropriate antibiotic prescribing using the Four Moments framework; A) Make the diagnosis; B) Cultures and Empiric Therapy; C) Stop, Narrow; D) Change to Oral antibiotics; E) Duration. The use of promotional and attractive materials to promote the Four Moments of Antibiotic Decision-Making, such as posters, pocket cards, and screen savers, to advertise the Four Moments Framework. Antibiotic use was decreased by 30.3 DOT per 1000 PD (95% CI, −52.6 to −8.0 DOT; $P = 0.008$). Additionally, the incidence rate of hospital-onset C difficile laboratory-identified events decreased by 19.5% (95% CI, −33.5% to −2.4%; $P = 0.03$) [21].

Interestingly, in the study conducted in the United Kingdom (UK), 58 UK acute hospital organisations expressed an interest in participating. In England, the Department of Health's guidance Start Smart—Then Focus required prescribers to review and revise antibiotic prescriptions every 48–72 h.12. In the USA, the analogous term antibiotic timeouts is used. Still, revised Centres for Disease Control and Prevention guidance in 2019 prioritised pharmacist-led audits and feedback to prescribers. This study aimed to evaluate a multifaceted behaviour change intervention, i.e., the Antibiotic Review Kit (ARK), designed to reduce antibiotic use among adult acute general medical inpatients by increasing appropriate decisions to stop antibiotics at clinical review. It focused on decisions to stop rather than decisions to start antibiotics. Most AMS champions were microbiologists. There was no evidence that sites that achieved greater reductions in antibiotic DDDs per admission had larger increases in mortality than did sites with smaller reductions in antibiotic DDDs per admission. Interestingly, a study published in 2022 in the UK investigating the antibiotic review kit intervention resulted in sustained reductions in antibiotic use among adult acute general medical inpatients. The onset of the COVID-19 pandemic probably explains the weak, inconsistent intervention effects on mortality. Hospitals should use the antibiotic review kit to reduce antibiotic overuse. Despite its limitations, the final model adjusting for COVID-19, the ARK intervention resulted in mean reductions in antibiotic use of 4·8% per year but no immediate reduction [42].

#### Prospective audit and feedback

Another study conducted in Greece. It was focused on the prescription of carbapenems with regard to the indication, dosage and duration of treatment, combined with the judicious use of carbapenem-sparing antibiotics whenever appropriate. The programme is based on the prospective audit and feedback strategy, along with a case-based education of treating doctors. An infectious diseases (ID) specialist and an ID fellow are being alerted by the hospital pharmacy upon prescription request for carbapenem and provide unsolicited in-person ("handshake") consultation within 72 h for all patients for whom the treating doctors have prescribed carbapenem. The antibiotic review and ward rounds. Further ID consultation service upon request is available 7 days a week, 24 h a day, through telephone or in-person [29].

The Systematic implementation of AMS has shown promising outcomes. AMS was started by the Baseline Phase, which started from April to June 2017. It included a routine prospective audit, and feedback was undertaken. Followed by the Intervention Phase, which started from July–December 2017. In this phase, the following interventions were added: Timeout, Correction of doses, continued education for rational use of antimicrobials, and Care bundle approach for prevention of hospital-acquired infections (HAIs). During various interventions. 89 queries/suggestions were made during the baseline phase for 49 (52.1%) of 94 patients, while 196 queries/suggestions were made during the intervention phase for 94 (38.7%) of 243 patients. In both phases, the average number of queries raised was 2 per patient. Queries for de-escalation saw an increase in the intervention phase. This approach could be used in hospitals with limited resources in developing countries and show some benefits of such interventional strategies in resource-limited settings [27].

#### AMS supplemental strategies

The Streamlining/timely de-escalation of therapy strategy was found in five studies BP and only one study DP [30].

This strategy was implemented with an antimicrobial timeout of 48 h. It consists of re-evaluating the patients' empirical and/or definitive antimicrobial regimen, after which the antimicrobials were either continued, escalated or de-escalated according to the patient's clinical condition. This strategy was also part of the regular prospective audit and feedback, where the data-recording team kept track of the timelines and doctors in-charge regarding timeout for each patient [27].

Antibiotic de-escalation strategy in Community-Acquired Pneumonia (CAP) was one of the AMS activities that were significantly affected by the COVID-19 pandemic [30] (Table 4) (Fig. 2).

Both dose optimisation/antibiotic dose adjustment and parenteral-to-oral conversion protocols showed significant outcomes with P-values of 0.03 and 0.04, respectively, in the multi-centre study of California – US, which included 422 general acute care hospitals [19]. During the pandemic, dose optimisation could be used for the specific antibiotic, such as Carbapenems, which focused only on the prescription of carbapenems with regard to the indication, dosage and duration of treatment, combined with the judicious use of carbapenem-sparing antibiotics whenever appropriate. This approach was an essential part of AMS implementation DP [29]. Additionally, in the study assessing the Impact of COVID-19 on Antimicrobial Stewardship Activities/Programs among HCPs in the United Kingdom, respondents were concerned about increased antibiotic use, including increased use of broad-spectrum antibiotics, delayed parenteral-to-oral switch [30].

Guidelines and Clinical Pathways were the most used, as they were applied in 69% BP and DP. However, the organisational collaboration in applying the AMS guidelines and clinical pathways strategy was effectively implemented during the pandemic [30, 31]. In addition, adherence to the local, national, and international guideline recommendations is vital to prevent over- and inappropriate prescribing of antimicrobials. During the pandemic, we found that the availability of updated antimicrobial guidelines, such as the National Institute for Health and Care Excellence (NICE), as well as international guidelines from the WHO and the International Pharmaceutical Federation (FIP), were highly effective. The management of clinical pathways, such as pneumonia and respiratory tract infections in COVID-19 patients, should also be updated [30]. Additionally, the local or organisational clinical practice guidelines should be adapted based on the local antibiograms and resistogram in order to maintain the relevance of the antimicrobial guidelines, as recommended, which has an essential role in decreasing the inappropriate use of antibiotics and decreasing the AMR [22].

In Scotland, Concern regarding bacterial co-infection complicating SARS-CoV-2 has created a challenge for antimicrobial stewardship. Following the introduction of national antibiotic recommendations for suspected bacterial respiratory tract infections complicating COVID-19, a point prevalence survey of prescribing was conducted across acute hospitals in Scotland. Patients in designated COVID-19 units were included, and demographic, clinical and antimicrobial data were collected from 15 hospitals on a single day between 20 and 30th April 2020. Comparisons were made between SARS-CoV-2 positive and negative patients and patients in non-critical care and critical care units. Factors associated with antibiotic prescribing in SARS-CoV-2 positive patients were examined using Univariable and multivariable regression analyses. A relatively low prevalence of antibiotic prescribing in SARS-CoV-2 hospitalised patients and a low proportion of broad-spectrum antibiotics in non-critical care settings were observed, potentially reflecting national antimicrobial stewardship initiatives. Broad-spectrum antibiotic and antifungal prescribing in critical care units were observed, indicating the importance of infection prevention and control and stewardship initiatives in this setting [43].

### AMS education

Before the pandemic, AMS education using active learning activities showed promising results. For example, we found a study conducted across the United States (US) hospitals that applied educational activities and webinars that encouraged collaboration with the clinical microbiology laboratory, integrating nurses into stewardship activities and antibiotic allergies. This AMS educational program entitled 'Building Stewardship: A Team Approach Enhancing Antibiotic Stewardship in Acute Care Hospitals' offered by the Agency for Healthcare Research and Quality (AHRQ) safety program was highly effective, as it focused on the importance of Antimicrobial Stewardship Programs (ASPs), strategies for implementation, and operational issues, including an understanding of pharmacodynamics, business models, and electronic surveillance [23]. The AHRQ educational components were also used in another study in an innovative and easy way, such as 1-Page documents and accompanying user guides on infectious disease syndromes. The document could be used as (1) informational attractive display posters, (2) discussion points on clinical rounds, or (3) an outline for developing local guidelines [21]. However, during the pandemic, AMS education was found in only one study and showed an essential impact. There was a critical need for structured AMS education to deal effectively with any emergency/crisis [30].

Computer Decision Support & Surveillance and Antibiotic Order Form strategy was found only in two studies BP. However, only Computer decision support & surveillance was found in one study DP [30]. During the pandemic, the use of technology has a significant impact on AMS implementation. Positive outcomes of COVID-19 on AMS activities included: technology being increasingly used as a tool to facilitate stewardship, e.g., virtual meetings and ward rounds.

The use of hospital electronic prescribing systems facilitated AMS activities by antimicrobial pharmacists. There was a UK-wide decrease in audit activities undertaken by antimicrobial pharmacists. Additionally, PHE Fingertips data support the suspicion of increased 'just in case' prescribing of antimicrobials was decreased DP. The national surveillance database indicated a substantial increase in antibiotic prescribing (DDD/1000 admissions) in the COVID-19 period [30]. The use of integrated computerised systems was still effective in reducing AMR. Interestingly, the use of new technology ideas, such as mobile applications in updating the antimicrobial guidelines was effective, such as the Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS) App [30], antibiotic order forms, prescribing and availability of guidelines on smartphones [44].

Laboratory surveillance and feedback were found in 46% of the included studies. The surveillance of antimicrobial use and resistance has been used as a crucial part of AMS implementation, especially when accompanied by other strategies, such as antibiotic restriction, as shown in the study conducted in Germany. The formulary restriction of specific antibiotics (e.g., tigecycline and colistin), the creation of selective antibiotic resistogram profiles, the implementation and electronic access to antimicrobial prescribing guidelines, and mobile applications were used as AMS toolkit BP [22]. laboratory results and microbiology were essential data sources in AMS implementation [24]. During the Pandemic, reviewing the patient laboratory data was also an integral part of the patient's clinical examination by the ID specialist or ID fellow. It is also accompanied by a review of the patient's laboratory data, all prescribed antimicrobials, and a subsequent daily, rounding-based, in-person approach to feedback by the ID doctors. Additionally, it was used in AMS case-based education [29].

#### AMS measures and quality improvement

As mentioned in the result section, there should be measures/metrics to properly manage AMS implementation. This could be conducted by identifying the measures that can be used to evaluate the outcome of AMS implementation to improve antibiotic use and AMS intervention strategies. These measures or metrics can be used for many purposes, such as quality assurance, improvement, comparisons, and benchmarking. Measuring AMS can be divided into four categories: antimicrobial consumption, process measures, outcome measures, and financial [45]. The AMS strategies have significant value with beneficial clinical, resistance and economic impact(s) [46] (Table 4) (Fig. 2). For more details, see Supplementary Table S7.

Monitoring trends in antimicrobial use and resistance within a hospital over several years and also identifying small changes in a single ward over a one-month period are essential to adapting empiric treatment according to local resistance trends, demonstrating changes in practice over time and identifying wards with high antimicrobial usage or use of non-policy antimicrobials and define targeted interventions required [8]. Surveillance of antimicrobial use and resistance is important either at the hospital, local, regional, and national levels, such as in the UK [47], Wales [48], Sweden [49], Australia [50], and Canada [51] and at the global level, such as WHO [52, 53] and ECDC [54].

Quality improvement and indicators were the most commonly used measures among the included studies, as found in about 83% of the included studies. However, quality improvement projects were found in two studies during the COVID-19 pandemic [30, 31]. It could be used at any stage of the antibiotic use process. The quality improvement activity assists clinicians in selecting the appropriate antibiotic, dose, duration, and route of administration to optimise clinical outcomes while minimising the selection of pathogenic organisms and the emergence of resistance. Importantly, there was an increasing linkage between ASPs and 146 hospital patient safety and quality initiatives. Interestingly, it was important to follow up and monitor results using appropriate quality improvement committees [19]. A single-centre quality improvement study with a retrospective evaluation of the impact of antimicrobial stewardship measures on optimising antibacterial use in intra-abdominal infections requiring emergency surgery was performed [22]. The use of the performance of a PPS to provide feedback on validated quality indicators (QIs) for appropriate antibiotic use (PPS-QI) demonstrated a reduction in geometric mean LOS of 0.8 days in the multicentre cluster-randomized clinical trial to improve antibiotic use and reduce the length of stay in hospitals in the Netherlands [20]. Quality improvement activities, such as national quality improvement schemes, were one of the AMS measures that were negatively impacted by the COVID-19 pandemic [30]. It could also be used to measure the improvement of AMS activities, such as the use of PCT-based guidelines as a useful tool for rationalising the use of antibiotics in patients with COVID-19 [31]. The presence of ongoing AMS quality indicators is one of the essential factors in maintaining preparedness for any emergency or crisis, especially at the national level [54]. During the Pandemic, an interesting study was conducted at Sheffield Teaching Hospitals NHS Foundation Trust (STHNFT). The aim of this study was to evaluate the effectiveness of the implemented guideline, which recommended that antibiotics can be withheld in patients with COVID-19 with PCT < 0.25 ng/mL unless felt necessary by a senior clinician. Additionally, the PCT in an electronic 'COVID order set' facilitated AMS measures and surveillance was included. This study found that a PCT-based guideline can be a useful tool for rationalising the use of antibiotics in patients with COVID-19 [31].

Both LOS and Cost were found in three studies, only BP. The use of LOS had several advantages: it was easy to measure, could be applied to all admitted patients, reflected the recovery time of hospitalised patients and drove hospital costs [20]. LOS was used to examine the antimicrobial use and length of stay (LOS) before and after a change in AMS approach at the Hospital of the University of Pennsylvania, a 776-bed tertiary care academic medical centre in Philadelphia and showed a significant increase after the change in AMS strategy from Pre-authorization and Prospective Audit with Feedback [24]. Interestingly, when prior to authorisation, AMS strategy was conducted in costly antibiotics, such as including aztreonam, ceftazidime, daptomycin, levofloxacin, linezolid, and meropenem) and showed a promising outcome in decreasing the LOS and cost. LOS is an important factor in healthcare cost analysis. Based on the national health insurance claims database and specific health check-ups in Japan, the importance of appropriate use of antibiotics and AMS implementation was paramount [25].

Before 2019, there were no reliable means for measuring antimicrobial usage. The WHO promoted measurable tools, such as the defined daily dose (DDD) and Day of Therapy (DOT), to allow comparisons for antimicrobial usage among hospitals and countries [33, 55]. In the included studies, the DDD and DOT are the most common AMS measures, as it was used in 53% of BP and 28% of DP. Significantly, we found another study promoted the use of KPIs, such as the AMR local indicators—produced by the UKHSA among the National Health Service (NHS) hospitals in England, and it showed a significant outcome in AMS and provided a comparative measure for the antibiotic prescribing among different periods DP [30, 56].

On the other hand, the CDI rate was used in measuring the outcome of AMS implementation [19]. It was found that a reduction in antibiotic use and hospital-onset CDI rates was an outcome of implementing the Agency for Healthcare Research and Quality Safety Program across US hospitals [21]. During the pandemic, there was a concern about increasing CDI rates as a result of the COVID-19 pandemic across all National Health Service (NHS) acute trusts in England [30]. Interestingly, data on CDI was collected as a contribution to AMS activities DP [31].

A study published in Cambridge University Press aimed to develop and implement antibiotic stewardship activities in urgent care targeting non–antibiotic-appropriate acute respiratory tract infections (ARIs). The AMS activities were started in fiscal 2020 and included measure development, comparative feedback, and clinician and patient education. This study measured antibiotic prescribing in fiscal years 2019, 2020, and 2021 for the stewardship targets, potential diagnosis-shifting visits, and overall. Additionally, it collected patient satisfaction data for ARI visits. The antibiotic prescribing rate decreased for stewardship-measure visits from 34% in FY19 to 12% in FY21. Although AMS was affected by the COVID-19 pandemic, an ambulatory antimicrobial stewardship program that focused on improving non–antibiotic-appropriate ARI prescribing was associated with decreased prescribing for (1) the stewardship target, (2) a diagnosis-shifting measure, and (3) overall antibiotic [57]. The first step to improving the current situation is to measure how medicines areused and this forms the basis of advocacy for change [58]. Clinical pharmacist has a critical role in AMS, and can be effective in implemented sustainable change [59].

### Limitations of the systematic review

Searching only published databases could have resulted in missing some potentially relevant but unpublished studies from the review. Secondly, limiting studies to being published in English could have resulted in missing essential studies published in other languages.

### Limitations of the evidence

To the knowledge of the authors, this is the first systematic review to assess the AMS implementation of BP and DP. However, there are insufficient studies using AMS strategies and measures. The authors did their best to compare the AMS strategies and measures, but variations in their use affected the comparability of findings across studies.

### Comparison with existing literature

A few reviews have assessed AMS in hospitalised patients. However, none of the reviewers has focused on the core and supplemental AMS strategies, nor the AMS measures in secondary care and acute care settings BP and DP as explored in this present systematic review.

**Implications for research and practice**

Few studies identified the AMS measures, the use of AMS indicators and quality improvement projects which are relevant to this systematic review. Therefore, further studies are required to provide measurable indicators for assessing AMS implementation. It will also enable the planning and evaluation of suitable AMS interventions. Secondly, further research is required to develop methods for standardised measurements for AMS implementation that will allow greater comparability of AMS outcomes and measures across studies. Lastly, there was evidence that antibiotic use is best achieved with organisational collaboration, especially during an emergency or pandemic.

## Conclusion and recommendations

This systematic literature review investigated the AMS strategies and measures used in the acute care settings BP and DP. Advocacy for AMS must continue in the post-pandemic era to assure the safety of patient care. There are so many lessons learnt from the COVID-19 pandemic. These lessons and further recommendations from this systematic review were as follows:

1. In order to set up AMS, a multidisciplinary team is one of the key components of the structure and governance of the ASP in acute care settings BP and DP.
2. When establishing a new stewardship program, it is best to start with the core strategies and focus on achieving and maintaining them before adding some of the supplemental strategies.
3. Each Hospital should select the relevant AMS intervention tools to maintain the appropriate use of antibiotics and decrease the AMR. The types of interventions selected, how to be delivered, and by whom will be determined by local resources need and available expertise.
4. A prospective Audit with Feedback and Antibiotic Review core strategies showed promising outcomes in AMS implementation DP.
5. Guidelines, & Clinical Pathways, Guidelines and Education strategies were important to maintain the successful implementation of AMS BP and DP.
6. The development of national prescribing indicators helped to promote the appropriate antibiotic use during-the-pandemic, such as the UK five-year National Action Plan 2019–2024, with ambitions to reduce UK antimicrobial use in humans by 15% by 2024.
7. Novel AMS measures, such as Procalcitonin-guided antibiotic prescribing, showed a promising effect on AMS implementation. Results showed reduced antibiotic consumption in patients with PCT 0.25 ng/mL with no increase in mortality. Further research is recommended to identify the optimal cut-off value for PCT in this setting.
8. DDD and DOT are the most common AMS measures among the other measures. There is a need to standardise AMS measures in order to provide a comparison of outcomes and planning of effective AMS implementation.
9. The use of an integrated Computerised Decision Support System and Surveillance is required to maximise the use of technical support in sustained AMS implementation and measuring, which would be beneficial in preparing for any future crisis or emergencies.

**Abbreviations**

| | |
|---|---|
| ABT | Antibiotic Therapy |
| AHRQ | Agency for Healthcare Research and Quality |
| AMS | Antimicrobial Stewardship |
| AMS | Antimicrobial Stewardship |
| ARK | Antibiotic Kit Review |
| ASP | Antimicrobial Stewardship Program |
| AMR | Antimicrobial Resistance |
| ARIs | Acute respiratory tract infections |
| BP | Before-the-pandemic |
| BSAC | British Society for Antimicrobial Chemotherapy |
| CAP | Community-Acquired Pneumonia |
| CBA | Controlled Before-After |
| CDI | Clostridioides Difficile Infection |
| CI | Confidence Interval |
| COVID-19 | Coronavirus |
| CwPAMS | Commonwealth Partnerships for Antimicrobial Stewardship |
| DDD | Defined Daily Doses |
| DOT | Days of Therapy |
| DP | During-the-pandemic |
| ECDC | European Centre for Disease Prevention and Control |
| FIP | International Pharmaceutical Federation |
| HAIs | Hospital-Acquired Infections |
| HCPs | Healthcare Professionals |
| ICU | Intensive Care Unit |
| IVOST | IV to oral switches |
| IDSA | The Infectious Diseases Society of America |
| IV | Intravenous |
| ISRCTN | International Standard Randomised Controlled Trial Number |
| LOS | Length of Stay |
| LOT | Length of Therapy |
| MMAT | Mixed Method Appraisal Tool |
| NHS | National Health Service |
| NICE | National Institute for Health and Care Excellence |
| STHNFT | Sheffield Teaching Hospitals NHS Foundation Trust |
| OPAT | Outpatient Parenteral Antibiotic Therapy |
| PAT | Postoperative Antibiotic Therapy |
| PCT | Procalcitonin |
| PPE | Personal Protective Equipment |
| PPS-ECDC | Point Prevalence Study of the European Centre for Disease Prevention and Control |
| PPS-QI | Point Prevalence Surveys; LOS—Length of Stay; ICU—Intensive Care Unit; ABT—Antibiotic Therapy |
| PHE | Public Health England |
| PICOS | Population, Intervention, Comparison, Outcome, Setting |
| PRISMA | Preferred Reporting Items for Systematic Reviews |

| | |
|---|---|
| PPS-ECDC | Point Prevalence Study of the European Centre for Disease Prevention and Control |
| PPRF | Post-prescription review and feedback |
| QIs | Quality Indicators |
| RCTs | Randomized Controlled Trials |
| STHNFT | Sheffield Teaching Hospitals NHS Foundation Trust |
| SARS-CoV-2; COVID-19 | Severe acute respiratory syndrome coronavirus-2 |
| TARF | Team Antibiotic Review Form |
| URTIs | Upper Respiratory Tract Infections |
| US | United States |
| UK | United Kingdom |
| UH | University of Hertfordshire |
| WHO | World Health Organization |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-023-15072-5.

**Additional file 1: Supplementary Table S1.** Descriptive definitions of Antimicrobial Stewardship. **Supplementary Table S2.** Rationale behind selecting each database used to conduct the systematic literature review. **Supplementary Table S3**. The systematic review of the search terms in different databases. **Supplementary Table S4.** The quality of the included studies using MAAT. **Supplementary Table S5.** Antimicrobial Stewardship Core and Supplemental Strategies. **Supplementary Table S6.** Definition of some of AMS strategies. **Supplementary Table S7.** AMS Strategies and their related outcomes. **Supplementary Table S8.** Suggested measures for antimicrobial stewardship. **Supplementary Table S9.** ASP Metrics Example. **Supplementary Figure S1.** Data extraction Form. **Supplementary Figure S2.** A multidisciplinary approach to antimicrobial stewardship implementation.

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### Authors' contributions

RAE participated in protocol development, literature searching, data extraction, data analysis and manuscript preparation; NU participated in protocol development and data analysis and independently reviewed the quality of studies and manuscript preparation. ZA participated in protocol development, literature searching, and data extraction, independently reviewed the quality of studies, selection, and driving ideas, and provided subject-specific comments to update the manuscript. ABA conducted the data extraction for the included studies independently. The author(s) read and approved the final manuscript.

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## Declarations

### Ethics approval and consent to participate

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### Consent for publication

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### Competing interests

The authors declare that they have no competing interests.

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# Appendix 64.

WHO AWaRe classification for antibiotic stewardship: tackling antimicrobial resistance — a descriptive study from an English NHS Foundation Trust prior to and during the COVID-19 pandemic.

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# WHO AWaRe classification for antibiotic stewardship: tackling antimicrobial resistance – a descriptive study from an English NHS Foundation Trust prior to and during the COVID-19 pandemic

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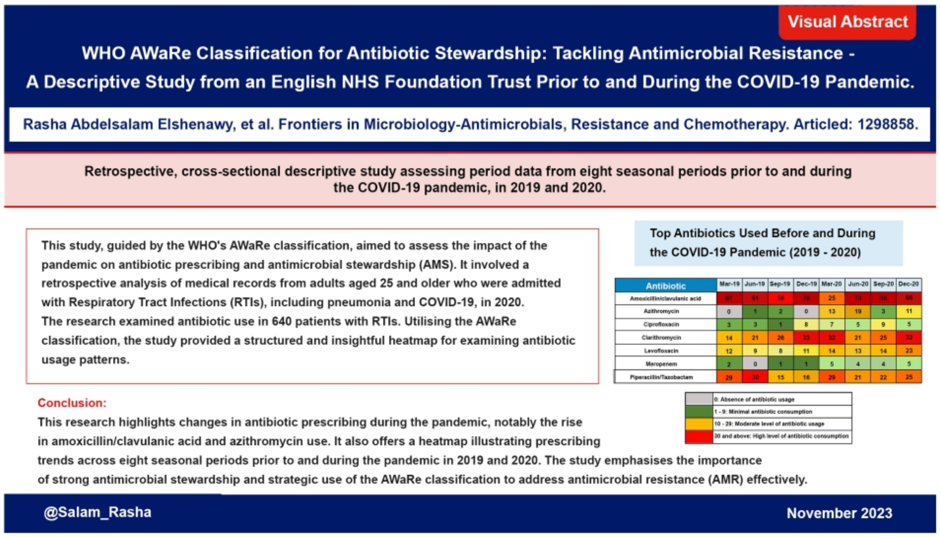
Antimicrobial resistance (AMR) is a silent and rapidly escalating pandemic, presenting a critical challenge to global health security. During the pandemic, this study was undertaken at a NHS Foundation Trust in the United Kingdom to explore antibiotic prescribing trends for respiratory tract infections (RTIs), including pneumonia, and the COVID-19 pandemic across the years 2019 and 2020. This study, guided by the WHO's AWaRe classification, sought to understand the impact of the pandemic on antibiotic prescribing and antimicrobial stewardship (AMS). The research methodology involved a retrospective review of medical records from adults aged 25 and older admitted with RTIs, including pneumonia, in 2019 and 2020. The application of the AWaRe classification enabled a structured description of antibiotic use. The study evaluated antibiotic use in 640 patients with RTIs. Notably, it observed a slight increase in the use of amoxicillin/clavulanic acid and a substantial rise in azithromycin prescriptions, highlighting shifts in prescribing trends. Despite these changes, some antibiotics displayed steady consumption rates. These findings highlight the importance of understanding antibiotic use patterns during the AMR threat. The increase in the usage of "Watch" category antibiotics during the pandemic emphasises the urgency of robust AMS measures. The research confirms that incorporating the AWaRe classification in prescribing decisions is crucial for patient safety and combating antibiotic misuse. This study provides essential insights into the changing landscape of antibiotic prescribing during a global health crisis, reinforcing the necessity for ongoing AMS vigilance to effectively address AMR challenges.

KEYWORDS
**AWaRe, antibiotic stewardship, COVID-19, NHS, hospitals, antimicrobial resistance**




GRAPHICAL ABSTRACT

## Introduction

Antimicrobial resistance (AMR) constitutes a silent and rapidly escalating pandemic, presenting a critical challenge to global health security (Salam et al., 2023). The introduction of penicillin in the 1920s was a transformative era in the field of infection management, significantly diminishing mortality rates associated with infections (Elshenawy et al., 2023). Despite these advances, the emergence and escalation of AMR, primarily attributed to the inappropriate prescription of antibiotics, casts a long shadow over these achievements. It was projected that AMR infection rates could escalate to 10 million cases by the year 2050 (O'Neill, 2014). Notably, in 2019, AMR was implicated in the deaths of over 1.2 million individuals globally. In response to this growing crisis, the implementation of antimicrobial stewardship (AMS) has become increasingly imperative (Murray, 2022). AMS advocates for the judicious use of antibiotics, thereby optimising treatment outcomes and minimising the development of resistance (National Institute for Health and Care Excellence, 2015). The World Health Organization (WHO) has actively contributed to this endeavour by developing the AWaRe classification system (www.who.int, 2023). This framework is instrumental in guiding the global implementation of AMS and promoting responsible antibiotic usage, aligning with the strategic objectives outlined in the UK's Five-Year AMR Strategic Plan (Department of Health and Social Care, 2019). This alignment emphasised an integrated international commitment to addressing and mitigating the challenges posed by AMR (Tejpar et al., 2022).

In the AWaRe tool, antibiotics are divided into three categories: access, watch, and reserve. Each category is based on its respective effect on AMR. The "Access" antibiotics are characterised by their narrow spectrum of activity, typically resulting in fewer side effects, a reduced likelihood of antimicrobial resistance selection, and lower costs. They are strongly recommended for empiric treatment of common infections and should be readily available. Conversely, "Watch" antibiotics carry a higher risk of promoting antimicrobial resistance and are primarily prescribed for patients with more severe conditions, predominantly within hospital settings. Vigilant monitoring of these antibiotics is vital to prevent their overuse. "Reserve" antibiotics, however, are considered the last resort and should be employed only when dealing with severe infections caused by multidrug-resistant pathogens. Their use should be reserved for critical situations. The AWaRe classification underscores the importance of restricting the use of "Watch" and "Reserve" category antibiotics. By 2023, the WHO aims for at least 60% of all antibiotic consumption to come from the Access group (www.who.int, 2023).

The COVID-19 pandemic has profoundly impacted global healthcare systems and various aspects of people's lives worldwide (World Health Organization, 2021). An inevitable consequence of the pandemic has been the increase in inappropriate antibiotic use, contributing to rising AMR rates (Subramanya et al., 2021). This is despite WHO guidelines advising against antibiotics unless there is strong evidence of a secondary bacterial infection (World Health Organization, 2020). Surprisingly, it was found that 70% of COVID-19 patients were administered antimicrobials (Pérez de la Lastra et al., 2022). Consequently, the inappropriate use of antibiotics during the COVID-19 pandemic may exacerbate the global challenge of AMR (Nandi et al., 2023). This research aimed to examine the use of antibiotics in the initial and subsequent treatment stages of RTIs, including pneumonia, both prior to pandemic (PP) and during the pandemic (DP) at one English National Health Service (NHS) Foundation Trust. In order to provide an in-depth understanding of the impact of the pandemic on antibiotic prescribing, we analysed data from eight seasonal time points in 2019 and 2020.

# Method

## Study design

A retrospective cross-sectional patient records review study was conducted to investigate AMS and the AWaRe classification of antibiotics in adult patients aged 25 and older. These patients were admitted to an English NHS Foundation Trust in the United Kingdom during 2019 and 2020. The study comprehensively describes antibiotic prescribing patterns utilising a methodological approach based on retrospective cross-sectional analysis. For sampling, the systematic method was employed to consistently select patient medical record data from a larger dataset at the Trust. Initially, data from 4,830 records (2,755 from 2019 and 2,075 from 2020) were extracted. After applying inclusion and exclusion criteria and eliminating duplicate records, the numbers were narrowed down to 1,188 for 2019 and 939 for 2020. Subsequently, a random selection of 80 records for each of the four-time points in 2019, as well as 80 records from 2020, was conducted using Excel's Random function. This resulted in a total of 640 patient records (as shown in Figure 1). The systematic sampling method ensured equal representation across the patient population and was consistently applied across all eight seasonal time points, spanning from Spring 2019 to Winter 2020. This approach streamlined the sampling process whilst ensuring a comprehensive representation of the patient population.

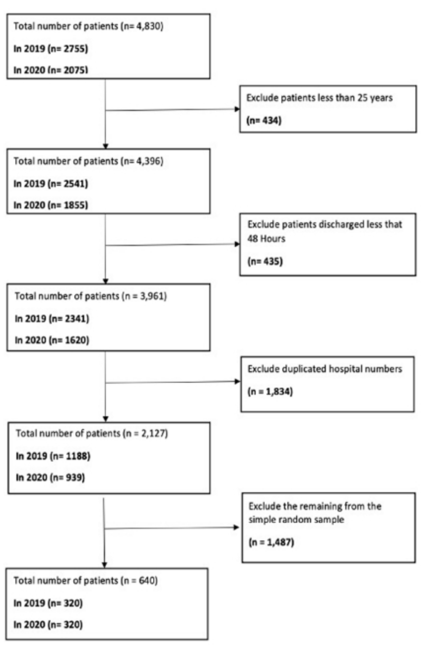



FIGURE 1
Data filtering algorithm for extracting a representative sample of 640 patient medical records from 2019 and 2020.

## Sample size

According to estimations by Public Health England, approximately 20% of antibiotic prescriptions in the UK are potentially inappropriate. For this study, the sample size was determined using Minitab statistical software, taking into account the total population size, a margin of error set at 10%, and a confidence interval of 95%. The data collection involved patient records across eight different seasonal time points spanning 2019 and 2020. The analysis encompassed a total of 640 medical records, divided evenly between 2019 (pre-pandemic period) and 2020 (during the pandemic period), with each year comprising four seasonal time points. To ensure a robust and representative sample, a systematic sampling method was employed to select 80 patients for each of these intervals.

## Study population (inclusion/exclusion criteria)

A stratified sampling strategy was employed to ensure maximum diversity amongst the included medical records. The inclusion criteria comprise the following: (i) adult patients aged 25 years and older; (ii) patients admitted to the Trust; (iii) patients admitted in 2019 and 2020; (iv) patients prescribed antibiotics for RTIs, including pneumonia; and (v) pregnant women and immunocompromised patients. However, patients who spent less than 48–72 h in the Accident and Emergency (A&E) department, patients who were not prescribed antibiotics, and children were excluded from this study.

## Data source

The primary author (RAE) was responsible for gathering data from the patient's electronic patient records within the Trust, strictly following the inclusion and exclusion criteria established for the study.

## Data collection

Data were collected from the medical records of 640 patients within the Foundation Trust in accordance with the specified inclusion and exclusion guidelines. Data were collected from eight-time points, with four-time points PP: (i) March (Spring 2019); (ii) June (Summer 2019); (iii) September (Autumn 2019); and (iv) December (Winter 2019). Additionally, four-time points occurred DP: (i) March (Spring 2020) – the first wave of COVID-19; (ii) June (Summer 2020) – the first lockdown; (iii) September (Autumn 2020) – the second wave of the pandemic; and (iv) December (Winter 2020) – the vaccination rollout.

## Data extraction

A data extraction tool was utilised to retrieve essential information from 320 medical records of patients diagnosed with RTIs, such as pneumonia, in the pre-pandemic year of 2019. Additionally, the same tool was used to extract data from another set of 320 records of patients diagnosed with RTIs, including pneumonia and COVID-19, during the pandemic in 2020. The data extraction tool was set up in line with the guidelines of the WHO AWaRe Tool1 (www.who.int, 2023). This study focussed exclusively on antibiotics utilised for treating RTIs. Following the categorisation by the WHO AWaRe Tool, 10 antibiotics were classified under the "Access" group, 11 were identified as "Watch" antibiotics, and 3 were allocated to the "Reserve" category, as shown in Figure 2. The data extraction tool encompassed comprehensive details, including patient demographics, initial diagnosis, and the usage of first- and second-course antibiotics. Adhering to the guidelines of the WHO AWaRe Tool, the primary author dedicated approximately 45 min to each patient's medical record for the successful extraction of the required data.

## Pilot study

The primary author conducted a pilot study in which data were derived from 10 patient medical records at each time point,

**WHO Access, Watch, Reserve (AWaRe) classification for antibiotics evaluation and monitoring before and during the COVID-19 pandemic**

| Access | Mar-19 | Jun-19 | Sep-19 | Dec-19 | Mar-20 | Jun-20 | Sep-20 | Dec-20 |
|---|---|---|---|---|---|---|---|---|
| Amoxicillin | 2 | 1 | 2 | 3 | 6 | 6 | 0 | 1 |
| Amoxicillin/clavulanic acid | 67 | 61 | 56 | 76 | 25 | 70 | 86 | 66 |
| Benzylpenicillin | 1 | 0 | 2 | 0 | 3 | 0 | 0 | 0 |
| Doxycycline | 1 | 1 | 3 | 2 | 1 | 2 | 0 | 1 |
| Flucloxacillin | 2 | 2 | 3 | 2 | 0 | 5 | 2 | 1 |
| Gentamicin | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 |
| Metronidazole | 3 | 7 | 2 | 0 | 4 | 4 | 2 | 4 |
| Sulfamethoxazole/Trimethoprim | 0 | 1 | 1 | 0 | 4 | 2 | 0 | 0 |
| Clindamycin | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cephalexin | 0 | 0 | 2 | 1 | 1 | 0 | 0 | 0 |
| **Watch** | | | | | | | | |
| Azithromycin | 0 | 1 | 2 | 0 | 13 | 19 | 3 | 11 |
| Ceftazidime | 2 | 2 | 0 | 0 | 0 | 1 | 0 | 0 |
| Ceftriaxone | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 |
| Cefuroxime | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Ciprofloxacin | 3 | 3 | 1 | 8 | 7 | 5 | 9 | 5 |
| Clarithromycin | 14 | 21 | 26 | 33 | 32 | 21 | 25 | 32 |
| Levofloxacin | 12 | 9 | 8 | 11 | 14 | 13 | 14 | 23 |
| Meropenem | 2 | 0 | 1 | 1 | 5 | 4 | 4 | 5 |
| Piperacillin/Tazobactam | 29 | 30 | 15 | 16 | 29 | 21 | 22 | 25 |
| Teicoplanin | 0 | 0 | 1 | 0 | 3 | 0 | 0 | 0 |
| Vancomycin | 1 | 4 | 0 | 1 | 0 | 1 | 0 | 0 |
| **Reserve** | | | | | | | | |
| Aztreonam | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| Cefazidime/Azobactam | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| Linezolid | 3 | 2 | 1 | 1 | 0 | 0 | 1 | 1 |

| | |
|---|---|
| (grey) | 0: Absence of antibiotic usage |
| (green) | 1 - 9: Minimal antibiotic consumption |
| (yellow) | 10 - 29: Moderate level of antibiotic usage |
| (red) | 30 and above: High level of antibiotic consumption |

FIGURE 2
Heatmap for antibiotic use in 2019 and 2020 according to AWaRe criteria.

accumulating 80 patient medical records in 2019 and 2020. The primary objectives of this pilot study were to provide an initial characterisation of the data and to evaluate the viability of the data extraction instrument in addressing the research queries. Descriptive statistical analysis was employed to interpret this initial data. The findings from this pilot study indicated that the data extraction tool was effective in meeting all the objectives of the study. The data generated and extracted during the pilot phase were not included in the study's final analysis.

## Validity and reliability of the data extraction tool

The lead author (RAE) developed the data extraction tool using literature sources, the AMS toolkit from Public Health England (PHE), and the World Health Organization's (WHO) AWaRe Tool. The tool's components were finalised through collaborative discussions amongst the authors. To validate the tool, RAE and an AMS pharmacist at the research NHS Foundation Trust independently extracted data from 10 medical records at each sample time point. A minimum agreement rate of 80% was set as the standard for tool validation. Additionally, to assess the tool's reliability, RAE and the AMS pharmacist separately conducted data extractions from the same set of samples. The inter-rater reliability was measured by the percentage of agreement in their independently extracted data, with any variances resolved through joint discussions.

## Patient characteristics

Data were extracted from patient medical records for those admitted in 2019 and 2020, specifically focussing on patients diagnosed primarily with RTIs, including pneumonia, and COVID-19 positive cases, as COVID-19 has the potential to cause secondary bacterial infections that necessitate antibiotic treatment. For patients admitted in 2020, during the pandemic, cases of COVID-19 were also included in the data extraction. The selection of primary RTI diagnoses was guided by the pertinent categories in the International Classification of Diseases, 10th Revision (ICD-10). The extracted data focussed on antibiotics given at admission, empirical antibiotic treatments, and antibiotics prescribed within 48–72 h or 5–7 days following admission.

## Patient and public involvement

The study protocol was submitted to the Citizens Senate, an organization focussed on patient care with a considerable representation of elderly individuals. They provided useful suggestions and comments.

## Registration

This study has been officially registered with the ISRCTN registry. The ISRCTN registry is a primary registry acknowledged by the WHO and the International Committee of Medical Journal Editors (ICMJE), accepting all clinical research studies (www.isrctn.com, 2022). Moreover, it was registered in Octopus, the global primary research record (Octopus, 2019).

## Data analysis

This study identified the initial antibiotic prescribed for each patient according to the main diagnosis of RTIs, PP, and DP. Additionally, AMS was evaluated using the AWaRe classification, descriptive statistics, and data analysis software, Excel 2019 for Windows (www.microsoft.com, 2019).

# Results

## WHO AWaRe tool: antibiotic usage in RTIs

This research examined the antibiotics prescribed for RTIs in 640 patients admitted between 2019 and 2020. In the Figure 1 heatmap, each row represents a different antibiotic, whilst each column corresponds to a specific seasonal month from 2019 to 2020. The colour intensity of each cell in the heatmap represents the frequency of prescriptions for each antibiotic used in treating RTIs, including pneumonia and COVID-19-positive cases, across the 640 patients admitted during those years. This visualization is particularly informative given that COVID-19 can lead to secondary bacterial infections requiring antibiotic intervention. Darker colours indicate higher prescription rates, providing a visual representation of prescribing trends over time. The heatmap uses a colour-coded system to reflect the levels of antibiotic consumption over several months, from March 2019 to December 2020. Antibiotics are categorised into three groups based on the World Health Organization's Access, Watch, and Reserve (AWaRe) classification, which is designed to promote the proper use of antibiotics to combat resistance. In this heatmap figure, antibiotic consumption was categorised into four levels based on values, with the highest value being 86 and the lowest value being 0. These categories were as follows: 0 represented the absence of antibiotic usage, 1–9 represented minimal antibiotic consumption, 10–29 represented a moderate level of antibiotic usage, and 30 and above represented the highest level of antibiotic consumption (Figure 2). The categorisation of data in Figure 2 is derived from a literature review and the clinical relevance of antibiotic prescribing trends.

The "Access" category includes essential antibiotics that should be widely available. In this category, amoxicillin/clavulanic acid showed a substantial increase, starting at 67 in March 2019 and peaking at 86 in September 2020, indicating high usage. Flucloxacillin also demonstrated an increase from 2 in March 2019 to 5 in June 2020, suggesting moderate use. The "Watch" group comprises antibiotics that have the higher potential for resistance and should be used more cautiously. In this study, azithromycin usage escalated from zero in March 2019 to 19 in June 2020, showing a high level of use. Clarithromycin started at 21 in June 2019 and increased to 32 by December 2020. Ciprofloxacin and levofloxacin also saw increases in their consumption levels over the study period. Piperacillin/tazobactam maintained a consistently high consumption level of 29 in March 2019 and March 2020. Meropenem showed a modest increase from 2 in March 2019 to 5 in December 2020. In the "Reserve" category, which includes antibiotics that should be reserved for treating infections caused by multidrug-resistant organisms, linezolid maintained a high consumption level of 3 in March 2019 without any substantial increase through 2020. Aztreonam and ceftazidime/avibactam show minimal increases in usage.

Notably, there was an increase in the total usage of antibiotics in the "Access" category, reaching 305 in 2019 and slightly decreasing to 298 in 2020. In contrast, the "Reserve" category saw a reduction in use, declining from 9 to 3. Meanwhile, the "Watch" category experienced a significant increase in 2020, with usage escalating to 386, up from 259 in the previous year.

## The top seven prescribed antibiotics before and during the COVID-19 pandemic

Figure 3 shows the use of the seven most commonly prescribed antibiotics in both PP and DP, further detailed in Supplement 1. In 2019, amoxicillin/clavulanic acid was the most frequently prescribed antibiotic, accounting for 247 instances. This trend persisted in 2020 with 260 instances, maintaining its top position. In 2020, compared to 2019, there was an increase in prescriptions for most of the other antibiotics. For instance, clarithromycin saw an increase from 94 prescriptions in 2019 to 100 in 2020. Piperacillin/tazobactam also witnessed a slight increase, from 90 instances in 2019 to 97 in 2020. Additionally, 2020 showed increased prescriptions of levofloxacin, azithromycin, and ciprofloxacin compared to 2019. Levofloxacin prescriptions increased from 40 in 2019 to 64 in 2020. Azithromycin had a surge, increasing from 12 in 2019 to 46 in 2020. Ciprofloxacin also displayed a increasing trend, going from 15 in 2019 to 26 in 2020, whilst meropenem's usage modestly increased in 2020, from 10 to 18 instances.

## Discussion

This study examined the prescribing patterns of antibiotics at an English NHS Foundation Trust, employing the AWaRe classification system for antibiotics used in treating RTIs, including pneumonia, and taking into account cases positive for COVID-19 in the year 2020. This AWaRe classification serves as an effective means for tracking antibiotic usage, establishing goals, and observing the impact of stewardship initiatives aimed at enhancing antibiotic utilisation and combating antimicrobial resistance. The WHO's 13th General Programme of Work for the years 2019–2023 sets a target for countries to achieve at least 60% of their total antibiotic consumption from antibiotics categorised in the access group (www.who.int, 2021). COVID-19 highlighted the effectiveness of antimicrobial stewardship (AMS) in combating AMR by guiding strategic choices during the pandemic and encouraging judicious antibiotic use. Findings from this study showed that amoxicillin/clavulanic acid, classified in the "Access group," emerged as the most frequently prescribed antibiotic (Elshenawy et al., 2023).

This study observed a significant increase in the use of azithromycin, an antibiotic categorised in the "Watch" group. This categorisation indicates a need for more cautious use due to a higher potential for resistance development. This upward trend in azithromycin usage aligns with findings from a variety of international research efforts. In India, studies by Mugada et al. (2021) and Sharma et al. (2021) reported similar patterns, reflecting a broader shift in antibiotic prescription practices. In Malaysia, Mohamad et al. (2022) also observed an increase. In Zambia, findings by Mudenda et al. (2022, 2023) further corroborate these findings, suggesting both a regional and a global increase in reliance on azithromycin. Additionally, research conducted in several Eastern Mediterranean countries, including studies by Kalungia et al. (2022) and Jirjees et al. (2022), and in other regions such as Ghana, as noted by Amponsah et al. (2022), has also observed this trend, highlighting a consistent global shift towards increased usage of this particular antibiotic. These studies collectively emphasise the growing preference for azithromycin

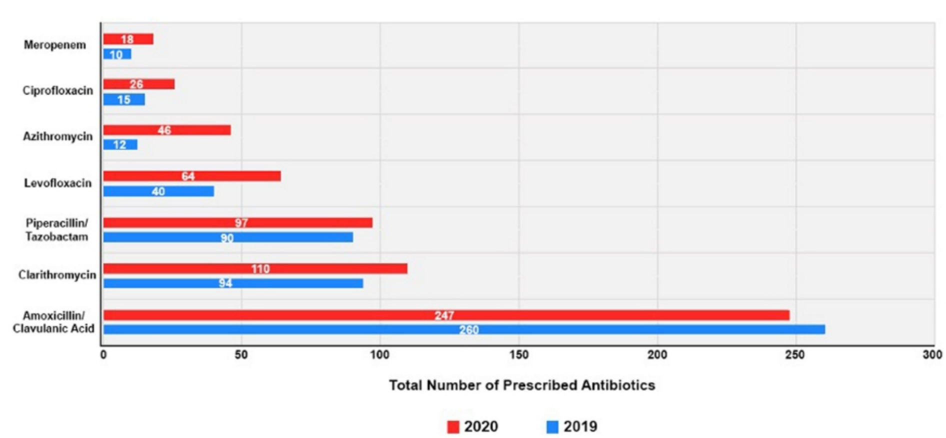



FIGURE 3
Seven commonly prescribed antibiotics prior to and during the COVID-19 pandemic.

across diverse geographical and clinical settings (Mugada et al., 2021; Sharma et al., 2021; Amponsah et al., 2022; Jirjees et al., 2022; Kalungia et al., 2022; Mohamad et al., 2022; Mudenda et al., 2022; Mudenda et al., 2023).

Possible reasons for this increase could be the rise in respiratory tract infections, including pneumonia, suspected to be COVID-19 during the pandemic, as well as the early inclusion of antibiotics, such as azithromycin, in COVID-19 treatment protocols (Mugada et al., 2021). A study conducted in Zambia in 2022 analysed antibiotic prescriptions (443 instances) and found that ceftriaxone and metronidazole were the most commonly prescribed antibiotics. A total of 42.1% of antibiotics in the "Watch" category exceeded recommended limits, emphasising the urgent need for improved antimicrobial stewardship and adherence to guidelines (Mudenda et al., 2023). An increasing trend in the use of antibiotics categorised in the "Watch group" has been observed in this study. This trend may stem from concerns regarding the effectiveness of "Access group" antibiotics, their availability, and patient demands. It highlights the necessity for enhanced availability of "Access group" antibiotics and a reduction in the utilisation of "Watch group" antibiotics, which are more prone to resistance.

In the "Watch" category, antibiotic use significantly increased during the COVID-19 pandemic in 2020, totalling 386 compared to 259 in the pre-pandemic year of 2019. This trend illuminates evolving prescribing practices and highlights the necessity of enhanced antibiotic stewardship. The study also revealed that antibiotics in the "Watch" group were the most used, accounting for 45.8% of the total, with the "Access" group following at 42.7% and the "Reserve" group comprising 12.5% of the usage. In Ghana, a study conducted in 2022 revealed that there was a notable inclination towards prescribing antibiotics from the "Access" group. This trend reflects specific regional prescribing patterns and underscores the dominant role of "Access" group antibiotics in these countries' healthcare practices. In India, antibiotic use was compared over 2 years using the AWaRe index tool. The study, retrospective in nature, analysed data from January 2017 to December 2018. Results showed a shift in antibiotic consumption: in 2017, 53.31% of antibiotics used were from the "Access" category, 40.09% from "Watch", and 3.40% from "Reserve". In 2018, these figures changed to 41.21, 46.94, and 8.15%, respectively, indicating a 17% increase in "Watch" and 140% in "Reserve" category usage, suggesting evolving resistance (Sharma et al., 2021). The study revealed that in 2020, during the COVID-19 pandemic, there was a substantial increase in the usage of levofloxacin, azithromycin, and ciprofloxacin compared to their consumption levels in 2019, highlighting a shift in antibiotic prescribing patterns during the health crisis.

Analysing the impact of the COVID-19 pandemic on antibiotic prescribing patterns within the UK NHS Trust during 2019 and 2020 presents a multifaceted challenge. The study indicates an increased use of specific antibiotics such as levofloxacin, azithromycin, and ciprofloxacin in 2020, which might be linked to the treatment approaches and uncertainties prevalent in the early stages of the pandemic. Additionally, the pandemic led to notable shifts in healthcare practices, potentially influencing these prescribing behaviours. However, the study's retrospective and cross-sectional nature may not fully capture all the confounding factors, such as the severity of infections or varied patient health conditions. The data, whilst indicative, might not comprehensively represent all cases or the complete spectrum of clinical decision-making, making it difficult to precisely quantify the direct impact of the pandemic on antibiotic prescribing patterns. This study is descriptive, providing a visual tool to observe antibiotic prescriptions in 2019 and 2020, as well as to visualise how the COVID-19 pandemic impacted antibiotic prescribing. It also identifies areas requiring AMS implementation. Additionally, identify the areas required for AMS implementation. Although estimating patient days was vital, it presented challenges in this study, necessitating further research on this aspect.

### Limitations

The study has several limitations. It excludes children under 12 years old and faces challenges in accurately calculating patient days, potentially affecting the evaluation of antibiotic use compared to patient volume. The study's focus on a limited number of prescriptions may not encompass the entire range of prescribing behaviours. As a retrospective and cross-sectional analysis, it has limitations in considering the varied health statuses and treatment reactions of patients and may not effectively measure compliance with clinical prescribing guidelines. These factors indicate that the study might not provide a comprehensive assessment of the impact of antibiotic prescribing on patient outcomes.

## Conclusion

This study provides valuable insights into the dynamics of antibiotic prescribing within a UK NHS Foundation Trust during the COVID-19 era. Analysing data from 640 patients, it reveals shifts in antibiotic use for respiratory infections, including pneumonia and COVID-19, across four seasonal phases. Key findings reveal a progressive increase in the use of amoxicillin/clavulanic acid in the Access category from March 2019 to September 2020. In the Watch category, there was a notable increase in the consumption of antibiotics such as azithromycin, clarithromycin, ciprofloxacin, and levofloxacin within the same timeframe. Piperacillin/tazobactam usage remained consistently high, whilst meropenem saw a slight uptick. This pivotal study not only traces the evolution of prescribing practices during the pandemic but also highlights the critical need for vigilant antimicrobial stewardship to combat resistance and safeguard patient health.

## Data availability statement

The datasets presented in this article are not readily available because this data is restricted and confidential with the institution policy. Requests to access the datasets should be directed to r.a.elshenawy@herts.ac.uk.

## Ethics statement

The studies involving humans were approved by Ethical approval for this study was granted by the Health Research Authority (HRA), with the Research Ethics Committee (REC) assigning reference number 22/EM/0161. In compliance with this approval, the study protocol underwent review and received approval from the University of Hertfordshire (UH) ethics committee under the reference LMS/PGR/NHS/02975. The authors have no conflicts of interest to disclose. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

## Author contributions

RE: Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft. NU: Supervision, Visualization, Writing – review & editing. ZA: Supervision, Visualization, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmicb.2023.1298858/full#supplementary-material

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# Appendix 65.

An evaluation of the five-rights antibiotic safety before and during COVID-19 at an NHS Foundation Trust in the United Kingdom.

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SARS CoV-2 Dispatches

# An evaluation of the five rights antibiotic safety before and during COVID-19 at an NHS Foundation Trust in the United Kingdom

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ABSTRACT

*Introduction:* Antimicrobial Resistance (AMR) poses a significant global health threat, with AMR-related deaths projected to reach 10 million annually by 2050. The COVID-19 pandemic has further exacerbated this crisis. This study focuses on evaluating the 'Five Rights of Antibiotic Safety' in an NHS Foundation Trust in England, assessing the impact of the COVID-19 pandemic on antibiotic prescribing and Antimicrobial Stewardship (AMS) practices in 2019 and 2020.

*Methods:* A cross-sectional retrospective study was conducted, focusing on adult patients aged 25 and older admitted to the NHS Foundation Trust and prescribed antibiotics for respiratory tract infections in 2019 and 2020. The study involved a retrospective review of 640 patient records, using descriptive analysis to evaluate the adherence to the 'Five Rights of Antibiotics' and assess the impact of COVID-19 on antibiotic safety practices.

*Results:* The study observed significant shifts in antibiotic prescribing practices during the study period. There was an increase in instances of inappropriate dosing and route of administration, alongside a slight improvement in prescribing durations. The study also noted a stable rate of appropriate antibiotic selection according to antimicrobial guidelines, indicating a concerning rise in inappropriate prescribing patterns during the COVID-19 pandemic.

*Conclusion:* The study revealed notable changes in antibiotic prescribing practices during the COVID-19 pandemic, advocating the importance of robust AMS to ensure appropriate use of antibiotics. The findings highlight the need for enhanced AMS educational initiatives and systematic oversight to combat AMR and protect public health in future health crises.



## 1. Introduction

By 2050, the annual death toll from multi-drug-resistant infections is projected to reach 10 million. In 2019, Antimicrobial Resistance (AMR) was responsible for 1.2 million deaths [1]. This number, exacerbated by the COVID-19 pandemic, is projected to reach 6 million by 2023. Antimicrobial Stewardship (AMS) advocates for judicious antibiotic use [2]. 'The Five Rights of Antibiotic Safety' ensure appropriate usage. It encompasses the right patient, drug, dose, time, and duration [3]. This study aimed to evaluate antibiotic safety and AMS practices in accordance with the 'Five Rights of Antibiotic Safety' at one English NHS Foundation Trust before and during the COVID-19 pandemic in 2019 and 2020. This evaluation is based on local antimicrobial guidelines ensuring appropriate and right antibiotic use, encompassing the patient, drug, dose, time, and duration.

## 2. Methods

While it is acknowledged that the COVID-19 pandemic significantly impacted antibiotic safety and AMS activities, there remains limited evidence regarding its precise effects. There was an immediate call for further studies to explore AMS implementation during the pandemic. A cross-sectional retrospective study was conducted, focusing on adult patients aged 25 and older who were admitted to one NHS Foundation Trust in the UK and prescribed antibiotics for respiratory tract infections, including pneumonia and COVID-19, during 2019 and 2020. The study excluded outpatients, individuals hospitalised for less than 48-72 hours, patients not prescribed antibiotics, and children. To ensure diversity, 640 patient records were reviewed using systematic and stratified sampling methods. Descriptive analysis was utilised to evaluate the 5Rs of

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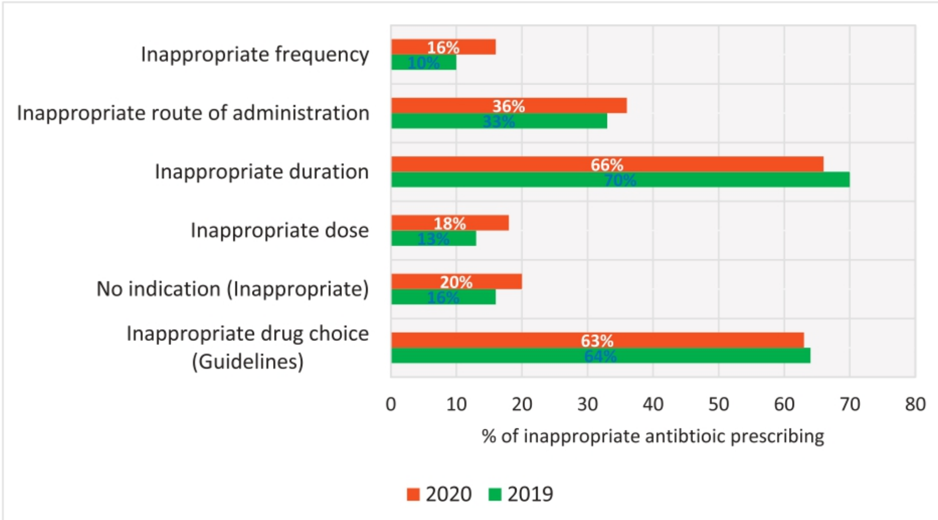


**Fig. 1.** Proportion of Five Rights of Antibiotic Safety: A comparison of 2019 and 2020 during the COVID-19 pandemic.

antibiotic safety and to assess the impact of COVID-19 on antibiotic safety practices. Data collection utilized a validated tool, and the study was registered in ISRCTN, adhering to WHO criteria (ISRCTN 14825813).

## 3. Results

In our study, we evaluated adherence to the 'Five Rights of Antibiotics' for the years 2019 and 2020. As illustrated in Fig. 1, there were significant shifts in the proportions of inappropriate antibiotic prescribing during this period. The inappropriate route of antibiotic administration saw a slight increase from 33% in 2019 to 36% in 2020. Similarly, instances of inappropriate dosing rose from 13% in 2019 to 18% in 2020. However, the proportion of inappropriate duration prescriptions showed improvement, decreasing from 70% in 2019 to 66% in 2020. However, prescriptions made without clear indications increased from 16% in 2019 to 20% in 2020.

Interestingly, the selection of the antibiotic, in accordance with antimicrobial guidelines, remained relatively stable, hovering at 63%–64% across both years. These findings highlight a concerning rise in inappropriate antibiotic prescribing patterns, especially during the 2020 COVID-19 pandemic. The results emphasise the critical importance of adhering to the 'Five Rights of Antibiotic Safety'. The observed fluctuations, including the increase in dosing errors by 3%–5% and the reduction in inappropriate durations, combined with steady drug choice rates, highlight the urgent need for oversight or antibiotic review. Moreover, to safeguard antibiotic efficacy, uphold patient wellness, and combat the looming threat of antimicrobial resistance, enlightening AMS educational initiatives in antibiotic prescribing is paramount.

## 4. Conclusion

The evaluation of antibiotic prescribing adherence to the 'Five Rights of Antibiotics' over 2019 and 2020 in this study revealed significant shifts, particularly during the COVID-19 pandemic. An increase in prescriptions without clear indications from 16% to 20% highlights potential changes in prescribing behaviour during the pandemic. The pandemic's impact on prescribing practices highlights the urgency of correlating antibiotic consumption with prescribing appropriateness. This necessitates robust AMS to ensure appropriate antibiotic use, combat antimicrobial resistance, and protect patient health against future health crises. Effective AMS is crucial for enhancing patient safety and public health.

## Funding

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## Ethical approval

The study received ethical approval from the University of Hertfordshire ethics committee and Health Research Authority (HRA) (REC reference number 22/EM/0161).

## Competing interest

None declared.

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## Appendix 66.

Impact of COVID-19 on ‘Start Smart, Then Focus’ Antimicrobial Stewardship at One NHS Foundation Trust in England Prior to and during the Pandemic.

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# Impact of COVID-19 on 'Start Smart, Then Focus' Antimicrobial Stewardship at One NHS Foundation Trust in England Prior to and during the Pandemic

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**Abstract:** Background: Antimicrobial resistance (AMR), a major global public health threat that has caused 1.2 million deaths, calls for immediate action. Antimicrobial stewardship (AMS) promotes judicious antibiotic use, but the COVID-19 pandemic increased AMR by 15%. Although there are paramount data on the impact of COVID-19 on AMS, empirical data on AMS implementation during the pandemic are lacking. This study aimed to investigate antibiotic prescribing and AMS implementation prior to the pandemic (PP) in 2019 and during the pandemic (DP) in 2020 at one NHS Foundation Trust in England. Method: This cross-sectional study involved adult patients admitted to one NHS Foundation Trust in England, focusing on those prescribed antibiotics for respiratory tract infections (RTIs). This included cases of pneumonia in both years under study and COVID-19 cases in 2020. Data were retrospectively extracted from medical records using a validated data extraction tool, which was developed based on the 'Start Smart, Then Focus' (SSTF) approach of the AMS Toolkit. Results: This study included 640 patients. The largest age group in the study was 66–85 years, comprising 156 individuals (48.8%) PP in 2019 and 148 (46.3%) DP in 2020. CAP was the predominant diagnosis, affecting approximately 126 (39.4%) PP and 136 (42.5%) DP patients. Regarding the timing of antibiotic review post-admission, reviews were typically conducted within 48–72 h, with no significant difference between 2019 and 2020, with an odds ratio of 1.02 (95% CI 0.97 to 1.08, *p*-Value = 0.461). During the pandemic, there was a significant difference in both AMS interventions, 'Continue Antibiotics' and 'De-escalation', with odds ratios of 3.36 (95% CI 1.30–9.25, $p = 0.015$) and 2.77 (95% CI 1.37–5.70, $p = 0.005$), respectively. Conclusion: This study emphasises the need for robust AMS to ensure adherence to guidelines. It acknowledges the impact of comorbidities and advocates for sustained stewardship efforts to combat resistance both during and after the pandemic era.

**Keywords:** antimicrobial stewardship (AMS); antibiotic prescribing; respiratory tract infections (RTIs); pneumonia; COVID-19 pandemic; antimicrobial resistance (AMR)

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## 1. Introduction

Antimicrobial resistance (AMR) poses an urgent global threat necessitating immediate action. The rising prevalence of multi-drug-resistant infections worldwide presents immense health consequences, including escalating morbidity, mortality, and economic burden [1]. The 2016 O'Neill review sounded the alarm on an impending 'silent pandemic', projecting over 10 million annual deaths from AMR by 2050, amounting to one death every three seconds [2]. This alarming prediction highlights the critical need for coordinated efforts and innovations to avert this public health crisis. In 2019, the World Health Organisation (WHO) identified AMR as one of the top ten global health threats requiring prompt intervention [3]. That same year, AMR-related deaths had already reached 1.2 million worldwide, emphasising the need for action [1].

Antimicrobial stewardship (AMS), an organisational approach promoting judicious antibiotic use, is pivotal to the UK's 5-year AMR strategy [4]. The UK Health Security Agency (UKHSA) has recognised antimicrobial stewardship's vital role in tackling AMR, providing the 'Start Smart, Then Focus' toolkit to implement stewardship in acute-care settings [5]. This toolkit promotes timely, responsible antibiotic use by initiating effective therapies and then actively reviewing regimens within 24–72 h. The 'Start Smart, Then Focus' principles apply to all antibiotic prescriptions to streamline antimicrobial use. Antimicrobial stewardship encompasses interventions aimed at improving appropriate antibiotic prescribing across all healthcare settings [6,7].

The COVID-19 pandemic, triggered by SARS-CoV-2, and starting in China in December 2019, rapidly spread globally [8]. By June 2023, around 644 million people had tested positive for COVID-19, resulting in approximately 6 million deaths [9]. Research suggests increased antimicrobial use during the pandemic may have contributed to rising resistant infections worldwide [10]. In 2021, the US Centres for Disease Control and Prevention (CDC) reported a 15% pandemic-related increase in AMR deaths in 2020, underscoring the need for more research and action [11]. In the UK, bloodstream infections rose 11.7% from 2018 to 2022 [12]. As healthcare returns to pre-pandemic patterns, maintaining focus on AMR as the 'silent pandemic' is critical. While secondary-care antibiotic use rose slightly in 2021, usage per admission declined, suggesting increases reflected expanding hospital activity rather than more prescriptions. However, with relaxed pandemic mitigations in 2022, substantial jumps occurred in pathogen and antibiotic-usage rates [13]. Therefore, providing empirical data on the pandemic's influence on antimicrobial prescribing and stewardship is essential to re-evaluate and update policies and antimicrobial stewardship roadmaps. This will mitigate future emergency impacts on stewardship in acute-care settings and alleviate the AMR threat. This cross-sectional retrospective study was conducted on an English NHS Trust.

This study aims to investigate antibiotic prescribing and AMS implementation prior to the pandemic (PP) in 2019 and during the pandemic (DP) in 2020 at one NHS Foundation Trust in England. The objectives were as follows:

(1) To evaluate AMS implementation between PP and DP periods using the SSTF toolkit;
(2) To determine the prevalence of inappropriately prescribed antibiotics PP and DP;
(3) To identify factors influencing antibiotic prescribing and AMS implementation both PP and DP.

This study contributes to addressing gaps in the literature by providing a comparative analysis of AMS implementation and antibiotic prescribing patterns prior to and during the COVID-19 pandemic. Its findings offer insights into the challenges and changes in antimicrobial stewardship during an unprecedented global health crisis, thus informing future strategies and policy updates in the context of AMR and global health emergencies.

## 2. Materials and Methods

### *2.1. Study Design and Setting*

This cross-sectional retrospective study was undertaken to estimate the prevalence of inappropriate antibiotic prescribing in adult patients aged 25 years and above who were admitted to one NHS Foundation Trust in England between 1 August 2021 and 28 February 2023. This secondary-care provider serves approximately 400,000 people and consists of about 742 beds. The data extraction tool was prepared based on the SSTF AMS Toolkit from UKHSA [5]. The study was reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement [14].

### *2.2. Participants*

To ensure maximum diversity, a stratified sampling approach was used for selecting medical records (MRs). The study included adult patients aged 25 and older, pregnant women, and immunocompromised patients admitted to the Trust. Admissions from both 2019 and 2020 were included, with a specific focus on patients prescribed antibiotics for respiratory tract infections (RTIs), including pneumonia cases in both years and COVID-19 in 2020. Exclusions were made for patients who spent less than 48–72 h in the accident and emergency (A&E) department, those not prescribed antibiotics, and children. The study protocol was sent to representatives of the Citizens' Senate, a patient care organisation with a good representation of many older people. They reviewed it and provided feedback. This study has been officially registered with the ISRCTN registry. The ISRCTN registry is a primary registry acknowledged by the WHO and the International Committee of Medical Journal Editors (ICMJE), accepting all clinical research studies [15]. Further details on participant eligibility are provided in the study protocol, which is published on the ISRCTN website [15]. Additionally, this study was registered in Octopus, the global primary research record [16].

### 2.3. Data Sources and Variables

The primary author (RA) extracted data from the electronic medical records of patients within the Trust. These data encompassed age, sex, allergies (which were classified into 'allergy', 'side-effect', or 'no documentation') [17], indications for treatment, comorbidities, C-reactive protein (CRP) levels [18], white blood cell (WBC) count, serum creatinine levels, chest X-ray results, and the duration of antibiotic treatment, categorised as $\leq$3 days (shorter duration) and $\geq$6 days (longer duration). Additionally, the length of hospital stay (LOS) and patient outcomes, whether discharged or deceased, were also included.

Patient selection was based on electronic health record (EHR) entries identified by their respective ICD-10 codes for respiratory tract infections (RTIs). This encompassed a range of conditions, including both specific and indeterminate diagnoses. Specific conditions included community-acquired pneumonia (CAP), chronic obstructive pulmonary disease (COPD), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP). Notably, in 2020, the selection also extended to cases of COVID-19 pneumonia. Alongside these, indeterminate diagnoses such as upper respiratory tract infections (URTIs), lower respiratory tract infections (LRTIs), and unspecified pneumonia were also considered. The primary diagnosis of RTIs in these records was pivotal in determining the initial or empirical antibiotic prescribed to the patients.

In this NHS Foundation Trust, the initiation of empirical antibiotic treatment is based on an initial, tentative diagnosis at the time of patient admission. The primary author meticulously evaluated the alignment of the chosen empirical antibiotic treatments with the local antibiotic guidelines to ascertain their appropriateness. These local guidelines serve as a gold standard, detailing the criteria for selecting empirical antibiotics, encompassing considerations for the type of infection, patient-specific factors, and local resistance patterns. The assessment process involves a thorough review of the antibiotics prescribed, and examining aspects such as the type of antibiotic, its dosage, route of administration, and prescribed duration. This review extends beyond the initial diagnosis and is dynamically adapted based on the patient's clinical response, results from microbiological testing, and additional diagnostic procedures, like chest X-ray findings. This method ensures that the antibiotic therapy aligns not only with the preliminary diagnosis but also remains responsive to the evolving clinical scenario and diagnostic insights, thus optimising patient care whilst adhering to antimicrobial stewardship practices.

The study's sample size was carefully determined based on Public Health England's estimate that 20% of all antibiotics prescribed in the UK might be inappropriate [19]. Using Minitab statistical software, the sample size was computed, factoring in the overall population size, a 10% margin of error, and a 95% confidence interval. Data were collected from medical records PP and DP. The study involved a systematic sampling of 320 patient records from 2019 PP and an equal number from 2020 DP, totalling 640 records. Data from each year were systematically sampled to ensure representativeness and to provide a robust dataset for analysing antibiotic prescribing trends.

A data extraction tool was employed to obtain the necessary data from patients' medical records. A mind map was created to help organise the data extraction tool in relation to the antibiotic use process and the UKHSA toolkit for AMS [12], as presented in the Supplementary Materials of Figure S1. In order to extract data from patients fitting the inclusion criteria, access to the Trust's electronic system was required. Prior to commencing 'Data Extraction', the primary author completed training modules for all these systems and subsequently gained access to them. The data extraction tool was prepared in order to obtain the necessary information from the patient's medical records. The AMS data extraction tool was prepared, encompassing demographic information, primary diagnosis, SSTF criteria, AMS interventions, investigations, and patient outcomes. The extraction process took approximately 45 min per patient medical record for the primary author to gather the required data. The data extraction for each patient is shown in Table S1 of the Supplementary Materials.

The primary author reviewed the literature and the UKHSA's AMS Toolkit to develop the data extraction tool. The authors discussed, recognised, and agreed to the the elements within the tool. A pilot study was conducted to provide an initial overview of the data and to evaluate the feasibility of the data extraction tool in addressing the research questions. To validate the tool, two independent authors separately extracted data from 1% of the sample (four patient records). An agreement rate of 80% or higher was used as a measure of the tool's validity. Additionally, to assess the tool's reliability, both authors independently extracted data from another 1% of the sample (four records). Inter-rater reliability was determined by comparing the percentage agreement in data extracted independently. Any disagreements were resolved through discussion.

### *2.4. Statistical Methods*

Descriptive analyses were conducted. Data on categorical or binary variables were presented as numbers (n) and proportions (%), while continuous variables with non-normal distributions were summarised using mean and standard deviation (SD). The 'Start Smart' approach data, including age, gender, allergies, indication, comorbidities, and duration, were described using numbers (n) and percentages (%) and further analysed via logistic regression. Similarly, the 'Then Focus' approach data, covering WBCs, CRP, serum creatinine, chest X-rays, day of antibiotic review, and type of AMS intervention, were presented in numbers (n) and percentages (%) and underwent advanced analysis via logistic regression.

In this study, the prevalence of inappropriate antibiotic prescribing was evaluated based on local antimicrobial prescribing guidelines. Inappropriate antibiotic prescribing was assessed by comparing prescriptions to hospital antimicrobial guidelines both PP and DP. The appropriateness of antibiotic prescribing according to local guidelines was assessed for both empirical antibiotic selection ('Start Smart') and the antibiotics prescribed post-review ('Then Focus'). Additionally, AMS implementation was assessed using the AMS Toolkit from UKHSA [12]. The decisions made following this review were utilised to determine the type of AMS intervention and the appropriateness of antibiotic prescribing in relation to the local guidelines [20]. A framework for data analysis was established and is presented in the Supplementary Materials as Figure S2. For more advanced statistical analysis, IBM SPSS Statistics version 22.0, RStudio version 2022, and R version 4.2.2 were employed [21,22].

## 3. Results

### *3.1. Clinical and Demographic Characteristics*

A retrospective analysis was performed on 640 patients' medical records from the Trust. The demographics of these patients are presented in Table 1. The comprehensive analysis of various variables did not reveal any statistically significant differences between the years 2019 and 2020. Patients admitted for RTIs during these years ranged in age from 25 to 99 years. A slight variation was observed in gender distribution: in 2019, females accounted for 49.4% (158) of the cases, increasing slightly to 49.7% (159) in 2020. The length of hospital stays (LOS) averaged around 13.7% in 2019 and decreased to 12.3% in 2020. The

LOS ranged from a minimum of one day to a maximum of 119 days in 2019. Regarding patient outcomes, the data indicated that the mortality rate (the proportion of deceased patients) remained steady at approximately 15% during the two-year study period, as shown in Table 1.

**Table 1.** Characteristics and demographics of patients admitted prior to the COVID-19 pandemic ($n$ = 320) and during the pandemic ($n$ = 320) (in 2019 and 2020).

| Patient Characteristics | | Prior to the Pandemic—2019 $n$ (%) | During the Pandemic—2020 $n$ (%) | $p$-Value |
|---|---|---|---|---|
| Age (Range = 25–99) | Mean (SD) | 74.3 (16.0) | 76.2 (15.5) | 0.127 |
| Gender | Female (%) | 158 (49.4) | 159 (49.7) | |
| | Male (%) | 162 (50.6) | 161 (50.3) | |
| Patient Outcome | Deceased (%) | 48 (15.0) | 50 (15.4) | 0.886 |
| | Discharged (%) | 272 (85.0) | 270 (84.4) | |
| LOS * (Range = 1–119) | Mean (SD) | 13.7 (13.7) | 13.1 (12.3) | 0.525 |

* Length of hospital stay (LOS); CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus; HAP, hospital-acquired pneumonia; LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection; VAP, ventilator-associated pneumonia.

Comparing the $p$-Value of the patient demographics and outcomes between PP (2019) and DP (2020) showed no significant changes. Mean age differed slightly (PP: 74.3, DP: 76.2; $p = 0.127$), with no significant difference between gender distribution (female $p = 0.886$, male $p = 0.525$) or shift in outcomes (deceased ($p = 0.886$) and discharged ($p = 0.525$)). LOS remained consistent (PP: 13.7 days, DP: 13.1 days; $p = 0.525$), demonstrating consistency in the characteristics of patients and the impact of their conditions on hospitalisation (Table 1).

### *3.2. Antibiotic Prescription 'Start Smart' Approach*

The term 'Start Smart' denotes the initial stage of antibiotic administration or empirical therapy [12]. The difference between the appropriateness of antibiotic prescriptions prior to and during the COVID-19 pandemic seems statistically insignificant. Age and gender do not appear to impact antibiotic prescribing patterns significantly. However, the age group of 66–85 years represented the largest segment of the study population, with 156 individuals (48.8%) PP in 2019 and 148 (46.3%) DP in 2020. For antibiotic allergy classification, only the 'side effects' category showed a significant difference between 2019 and 2020, with an odds ratio (OR) of 7.23 (95% CI 1.54 to 53.37, $p$-Value = 0.023).

Additionally, several factors influenced this initial antibiotic prescribing or empirical therapy ('Start Smart'), including the initial diagnosis 'indication'. For example, CAP was the predominant diagnosis in approximately 126 (39.4%) individuals PP and 136 (42.5%) DP. Uncertain diagnoses, including URTIs, LRTIs, and pneumonia, impact the selection of appropriate antibiotics at admission. These unclear or non-specific diagnoses accounted for 28.8% of admissions PP and 22.8% DP. Regarding COPD, a statistically significant difference was observed between PP and DP, with an odds ratio (OR) of 0.42 (0.19–0.90, $p = 0.029$). Additionally, the analysis revealed a statistically significant difference in the incidence of COVID-19 pneumonia between 2019 and 2020, with an odds ratio (OR) of 20.24 (95% CI 5.82–128.19, $p$-Value < 0.001). Concerning adherence to the empirical antibiotic treatment guidelines, it was observed that guidelines for empirical therapy were followed by 50% of the RTI study population in 2019 and 51% DP in 2020.

In comparing comorbidities prior to and during the pandemic, significant differences were observed in several conditions. Heart failure demonstrated a notable increase with an odds ratio (OR) of 2.06 (95% CI 1.23–3.52, $p = 0.007$). Hypercholesterolemia also showed a significant difference with an OR of 1.90 (95% CI 1.14 to 3.20, $p$-Value = 0.014). In contrast, kidney diseases exhibited a lower OR of 0.52 (95% CI 0.32 to 0.84, *p*-Value = 0.008). Similarly, liver diseases revealed an increased OR of 3.55 (95% CI 1.41–9.82, *p*-Value = 0.010), while asthma had a reduced OR of 0.50 (95% CI 0.25 to 0.95, *p*-Value = 0.038). Regarding the duration of antibiotic therapy, there were no significant differences in the duration, whether shorter (≤3 days) or longer (≥6 days), between PP and DP (Table 2).

**Table 2.** Adjusted ORs of factors affecting 'Start Smart' initial antibiotic prescribing prior to the COVID-19 pandemic ($n$ = 320) and during the pandemic ($n$ = 320) (in 2019 and 2020).

| | | Prior to Pandemic—2019 $n$ (%) | During the Pandemic—2020 $n$ (%) | Adjusted OR (95% CI) |
|---|---|---|---|---|
| Age | 25–45 | 22 (6.9) | 22 (6.9) | - |
| | 46–65 | 52 (16.3) | 46 (14.4) | 1.13 (0.49–2.68, $p$ = 0.775) |
| | 66–85 | 156 (48.8) | 148 (46.3) | 1.35 (0.62–3.04, $p$ = 0.455) |
| | >85 | 90 (28.0) | 104 (32.4) | 1.75 (0.77–4.08, $p$ = 0.186) |
| Gender | Female | 158 (49.4) | 161 (50.3) | - |
| | Male | 162 (50.6) | 159 (49.7) | 0.98 (0.67–1.42, $p$ = 0.910) |
| Allergy | Allergy | 18 (5.6) | 17 (5.3) | - |
| | No Allergy | 254 (79.4) | 258 (80.6) | 1.00 (0.46–2.20, $p$ = 1.000) |
| | Not Documented | 46 (14.4) | 29 (9.1) | 0.58 (0.23–1.45, $p$ = 0.243) |
| | Side Effects | 2 (0.6) | 16 (5.0) | 7.23 (1.54–53.37, $p$ = 0.023) * |
| Indication | CAP | 126 (39.4) | 136 (42.5) | - |
| | COPD | 30 (9.4) | 14 (4.4) | 0.42 (0.19–0.90, $p$ = 0.029) * |
| | HAP | 67 (20.9) | 52 (16.2) | 0.74 (0.46–1.20, $p$ = 0.221) |
| | VAP | 5 (1.5) | 1 (0.3) | 0.20 (0.01–1.38, $p$ = 0.156) |
| | URTI | 6 (1.9) | 8 (2.5) | 1.61 (0.46–5.85, $p$ = 0.455) |
| | LRTI | 30 (9.4) | 23 (7.2) | 0.77 (0.39–1.51, $p$ = 0.452) |
| | Pneumonia | 56 (17.5) | 42 (13.1) | 0.92 (0.53–1.60, $p$ = 0.769) |
| | COVID-19 Pneumonia | - | 44 (13.8) | 20.24 (5.82–128.19, $p$ < 0.001) *** |
| Comorbidities | Hypertension | 143 (44.7) | 148 (46.2) | 1.17 (0.80–1.72, $p$ = 0.414) |
| | Hypotension | 13 (4.0) | 14 (4.4) | 1.20 (0.49–2.91, $p$ = 0.689) |
| | Atrial Fibrillation | 61 (19.0) | 64 (20.0) | 1.02 (0.64–1.63, $p$ = 0.922) |
| | Heart Failure | 32 (10.0) | 63 (19.6) | 2.06 (1.23–3.52, $p$ = 0.007) ** |
| | Hypercholesteremia | 40 (12.5) | 58 (18.1) | 1.90 (1.14–3.20, $p$ = 0.014) * |
| | Diabetes Mellitus | 65 (20.3) | 54 (16.9) | 0.76 (0.47–1.22, $p$ = 0.256) |
| | Hypothyroidism | 24 (7.5) | 20 (6.2) | 0.81 (0.40–1.63, $p$ = 0.555) |
| | Kidney Diseases | 75 (23.4) | 46 (14.4) | 0.52 (0.32–0.84, $p$ = 0.008) ** |
| | Liver Diseases | 8 (2.5) | 19 (5.9) | 3.55 (1.41–9.82, $p$ = 0.010) * |
| | Malignancy | 50 (15.6) | 43 (13.4) | 0.95 (0.57–1.57, $p$ = 0.850) |
| | Osteoarthritis | 31 (9.7) | 40 (12.5) | 1.06 (0.58–1.93, $p$ = 0.843) |
| | Asthma | 35 (10.9) | 21 (6.5) | 0.50 (0.25–0.95, $p$ = 0.038) * |
| | COPD | 42 (13.1) | 40 (12.5) | 1.38 (0.76–2.49, $p$ = 0.289) |
| | Dementia | 25 (7.8) | 23 (7.2) | 0.81 (0.41–1.59, $p$ = 0.538) |
| | Epilepsy | 10 (3.1) | 13 (4.1) | 1.32 (0.49–3.65, $p$ = 0.580) |
| | Depression | 12 (3.7) | 20 (6.2) | 1.81 (0.77–4.39, $p$ = 0.178) |

**Table 2.** *Cont.*

| | | Prior to Pandemic—2019 *n* (%) | During the Pandemic—2020 *n* (%) | Adjusted OR (95% CI) |
|---|---|---|---|---|
| Duration | ≤3 Days (Shorter) | 168 (52.5) | 164 (51.3) | - |
| | ≥6 Days (longer) | 152 (47.5) | 156 (48.7) | 1.16 (0.82–1.66, $p = 0.400$) |

HPN, hypertension; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus; HAP, hospital-acquired pneumonia; LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection; VAP, ventilator-associated pneumonia. Notes: *** $p < 0.001$; ** $0.001 \leq p < 0.01$; * $0.01 \leq p < 0.05$.

### 3.3. Antibiotic Prescription: 'Then Focus' Approach

Table 3 provides an overview of factors impacting 'Then Focus' antibiotic prescribing or pathogen-directed therapy in patients with RTIs prior to and during the COVID-19 pandemic. No significant differences were observed in laboratory tests for white blood cells (WBCs), C-reactive protein (CRP), or serum creatinine. The incidence of positive chest X-ray results indicating pneumonia was higher in 2020 compared to 2019, showing a statistically significant difference with an odds ratio of 1.75 (95% CI 1.04 to 2.97, *p*-Value = 0.037).

**Table 3.** Adjusted ORs of factors affecting the 'Then Focus' criteria for antibiotic prescribing prior to the COVID-19 pandemic ($n = 320$) and during the pandemic ($n = 320$) (in 2019 and 2020).

| | | Prior to Pandemic—2019 *n* (%) | During the Pandemic—2020 *n* (%) | Adjusted OR (95% CI) |
|---|---|---|---|---|
| WBCs | | 12 (3.8) | 11 (3.4) | |
| CRP | | 82 (25.6) | 78 (24.4) | 1.00 (1.00–1.00, $p = 0.595$) |
| Serum Creatinine | | 126 (39.4) | 123 (38.4) | 1.00 (1.00–1.00, $p = 0.860$) |
| Chest X-rays | Pneumonia % | 39 (12.2) | 54 (16.9) | 1.75 (1.04–2.97, $p = 0.037$) * |
| | No Pneumonia % | 82 (25.6) | 65 (20.3) | - |
| | Not taken % | 199 (62.2) | 201 (62.8) | 1.26 (0.86–1.85, $p = 0.231$) |
| Day of Antibiotic Review | Mean (SD) | 4.2 (2.8) | 4.4 (2.9) | 1.02 (0.97–1.08, $p = 0.461$) |
| Type of AMS Intervention | Change Antibiotics (Substitution) | 25 (7.8) | 20 (6.3) | - |
| | Continue Antibiotics | 14 (4.4) | 19 (5.9) | 3.36 (1.30–9.25, $p = 0.015$) * |
| | De-escalation | 37 (11.6) | 81 (25.3) | 2.77 (1.37–5.70, $p = 0.005$) ** |
| | Escalation | 65 (20.3) | 76 (23.8) | 1.50 (0.76–2.99, $p = 0.248$) |
| | IV-to-Oral Switch | 70 (21.9) | 58 (18.1) | 0.97 (0.48–1.96, $p = 0.928$) |
| | Stop Antibiotics | 94 (29.4) | 59 (18.4) | 0.86 (0.44–1.71, $p = 0.659$) |
| | No Intervention | 15 (4.6) | 7 (2.2) | - |

WBCs, white blood cells; CRP, C-reactive protein; AMS, antimicrobial stewardship. Notes: ** $0.001 \leq p < 0.01$; * $0.01 \leq p < 0.05$.

In terms of the timing for antibiotic review post-admission, it was noted that reviews were typically conducted within 48–72 h of admission. There was no significant difference in the timing of these reviews between 2019 and 2020, with an odds ratio of 1.02 (95% CI 0.97 to 1.08, *p*-Value = 0.461).

Regarding AMS interventions, significant changes were observed in only two interventions. The 'Continue Antibiotics' AMS intervention showed a significant difference during the pandemic, with an odds ratio of 3.36 (95% CI 1.30–9.25, $p = 0.015$). Additionally, there was a notable significant increase in the 'De-escalation' AMS intervention, evidenced by a statistically significant odds ratio of 2.77 (95% CI 1.37–5.70, $p = 0.005$) (Table 3).

In terms of adherence to local antibiotic treatment guidelines in the 'Then Focus' approach, it was found that antibiotic choices made post-review adhered to these guidelines in 64% of the RTI study population PP in 2019. This rate of adherence or appropriateness dropped to 36% DP in 2020.

### 3.4. Antimicrobial Stewardship Implementation

The bar chart below presents a comparison of antimicrobial stewardship interventions in the years prior to and during the COVID-19 pandemic, specifically 2019 and 2020. From the bar chart, we can see that the percentage of cases with 'No intervention' decreased slightly during the pandemic, from 5% to 2%. There was a noticeable decline in the practice of 'Stop Antibiotics', from 29% PP to 18% DP. The 'IV-to-Oral Switch' also saw a small decrease from 22% to 18%. On the other hand, the 'Escalations' intervention increased from 20% to 24%. Notably, the rate of 'De-escalation' nearly doubled, rising from 12% to 25%, and the practice of 'Continuing antibiotics' went up from 4% to 6%. The frequency of 'Changing antibiotics, or substitution', showed a minor decrease from 7% to 6% (Figure 1).

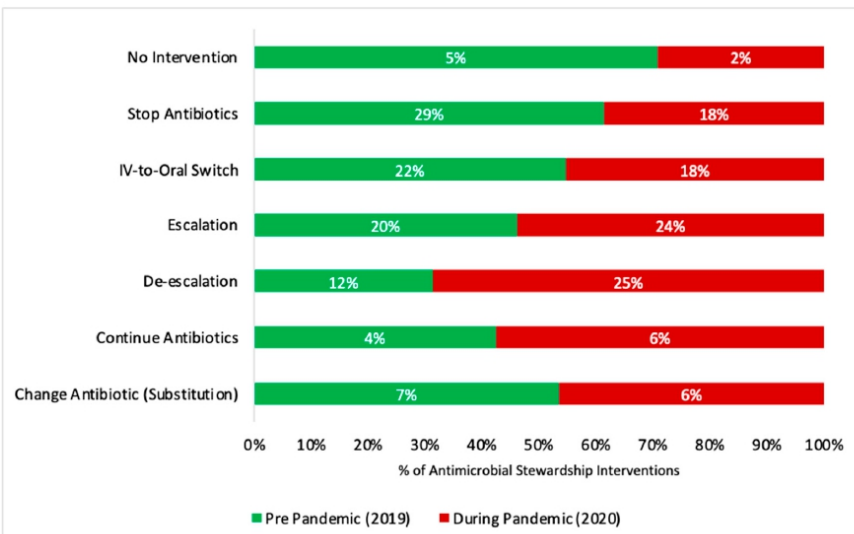


**Figure 1.** Antimicrobial stewardship interventions prior to and during the COVID-19 pandemic (pandemic (n = 320) and during the pandemic (n = 320) (in 2019 and 2020).

## 4. Discussion

This retrospective analysis evaluated the admissions of patients with RTIs both PP and DP. It also highlighted the implementation of AMS as a crucial part of the UK's five-year AMR strategy in order to enhance patient care and combat AMR [13]. It aimed to improve antibiotic prescribing, using an SSTF approach for antimicrobial stewardship [6]. As previously stated, while the toolkit proved invaluable for analysing AMS in this study, it necessitated additional revisions to encompass other variables that influence the prescription of antibiotics, precisely the initial course upon admission, known as 'Start Smart', and subsequent course(s) after hospitalisation, referred to as 'Then Focus.' By incorporating these updates, we aim to ensure the long-term viability of implementing AMS, particularly in emergencies, while concurrently reducing AMR.

Highlighting potential reasons for antibiotic stewardship is crucial. Recent data published by the European Centre for Disease Prevention and Control (ECDC) up to 2022 provide valuable insights, emphasising the need to understand and address factors contributing to antimicrobial resistance effectively [23]. When employing AWaRe 2022 as the standard for assessing antibiotic prescriptions during the COVID-19 pandemic, it becomes apparent that understanding antibiotic usage patterns in the face of the AMR threat is essential. The increase in the utilisation of 'Watch'-category antibiotics during the pandemic highlights the immediate need for robust AMS measures [24].

Antibiotics were prescribed to this study population either empirically at admission or after a 48–72 h period post-admission. CAP patients had the highest percentage of antibiotic prescriptions, with around 40% PP in 2019 and 43% DP in 2020. This aligns with a study in Denmark, where penicillin with beta-lactamase inhibitor was commonly prescribed for CAP. Only 31.3% (126 patients) of CAP cases were treated according to regional guidelines. Most patients received IV antibiotics within 4 h, and about three quarters switched to oral antibiotics by day 5 [19]. In a 2023 study conducted in England, high rates of antibiotic prescribing were observed alongside low rates of confirmed respiratory infections through cultures. Nearly one third of patients received multiple antibiotic courses, highlighting the impact of COVID-19 on antimicrobial stewardship [25].

Interestingly, another separate 2019 UK study discovered that antibiotic prescribing often deviated from guidelines, particularly for URTIs [21]. Our study has shown that when medical records contain indeterminate diagnoses, it becomes challenging to select appropriate antibiotics upon admission. For instance, a diagnosis might state 'pneumonia' without specifying whether it is community-acquired or hospital-acquired. This lack of detail also applies to URITs and LRTIs, where the exact type of infection is often not defined. This vagueness in diagnosis can substantially impact the appropriate selection of antibiotics upon admission.

In this study, the elderly demographic emerged as the most represented group, with individuals aged 66−85 years constituting the majority. This age bracket comprised 156 participants (48.8%) PP in 2019 and 148 (46.3%) DP in 2020, highlighting the need for safe AMS interventions in this age group. This finding is consistent with a 2023 study from the Netherlands, which demonstrated that a multifaceted antibiotic stewardship intervention effectively and safely reduced antibiotic prescribing in older adults. Successful implementation in various older-adult care settings necessitates active involvement from all healthcare professionals and adaptation to local circumstances [26].

In this study, adherence to local guidelines indicated that approximately 50% of patients received appropriate empirical antibiotics upon admission, with no significant difference between the PP and DP periods. However, there was a notable increase in non-adherence to these guidelines during the pandemic in 2020, with inappropriate antibiotic prescribing rising from 36% PP to 64% DP. This emphasises the necessity of sustaining AMS during pandemics or emergencies. This trend is similar to international research. In Sweden, which is renowned for one of the lowest rates of antibiotic prescriptions in Europe, a study across six sites revealed that 60% of inpatients (4119 out of 6812) were prescribed antimicrobials. By day five, 12.5% of these treatments had been escalated, whilst 21.5% were either narrowed or discontinued, influenced by initial culture collections and radiology results [27]. An English study assessing the risks and appropriateness of antibiotic prescribing in primary care during the COVID-19 pandemic analysed electronic health records from over 9 million patients.

Of the 29.2 million total prescriptions, approximately 29.1% were repeat prescriptions. For patients with same-day documented infections, lower rates of repeat prescribing were noted. Additionally, 8.6% of prescriptions were deemed potentially inappropriate based on the antibiotic type [28]. Despite the conditions of the pandemic, repeat prescribing rates did not significantly alter, highlighting the requirement for updated treatment guidelines and patient-specific information in light of the high and variable levels of repeat antibiotic prescribing observed. Although the English study focused on inappropriate antibiotic selection and repeat prescribing, our research distinctively investigated antibiotic appropriateness and AMS implementation in a secondary-care setting. The rise in inappropriate prescribing during the pandemic might be linked to the challenges faced by healthcare workers, including diagnostic uncertainties and increased patient loads. These issues, coupled with the evolving understanding of COVID-19 and its treatment protocols, influenced prescribing decisions, leading to a higher rate of non-adherence to established guidelines [28]. Our findings are in line with the broader context of AMR and antibiotic prescribing trends during the pandemic, emphasising the importance of robust AMS practices, particularly in times of healthcare crises.

Another 2021 study in England found that antibiotic prescribing patterns changed during the COVID-19 pandemic, with more early prescriptions. Different infection types were affected differently, and AMS was compromised. Future adaptations in infection management and stewardship are necessary [29]. The COVID-19 pandemic significantly influenced the number of patients admitted with RTIs. An increase in admissions in December 2019 could be attributed to the rapid spread of COVID-19 and its impact on respiratory health. Subsequent declines in March 2020 and June 2020 coincided with public health measures being put into place and the second national lockdown [13]. In England's 2021 winter season during the COVID-19 pandemic, there was a marked decrease in community antibiotic prescriptions for RTIs in primary care.

Contrary to previous winters, where such prescriptions typically increased, the 2020–2021 winter saw almost a 50% reduction compared to 2019–2020. This decline was not offset by increased prescriptions in secondary-care accident and emergency departments, suggesting fewer RTI cases and primary care visits, likely due to COVID-19 prevention measures [29]. In this study, we observed no substantial difference in appropriate antibiotic prescribing upon admission between 2019, prior to the pandemic, and 2020, during the COVID-19 pandemic. The prevalence of appropriate prescribing was 36% in 2019, compared to a similar 35% in 2020.

A nationwide cross-sectional study in Mexico in 2020 investigated the relationship between chronic conditions, comorbidities, and their impact on pneumonia and mortality in COVID-19 patients. The study revealed a clear association: chronic conditions such as cardiovascular diseases and chronic kidney disease heightened the risk of developing pneumonia. Similarly, these conditions, along with COPD, were linked to an increased likelihood of death in COVID-19 patients. Notably, the study found that the presence of multiple chronic conditions corresponded to a higher probability of either death or pneumonia in the patient sample, highlighting the critical impact of comorbidities on COVID-19 outcomes [30]. When comparing the prevalence of comorbidities PP and DP, significant differences were observed in chronic conditions. Cardiovascular diseases, such as heart failure, exhibited a notable increase during the pandemic (95% CI 1.23–3.52, $p = 0.007$), and hypercholesterolemia also demonstrated a significant rise (95% CI 1.14 to 3.20, $p$-Value = 0.014). Additionally, kidney diseases showed a statistically significant difference between the years PP and DP (95% CI 0.32 to 0.84, $p$-Value = 0.008). Liver diseases revealed a significant difference as well (95% CI 1.41–9.82, $p = 0.010$), while asthma was significantly different (95% CI 0.25 to 0.95, $p$-Value = 0.038). Furthermore, COPD was significantly different (95% CI 0.19 to 0.90, $p = 0.029$).

In a 2022 study conducted in Spain investigating the efficacy of chest X-rays in detecting COVID-19 pneumonia during the SARS-CoV-2 pandemic, it was determined that patients with low clinical suspicion and negative chest X-rays could be discharged with minimal risk of requiring consultation or developing severe COVID-19. The study also found that in patients who tested RT-PCR-positive for SARS-CoV-2, chest X-rays did not provide prognostic value [31]. Additionally, another 2021 study in England focusing on diagnosing COVID-19 from chest X-rays via a straightforward, rapid, and precise neural network revealed that it is feasible to accurately distinguish COVID-19 from other viral pneumonia and normal lung conditions in X-ray images. This method could aid clinicians in making more precise diagnostic decisions, underscoring the value of chest X-rays as an effective screening tool for the early and rapid identification of COVID-19 [32]. In this study, it was found that the prevalence of positive chest X-ray findings indicating pneumonia in 2021 was higher compared to 2019, as evidenced by an odds ratio of 1.75 (95% CI from 1.04 to 2.97, $p$-Value = 0.037). This indicates that patients were approximately 1.75 times more likely to have chest X-ray results positive for pneumonia during the pandemic in 2020 versus the pre-pandemic period in 2019. In a 2020 UK study, elevated CRP levels were found to predict bacterial and viral pathogens independently. However, their value, in addition to sputum purulence, was inconclusive [33]. Our study emphasises the importance of additional investigations like WBCs and chest X-rays to identify pneumonia patients who may benefit from antibiotics and ensure appropriate prescribing practices.

A 2021 study from Manchester showed that short and long antibiotic courses are equally effective in treating acute infections, indicating that shorter courses may help reduce antimicrobial resistance without leading to increased complications [34]. While this study did not investigate the effectiveness of different antibiotic course lengths, it was found that the proportion of patients receiving short ($\leq$3 days) versus longer ($\geq$6 days) courses of antibiotics was similar in the two years analysed PP and DP (2019 and 2020).

Across the six study sites in the USA, it was found that 12.5% of empirical antimicrobials were escalated, 21.5% were narrowed or discontinued, and 66.4% were unchanged. Narrowing or discontinuation was more likely when cultures were collected at the start of therapy (adjusted OR 1.68, 95% CI 1.05–2.70). Escalation was associated with multiple infection sites (2.54, 1.34–4.83) and a positive culture (1.99, 1.20–3.29) [35]. Furthermore, a study investigating AMS interventions during the COVID-19 pandemic discovered that 'de-escalation' and 'IV-to-Oral Switch' were significant interventions employed in acute-care settings during the pandemic period [6]. This study revealed statistically significant differences between the two AMS interventions when comparing 2019 and 2020. The odds of continuing antibiotics were 3.36 times higher in 2020 than 2019 (95% CI 1.30–9.25, $p = 0.015$). Additionally, the odds of de-escalating antibiotics were 2.77 times higher in 2020 (95% CI 1.37–5.70, $p = 0.005$). In contrast, other interventions, such as escalation, IV-to-oral switch, and stopping antibiotics, showed no significant differences between the two years ($p > 0.05$). Specifically, the odds ratios for escalation, IV-to-oral switch, and stopping antibiotics were 0.97 (0.48–1.96, $p = 0.928$) and 0.86 (0.44–1.71, $p = 0.659$), respectively. The COVID-19 pandemic impacted the implementation of AMS interventions. With the release of the National Institute for Health and Care Excellence (NICE) guidelines for pneumonia management in high-COVID-19-prevalence settings, the practices of intravenous-to-oral antibiotic switches (IVOS) and stopping unnecessary antibiotics decreased in 2020 compared to 2019 [36]. This highlights an urgent need to improve awareness and deliver further education on appropriate AMS interventions, with an emphasis on utilising IVOS, de-escalation, and antibiotic cessation aligned with individual patient factors and conditions. Focused efforts on these evidence-based AMS practices can help curb inappropriate antibiotic usage during public health crises. The COVID-19 pandemic has emphasised the economic and societal impact of uncontrolled infectious diseases, resembling predictions about AMR. Understanding the effects of changed antibiotic use, health-seeking behaviours, and infection control on AMR is crucial to promoting good practices and prioritising research [37]. Stewardship programs should prioritise core strategies and focus on their effectiveness before incorporating supplemental approaches. Quality indicators and improvement projects help maintain the sustainability of antimicrobial stewardship implementation, especially during the pandemic [6]. While healthcare professionals are dealing with the challenges of COVID-19, the ongoing crisis of AMR should not be neglected. Addressing AMR proactively can prevent future reactivity, similar to our response to COVID-19 [38]. In a 2022 Lancet study, the antibiotic review kit intervention method reduced antibiotic use among adult acute general medical inpatients. The COVID-19 pandemic likely influenced the inconsistent effects on mortality [39]. Hospitals should adopt the antibiotic review kit to curb antibiotic overuse. Although there was no significant difference in the day of antibiotic review before and during the pandemic, most reviews occurred after four days in both periods. This highlights the significance of multidisciplinary team ward rounds by the AMS team for proper antibiotic review and decision making for patients. SSTF audits yielded significant outcomes and valuable insights for other hospitals, resulting in improved antibiotic prescribing practices. Furthermore, incorporating other quality improvement methods can effectively sustainably enhance antibiotic prescribing [40,41].

*Strengths and Limitations*

Our study stands out for its comprehensive analysis of AMS in the context of the COVID-19 pandemic at an English NHS Trust, offering valuable empirical data on antibiotic prescribing practices and their seasonal variations. The robustness of our methodology, underpinned by rigorous follow-up and an established retrospective review process, coupled with a validated data extraction tool, ensures a thorough and reliable quantitative examination of AMS. However, the study is not without limitations. Its generalisability is restricted, being conducted in an acute-care setting within a secondary-care hospital, and primarily focusing on adult patients aged 75–84, excluding those under 25 and children. This limits the breadth of demographic applicability. The study's focus on RTIs also narrows its relevance to other infection types. Despite the sample size of 640 records, the examination was confined to the first and second courses of antibiotics, excluding longer courses. This might have left out vital information, especially considering the noted reduction in the maximum length of stay from 2019 to 2020. The systematic sampling methodology, while structured, might have inadvertently overlooked certain patient groups or unique cases, thereby not fully capturing the diversity in antibiotic prescribing practices. While our study provides significant insights into the practices of AMS prior to and during the pandemic, it is crucial to interpret its findings in light of these outlined limitations. The study paves the way for further research to broaden the understanding of healthcare professionals' perspectives on antibiotic prescribing in acute-care settings during the pandemic.

The study's limitations are noteworthy. It was conducted in an acute-care setting within a secondary-care hospital, which, coupled with the exclusion of children under 12 and challenges in calculating patient days, could impact the assessment of antibiotic usage and narrow its demographic scope. Moreover, its focus on RTIs limits its relevance to other infection types. Moreover, the study's limited timeframe does not fully explore ongoing changes in AMR and antibiotic stewardship. Additional research is necessary to better understand these ongoing developments and their impact on healthcare. Another major limitation arises when comparing data across seasons, considering the study's relatively short duration, the evolving virulence of SARS-CoV-2 variants, increasing treatment experience, and evolving AMR prevention measures. The analysis, based on 640 records, covers only the first and second antibiotic courses, potentially missing vital data, especially considering the reduced hospital stays from 2019 to 2020. The study's sampling approach may not fully capture the spectrum of antibiotic prescribing practices. As a retrospective, cross-sectional study, it may not precisely gauge the varied health conditions of patients and their adherence to prescribing guidelines. These limitations underscore the need for further research in this area.

Our study suggests that antimicrobial stewardship programs in acute-care settings should prioritise monitoring prescription patterns to enhance adherence to guidelines and mitigate AMR. A clear and specific diagnosis, particularly in cases of CAP, which predominated in our indications, significantly influences appropriate antibiotic selection and reduces AMR. Applying relevant severity scoring tools such as CURB-65 when initiating antimicrobial therapy and interpreting results appropriately is vital for ensuring proper antibiotic prescribing [34]. Maintaining AMS interventions, particularly 'De-escalation', is vital during antibiotic reviews in order to align with local guidelines and consider the severity of the infection. The study identified no significant difference between longer and shorter antibiotic durations PP and DP, suggesting that shorter courses of antibiotics could be considered in line with local guidelines. This consistency could be a key consideration in emergencies or crises but should always be balanced with local guidelines and clinical data, including lab results, cultures, and other diagnostic tests.

## 5. Conclusions

This retrospective study evaluates the impact of the COVID-19 pandemic on antibiotic prescribing and AMS practices, emphasising the pivotal role of AMS in healthcare, particularly in combating AMR. It highlights the importance of monitoring antibiotic use in accordance with local guidelines. It emphasises the importance of accurate diagnoses, such as in cases of community-acquired pneumonia, to select the appropriate antibiotics and mitigate AMR. Implementing sustainable AMS interventions, particularly 'De-escalation', is essential during emergencies like a pandemic. Additionally, the study emphasises the importance of considering chronic conditions in antibiotic decision-making for COVID-19 patients. It advocates for ongoing AMS efforts and the implementation of effective and comprehensive AMS programmes during the post-pandemic era, focusing on integrating immediate patient care with long-term strategies for fighting AMR in sustainable public healthcare.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/covid4010010/s1, Figure S1: Mind map organises data extraction for antimicrobial stewardship.; Figure S2: Framework used for data analysis used in this retrospective study; Table S1: Data extraction tool in this retrospective study.

**Author Contributions:** R.A.E. was responsible for data acquisition, with the study design and conceptualisation developed collaboratively by R.A.E., N.U. and Z.A.; R.A.E. carried out the literature review under N.U.'s and Z.A.'s supervision and further extracted relevant electronic data from patient records. The project dataset was constructed by R.A.E., who also verified, accessed, and analysed the data, guided significantly by N.U. and Z.A.; R.A.E. produced the initial draft of the study, guided by N.U. and Z.A. All authors contributed to data interpretation and the preparation and revision of the manuscript, sharing equal responsibility for the final decision to submit and approval of the final manuscript. Z.A. acted as the guarantor for the overall content of the research. Data were anonymised before analysis and securely stored within the University of Hertfordshire's (UH) dual secure system. R.A.E. analysed the anonymised data using UH's dual secure system. All authors have read and agreed to the published version of the manuscript.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The datasets presented in this article are not readily available, according to the institution's policy. Requests to access the datasets should be directed to r.a.elshenawy@herts.ac.uk.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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# Appendix 67.

Global Role of Pharmacists in Antimicrobial Stewardship Implementation in Hospitals Before and During the COVID-19 Pandemic: A Review Article Based on Systematic Literature Review.

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**Global Role of Pharmacists in Antimicrobial Stewardship Implementation in Hospitals Before and During the COVID-19 Pandemic: A Review Article Based on Systematic Literature Review**

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**Abstract:**

**Background:** The overuse of antibiotics has led to the rising problem of antimicrobial resistance (AMR) in healthcare. Antimicrobial stewardship (AMS) aims to promote the judicious use of antibiotics, ensuring the ongoing availability of effective therapy. Nevertheless, the essential role of pharmacists, particularly during the COVID-19 pandemic, has been insufficiently emphasised in AMS studies.

**Aim:** This research aims to emphasise the pharmacists' roles in AMS among different countries before and during the pandemic

**Summary:** This review article provides a comprehensive overview of the role of pharmacists in Antimicrobial Stewardship Implementation in Hospitals before and during the COVID-19 pandemic. Based on a twenty-year systematic literature review, only five studies were found to pinpoint pharmacists' contributions within AMS. The review classifies AMS implementation into various strategies and measures, highlighting crucial pharmacist-led initiatives such as aiding in emergencies, monitoring antibiotic use, promoting AMS implementation, and ensuring adherence to antimicrobial guidelines. It is often overlooked that pharmacists make critical contributions, especially during crises like COVID-19. Their pivotal role in AMS is essential, given the escalating threat of AMR. Effectively implementing AMS within healthcare is crucial to combatting antimicrobial resistance.

**Conclusion:** Pharmacists globally, especially during the COVID-19 pandemic, have proven their vital role in AMS. With the looming threat of AMR, enhancing pharmacist training and guidelines can boost their impact, positioning them as crucial players in addressing AMR. This research emphasises their multifaceted AMS role, and contributions from five countries aim to promote their role, particularly in crises.

## 1. Introduction:

Antimicrobial resistance (AMR) presents a critical global health emergency, responsible for at least 1.27 million deaths globally and contributing to around 5 million fatalities in 2019.[1] In the United States, over 2.8 million cases of antimicrobial-resistant infections are reported annually, leading to more than 35,000 deaths. In 2020, the first year of the COVID-19 pandemic, over 29,400 deaths were attributed to antimicrobial-resistant infections commonly associated with healthcare environments. Around 40% of these infections occurred among patients while they were hospitalized.[2] Pharmacists remain an underutilized resource in healthcare, and there is a critical need to focus on the development, implementation, and full utilization of pharmacy professional services at both national and global levels.[3] During the COVID-19 pandemic, global attention, including from the World Health Organization (WHO) and various media outlets, primarily focused on the commendable frontline efforts of physicians and nurses. However, the contributions of pharmacists were rarely highlighted. [4] Despite this, pharmacists around the world have been consistently working at the forefront of healthcare, delivering indispensable services throughout the pandemic. Their role in providing essential healthcare services during such critical times underscores their importance in the healthcare industry. Pharmacists are medication experts providing patient care in acute care settings, including hospitals.[4]

Antimicrobial stewardship (AMS) refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration.[5] The goals of AMS include improving patient outcomes, ensuring cost-effective therapy, and reducing adverse sequelae of antimicrobial use, including AMR.[6]

The historical story begins with Alexander Fleming's observation in 1940 about the decreasing efficacy of penicillin due to its overuse.[7] Figure 1 presents the history of AMS in the United States, outlining a timeline of significant events in the evolution of AMS. [8-9] This timeline is an essential illustration of how healthcare systems and regulatory bodies have responded to the growing threat of AMR.[10-11] By 1966, the first review of antibiotic use in Canadian hospitals suggested that 50% of antimicrobial use was unnecessary or inappropriate, a revelation that highlighted the need for stewardship.[12] In 1970, the first clinical pharmacy services were introduced in North American hospitals, marking the beginning of formalized AMS programs.[8] The timeline progresses to 1996, where specialists at Emory University School of Medicine suggested "large-scale, well-controlled trials of antimicrobial use regulation ensure optimal 'antimicrobial use stewardship'.[9] By 1997, the CDC, FDA, and NIH published an action plan to combat AMR.[13] The IDSA and SHEA published guidelines in 1997 for preventing and reducing AMR through antimicrobial stewardship program (ASP).[14] This was followed by the CDC's launch of the "12 Steps to prevent AMR in hospitals" in 2002, which provided a framework for hospitals to implement AMS programs.[15] In 2006, the CDC released guidelines for managing multi-drug resistant organisms (MDROs) in acute care settings[16], and IDSA in 2007 released guidelines for developing institutional stewardship programs.[17] The timeline concludes with a critical development in 2008, where Medicare announced that it would stop reimbursement for hospital-acquired infections related to inadequate infection prevention and control (IPC), signalling the financial imperative for hospitals to adopt AMS practices.[18]

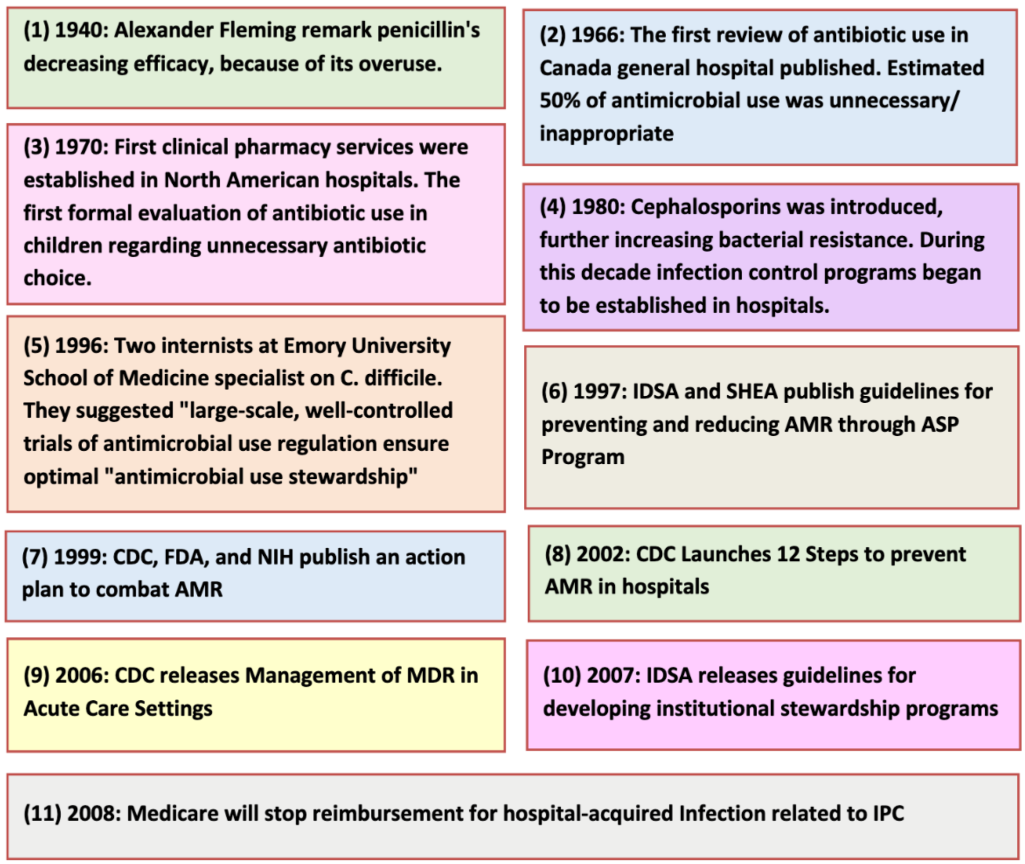


**FIGURE 1:** History of Antimicrobial Stewardship (AMS) in the United States

This investigation is a crucial part of a systematic literature review conducted in 2020, which explored the implementation, strategies, and measures of AMS over the past 20 years, between 2000 and 2021, including the era of the COVID-19 pandemic. The systematic review ultimately included 13 studies.[19] A more focused sub-analysis was then conducted, focusing on the contributions of pharmacists to AMS implementation strategies and measures worldwide, as reported by these studies. Of the 13 studies included, only six specifically addressed the role of pharmacists in AMS implementation, both before-the-pandemic (BP) and during-the-pandemic (DP). AMS strategies were categorized into core and supplemental strategies, along with AMS measures.[19] This article aims to examine the global contribution of pharmacists to the implementation of AMS within hospitals BP and DP, emphasizing the pivotal role pharmacists have played in AMS during times of emergency, such as the COVID-19 crisis. Inspired by the methodological approach of Debra A. Goff and colleagues' prior work, our findings are presented using a world map visual, spotlighting the key role of pharmacists in advancing AMS.[3] Pharmacists' participation in AMS implementation was observed across five countries.

In this article, the Public Health England (PHE) toolkit for AMS was utilized as a benchmark for analyzing AMS implementation. AMS strategies were categorized into core and supplemental strategies in accordance with the guidelines provided by the AMS toolkit.[20] Furthermore, a practical guide for the implementation and measurement of AMS was employed in the analysis.[21]

Strategies and interventions aimed at improving the appropriate prescription of antibiotics in all acute care settings are considered an essential part of “antimicrobial stewardship.” The literature presents many antimicrobial stewardship tools, interventions, and activities (collectively termed “strategies”) that can be employed to streamline and improve antimicrobial use and educate prescribers.[17] This article classifies a range of AMS strategies according to the implementation guidelines of the United States Infectious Diseases Society of America (IDSA) and the UK Public Health England AMS toolkit into core and supplemental strategies.[9, 20]

Measuring prescribing performance is crucial to evaluate the impact of AMS implementation in clinical practice and its demonstrable benefits for patients. The British scientist, Lord Kelvin (1824–1907), mentioned in his Popular Lecture, "If you cannot measure it, you cannot improve it".[22] To improve antimicrobial use, one must identify measurable elements/metrics that can evaluate the outcomes of AMS. These metrics serve various purposes, such as quality assurance, improvement, and comparisons/benchmarking, either within a hospital or between hospitals. Establishing what to measure is a critical step in maintaining sustainability in AMS intervention.[19]

Measuring stewardship can be divided into four categories: antimicrobial consumption, process measures, outcome measures, and financial.[23] Before 2019, there were no reliable means for measuring antimicrobial usage or correlating usage with resistance until the WHO promoted measurable tools that could be used worldwide to accurately reflect antimicrobial usage, such as the Defined Daily Dose (DDD).[23] The WHO defines DDD as the assumed average maintenance dose per day for an antibiotic used for its main indication in adults. To estimate the total number of days of antimicrobial therapy, healthcare personnel divide the total grams of each antimicrobial used over a given period by the WHO-defined DDD for the individual antimicrobials. Because DDD is a standardized unit of measure, it facilitates comparisons of antimicrobial usage with other hospitals and countries.[23] Each hospital should select appropriate measures/metrics that support the effective implementation of AMS. It is important to be aware of the advantages and disadvantages of each metric to ensure proper selection.[19]

## 2. Global Impact of Pharmacists in AMS Across Different Countries

Figure 2 shows a global map that emphasizes the contributions of pharmacists from these five countries.

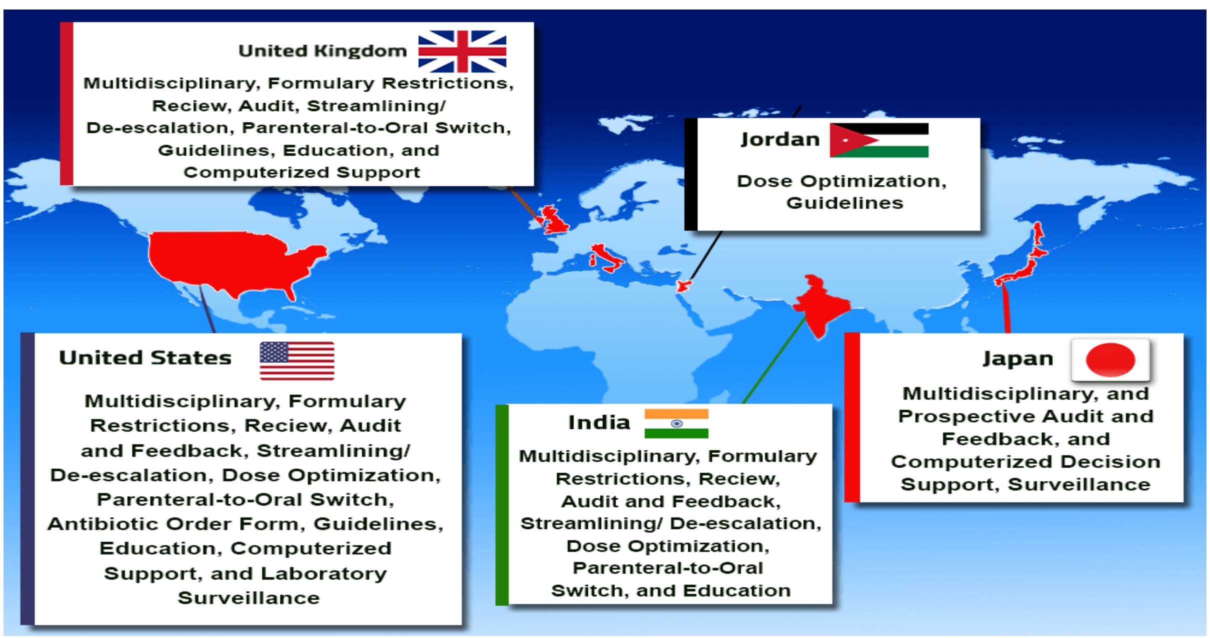


**FIGURE 2:** Map highlighting pharmacist's AMS global contributions before and during the COVID-19 pandemic in acute care settings.

### 2.1. United States

In the 2013 study by Trivedi et al., pharmacists in California played a pivotal role in AMS within acute care hospitals. They executed core AMS strategies, which included formulary restrictions, antibiotic reviews, and automatic stop orders, with 39% of hospitals monitoring AMR patterns and 36% tracking antimicrobial utilization. Supplementary strategies such as educational programs, dose optimization, and adherence to clinical pathways were also a focus, with pharmacists adjusting dosages for 17% of patients and streamlining therapies when possible. Pharmacists were central to the Antimicrobial Stewardship Program's application, which saw positive outcomes such as improved antimicrobial use in 74% of cases and a decrease in antimicrobial costs for 63% of the hospitals. Furthermore, 47% reported enhanced antimicrobial susceptibility patterns, and 38% integrated computer software with electronic records to support ASPs. This study highlights the essential contributions of pharmacists to AMS, showcasing their integral role in enhancing patient care and managing AMR, particularly during the time when public health faces significant challenges from antimicrobial resistance.[7]

In the 2014 study by Mehta et al., pharmacists played a key role in executing core AMS strategies within a Pennsylvania academic medical center. The research compared the effects of prior authorization and prospective audit with feedback on antimicrobial use. The transition from prior authorization to prospective audit with feedback resulted in a marked increase in antimicrobial usage, with total systemic antimicrobial use rising by 9.65 days of therapy per 1,000 patient-days (DOT/1,000-PD) monthly, and broad-spectrum anti-gram-negative antimicrobial use increasing by 4.80 DOT/1,000-PD monthly. Pharmacists were integral in quality improvement initiatives, including the parenteral-to-oral switch, ensuring the appropriate employment of restricted antibiotics. They monitored AMS quality indicators such as guideline-conformant empirical antibiotic selection, renal dose adjustment, switching from parenteral to oral therapy within 48–72 hours based on clinical conditions, and updating empirical antibiotic therapy to pathogen-specific therapy following culture results. The study observed significant upticks in the use of cefepime and piperacillin/tazobactam post-intervention and identified increases in hospital length of stay (LOS), both overall and after the first antimicrobial dose, following the strategy change.[24]

In the study by Tamma et al., pharmacists were key participants in the Agency for Healthcare Research and Quality (AHRQ) Safety Program, which aimed to evaluate the impact of Antibiotic Stewardship Programs (ASPs) on antibiotic usage across 437 U.S. hospitals. Over the course of a year, the program supported the establishment of ASPs and enhanced antibiotic decision-making among frontline clinicians. Pharmacists, alongside other clinicians, engaged in various educational initiatives including 17 webinars and additional training materials that covered the creation of ASPs, safety science, teamwork enhancement, communication, and infection management best practices. This comprehensive educational approach was a significant part of the program. Throughout the program's duration, adherence to essential ASP components such as pre- and post-antibiotic prescription interventions, access to local antibiotic guidelines, dedicated salary support for ASP leads, and quarterly antibiotic use reporting, improved dramatically from 8% to 74%. The hospitals that participated in the program saw a notable decrease in antibiotic use, measured as a reduction of 30.3 days of therapy per 1,000 patient days. In addition, there was a 19.5% decrease in the incidence rate of hospital-onset Clostridioides difficile events. The program's outcomes suggest that the educational and stewardship efforts led by pharmacists were effective in reducing overall antibiotic use and the rates of hospital-onset C. difficile infections. This indicates the vital role of pharmacists in the successful implementation of ASPs and in fostering responsible antibiotic use within hospital settings.[25]

### 2.2. United Kingdom (UK)

In the 2020 UK study led by Ashiru-Oredope et al., pharmacists played a critical role in adapting AMS activities during the COVID-19 pandemic. The study, which involved a questionnaire disseminated to AMS leads across the UK, found that 64% (61 out of 95 respondents) reported a decline in AMS activities due to the pandemic. This decline particularly impacted audits, educational initiatives, quality improvement projects, AMS meetings, and multidisciplinary efforts, including ward rounds. Despite these challenges, the study highlighted positive developments as pharmacists leveraged technology to overcome disruptions. There was a notable increase in the use of virtual platforms for meetings and ward rounds. Additionally, pharmacists expanded the use of procalcitonin tests to better differentiate between bacterial and viral infections, an important distinction during the pandemic. The study also examined the use of the Start Smart, Then Focus (SSTF) toolkit audit and CURB65 scoring by pharmacists, observed the dynamics of AMS teams, and reviewed the revisions to antimicrobial guidelines by NICE. It took into account the number of Clostridioides Difficile Infection (CDI) cases and the shift from parenteral to oral antimicrobial therapy. Significantly, the study highlighted the pandemic's mixed impact on pharmacist-led AMS practices. Out of 95 respondents, 65% felt negative effects, 7% perceived benefits, 25% saw both, and 2% noticed no change. Furthermore, pharmacists were involved in virtual AMS interventions and monitored Key Performance Indicators, including AMR local indicators set by The UK Health Security Agency (UKHSA). This study demonstrates the resilience and adaptability of pharmacists in maintaining AMS activities amidst the challenges posed by the pandemic and suggests potential areas for the further development of AMS in the post-pandemic era.[26]

### 2.3. India

In the study conducted from January 2018 to December 2019 by Thakkar et al., pharmacists played a crucial role in the antimicrobial stewardship program (AMSP) at a private tertiary care hospital in India. The AMSP focused on the prospective audit and feedback of restricted antimicrobials. During the 2-year period, 2,397 restricted antimicrobials were prescribed to 1,366 patients. A justification form, filled out for these prescriptions, was reviewed by the antimicrobial stewardship committee (AMSC) within 48 to 72 hours. Out of the total prescribed restricted antimicrobials, 1,801 prescriptions, accounting for 75%, were applicable for review. The study revealed that only 1.4% of admitted patients received restricted antimicrobials, with the total days of therapy with these drugs being 41 per 1,000 patient days. The AMSC found 12.5% of the prescriptions to be unjustified, and de-escalation recommendations were accepted in 89% of the cases. The program's outcomes, such as the days of therapy and compliance with AMSC recommendations, highlight the essential role that pharmacists and the AMSC play in overseeing the judicious use of antimicrobials and in curbing antimicrobial resistance.[27]

### 2.4. Japan

In the 2018 study by Moriyama et al. in Japan, the role of pharmacists in AMS and antifungal stewardship (AFS) programs was evaluated through a nationwide cross-sectional study. The study focused on interventions related to the use of broad-spectrum antimicrobials and antifungals in inpatient settings across the country. The survey, which was web-based and self-administered, received responses from 39 out of 240 hospitals, equalling a 16% response rate. Within these hospitals, 44% reported interventions in the use of broad-spectrum antimicrobials within the first 7 days, and 87% within 28 days. When it came to antifungals, interventions were reported by 8% of hospitals within 7 days and by 26% within 28 days. Notably, small to mid-sized hospitals, with ≤500 beds, were more likely to intervene within 7 days for broad-spectrum antimicrobial use compared to larger hospitals, with an odds ratio of 5.7. The study concluded that smaller hospitals in Japan were more prompt in their early intervention of AMS, demonstrating the proactive role of hospital pharmacists in these settings. However, it also highlighted a need for all hospitals, regardless of size, to put more effort into improving AFS. This suggests that pharmacists in Japanese hospitals are integral to the implementation and timely intervention of AMS and AFS programs, but there remains room for growth in antifungal management practices.[28]

### 2.5. Jordan

In the point prevalence study conducted by Ababneh et al. on August 13, 2018, in a tertiary academic hospital in northern Jordan, the role of pharmacists in the ASP involved quantifying the use of antimicrobials among inpatients. The study included data from 144 patients and utilized two key metrics: defined daily doses (DDDs) and days of therapy (DOTs). The findings revealed that carbapenems, glycopeptides, and piperacillin-tazobactam were the most used antimicrobials. The internal medicine wards had the highest prescription rate, with 49.8 DDDs per 100 admissions. This was followed by the surgery wards with 33.2 DDDs per 100 admissions, and the intensive care unit with 20.6 DDDs per 100 admissions. Pharmacists in this hospital were integral in reviewing antibiotic prescriptions through the electronic healthcare system (iSoft), obtain information, such as patient age, gender, ward location, antimicrobial agents, doses, routes, durations, and start/end dates. This study highlighted the pharmacists' contribution to surveillance as part of the ASP and highlighted the feasibility of such practices for routine adoption in ASPs. The role of pharmacists was critical in monitoring antimicrobial usage patterns and providing data to inform stewardship interventions aimed at optimizing antimicrobial use and combating resistance.[29]

### 3. Effective AMS Strategies and Measures Implemented by Pharmacists in Hospitals

In terms of AMS strategies and measures, Table 1 below showed the AMS measures and strategies among the five countries (Figure 1), that the pharmacists have pivotal role in implementing them before and during the pandemic. According to the table, pharmacists in the United Kingdom (UK), United States (USA), India, Japan, and Jordan have actively participated in core strategies of AMS, which are fundamental to initiating and maintaining effective antimicrobial use (Table 1). These core strategies include forming multidisciplinary stewardship teams, implementing formulary restrictions and preauthorization protocols to control the use of antimicrobials, reviewing antibiotic use to ensure appropriateness, and conducting prospective audits with feedback mechanisms.[30]

Table 1 displays the involvement of pharmacists in the implementation of AMS across five countries: the UK, the USA, India, Japan, and Jordan, in the timeframes before and during the COVID-19 pandemic. It emphasises that pharmacists in all these countries are integral to core AMS strategies, actively participating in multidisciplinary stewardship teams and conducting prospective audits and feedback, except of Jordan. The table further shows that pharmacists are involved in enforcing formulary restrictions and preauthorization in the USA, UK and India. Antibiotic reviews are a common practice in all the countries mentioned, with Japan and Jordan being the only exception.

Pharmacists contribute significantly to the implementation of supplementary AMS strategies, with practices varying across different countries. In the UK, USA, and India, pharmacists actively employ streamlining or de-escalation strategies and parenteral-to-oral switch methods. Dose optimization is another key strategy practiced by pharmacists in the USA, India, and Japan. The adherence to guidelines and clinical pathways, crucial for maintaining the quality and effectiveness of AMS programs, is a strategy adopted by pharmacists in the UK, USA, and Jordan. Unique to the USA is the implementation of antibiotic order forms, indicating a specialized approach in managing antimicrobial use. While AMS education is a common practice among pharmacists in most of these countries, it is not prominently featured in Jordan and Japan. Furthermore, the integration of technology in AMS through computerized decision support and surveillance systems is observed in the practices of pharmacists in the UK, USA and Jordan. Laboratory surveillance, an essential component for monitoring and responding to antimicrobial resistance, is utilized by pharmacists in the USA and India, highlighting their proactive role in AMS.

In terms of AMS measures, the Defined Daily Dose (DDD) is tracked by pharmacists in the USA and Jordan, illustrating their focus on quantifying antimicrobial usage. The Day of Therapy (DOT) metric is monitored in the USA, India, and Japan, providing insight into the duration of antimicrobial treatments. The Length of Stay (LOS) is an important metric measured exclusively by pharmacists in the USA, reflecting their role in assessing the impact of antimicrobial use on hospitalization duration. Notably, the measurement of Procalcitonin (PCT) is implemented in the UK, aiding in the evaluation of infection severity and antibiotic necessity. The cost associated with antimicrobial use, an essential aspect of stewardship, is considered by pharmacists in the USA and Japan. The rates of Clostridioides Difficile Infection (CDI), a critical marker for antibiotic-related complications, are monitored by pharmacists in the UK and Japan. Furthermore, pharmacists in the UK, USA, and Jordan utilize indicators or quality improvement measures, underlining their commitment to enhancing the effectiveness and safety of antimicrobial use. This comprehensive overview emphasises the integral role of pharmacists in AMS, revealing their commitment to core strategies and diverse adoption of supplementary strategies and measures across different healthcare systems.

**Table 1.** Pharmacists' role in AMS implementation before and during the COVID-19 pandemic

| Antimicrobial Stewardship (AMS) Implementation | UK | USA | India | Japan | Jordan |
|---|---|---|---|---|---|
| **Core Strategies** | | | | | |
| **Multidisciplinary Stewardship Team** | X | X | X | X | |
| **Formulary Restrictions and Preauthorisation** | X | X | X | | |
| **Antibiotic Review** | X | X | X | | |
| **Prospective Audit & Feedback** | X | X | X | X | |
| **Supplementary Strategies** | | | | | |
| **Streamlining/ De-escalation** | X | X | X | | |
| **Dose Optimisation** | | X | X | | X |
| **Parenteral-to-Oral Switch** | X | X | X | | |
| **Guidelines and Clinical Pathways** | X | X | | | X |
| **Antibiotic Order Form** | | X | | | |
| **AMS Education** | X | X | X | | |
| **Computerized Decision Support, Surveillance** | X | X | | | X |
| **Laboratory Surveillance and Feedback** | | X | | | |
| **AMS Measures** | | | | | |
| **Defined Daily Dose (DDD)** | | X | | | X |
| **Day of Therapy (DOT)** | | X | X | | X |
| **Length of Stay (LOS)** | | X | | | |
| **Cost** | | X | | X | |
| **Clostridioides Difficile Infection (CDI)** | X | X | | | |
| **Procalcitonin (PCT)** | X | | | | |
| **Indicators or Quality Improvement** | X | X | | | X |

This visual breakdown allows us to appreciate the multifaceted involvement of pharmacists in AMS, highlighting their essential role in managing antibiotics effectively, particularly during a time when the COVID-19 pandemic has placed additional strain on healthcare systems.[26] It is evident that pharmacists are not only key players in the frontline implementation of stewardship practices but also in ensuring their continuation and adaptation in response to the evolving healthcare landscape.[30]

**5. Pharmacists' Vital Role in Global AMS: Enhanced During COVID-19**

Figure 3 presents a comprehensive view of the critical role pharmacists play in AMS globally, a role that has been emphasized during the COVID-19 pandemic. Pharmacists have taken a forefront position in reviewing antibiotic use to ensure that prescriptions are appropriate and safe, a task that is fundamental in managing and mitigating antimicrobial resistance. They are instrumental in enforcing formulary restrictions, which helps direct the use of antimicrobials within clinical settings. Through prospective audits coupled with feedback mechanisms, pharmacists contribute to the ongoing evaluation and enhancement of AMS practices.

In the multidisciplinary landscape of healthcare, pharmacists collaborate with various teams, providing valuable insights and expertise to drive stewardship efforts. This collaboration extends to AMS rounds where they participate in direct patient care decisions. Their role in streamlining or de-escalating therapies is pivotal, optimizing antimicrobial therapy by shifting from broad to narrow-spectrum antibiotics when possible. AMS Education is another key aspect of their role, wherein pharmacists engage in training healthcare professionals and informing patients about the prudent use of antimicrobials. As AMS champions, they advocate for and lead stewardship initiatives, ensuring that these programs are integrated and valued within their institutions. They also contribute to the development of clinical guidelines that inform and standardize antimicrobial therapy.

Pharmacists often serve on AMS committees, where they help to shape the strategic direction of stewardship interventions. The importance of their role has been especially pronounced during the pandemic, as they have adapted to ensure the continuity and effectiveness of AMS programs in the face of unprecedented challenges. Their collaborative efforts with other healthcare professionals have been key to sustaining stewardship efforts and are indicative of their indispensable role in healthcare, both prior to and during the pandemic.

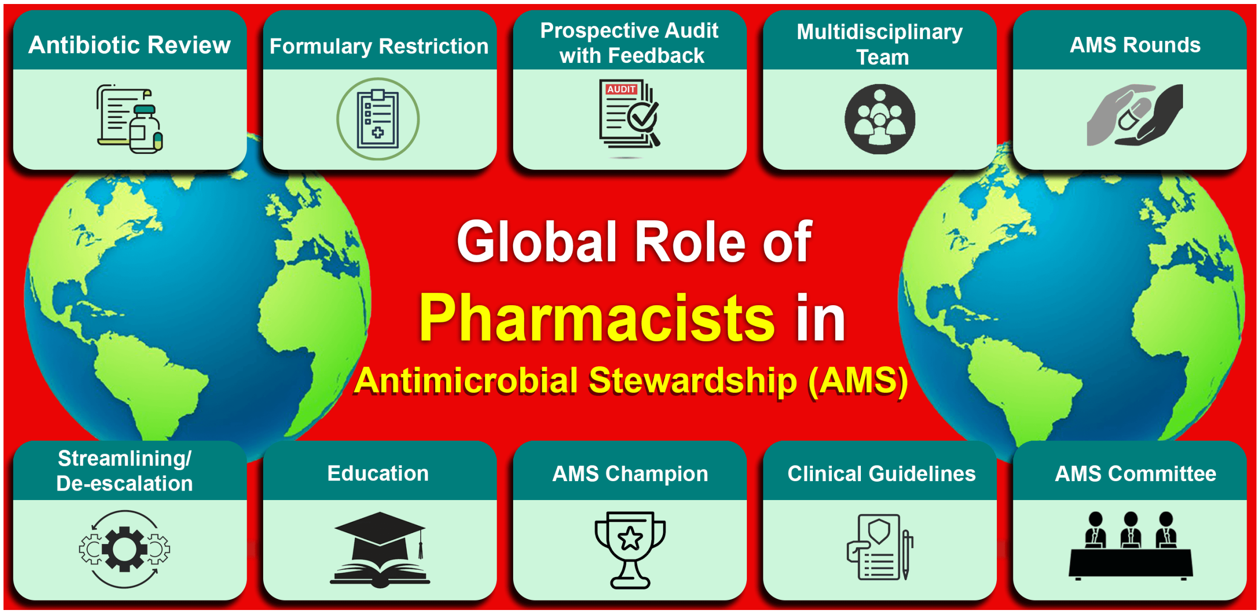


**FIGURE 3.** Infographic of the roles of pharmacists in AMS implementation before and during the COVID-19 pandemic

**6. Key Role of Pharmacists in Advancing AMS During COVID-19**

Before the COVID-19 pandemic, pharmacists in the USA and UK were essential in implementing various core and supplementary AMS strategies. These included forming multidisciplinary teams, conducting antibiotic reviews, streamlining or de-escalating antimicrobial therapies, enforcing formulary restrictions, educating healthcare professionals, and adjusting doses as needed. In the UK, pharmacists also engaged in quality improvement projects, adhered to national performance indicators, and conducted AMS audits to promote the judicious use of antimicrobials and adapt practices based on feedback. In the USA, pharmacists took lead roles in the Agency for Healthcare Research and Quality Safety Program, emphasizing improved teamwork, communication, and best practices in infection management. Meanwhile, in India, pharmacists pioneered prospective audit and feedback systems, ensuring the justified prescription of restricted antimicrobials and advocating for de-escalation when necessary. In Jordan, pharmacists were key in the continuous monitoring of antimicrobial use, providing essential data for AMS.

During the COVID-19 pandemic, UK pharmacists integrated technology to enhance stewardship efforts, utilizing virtual platforms for meetings, AMS Committee discussions, and ward rounds. The increased use of procalcitonin testing in the UK underscored the pharmacists' role in distinguishing bacterial from viral infections, a task that became particularly vital during the pandemic. However, the pandemic imposed a dual responsibility on pharmacists, who reported that the pandemic's adverse effects impacted routine AMS activities. Despite these challenges, 65% of UK pharmacists balanced their roles in pandemic response with ongoing AMS efforts.

In light of the pandemic, there was an urgent need to revise clinical guidelines to reflect new research and the challenges presented by COVID-19. Pharmacists were instrumental in updating these guidelines, ensuring they remained current with the pandemic's evolving nature while still addressing the need for effective antimicrobial stewardship.

**7. The Crucial Role of Pharmacists in AMS Implementation in the Post-Pandemic Era**

As the world moves beyond the COVID-19 pandemic, pharmacists are set to continue their critical work in AMS. Their involvement is expected to deepen, responding to the lessons learned during the pandemic and addressing the ongoing threats of AMR. Pharmacists will be instrumental in guiding a smooth transition back to regular healthcare practices, maintaining the momentum for global health improvement, and restoring the interconnectedness that was present before the pandemic.[19]

In the new normal, the role of pharmacists in implementing AMS will be more crucial than ever. Their efforts during the pandemic have highlighted the importance of effective antimicrobial use and the risks associated with AMR. As healthcare systems recalibrate, pharmacists are poised to work even more closely with multidisciplinary teams to refine AMS processes, ensure prudent antibiotic prescribing, and promote the judicious use of these critical drugs. During the challenging times of the pandemic, pharmacists have refined their expertise, positioning themselves as leaders in educational initiatives that explain the complexities of antimicrobial resistance to healthcare providers and the public. They stand at the forefront of monitoring antibiotic usage and are tasked with incorporating cutting-edge research into established AMS strategies. As guardians against the advancing tide of microbial threats, their alertness and flexibility are crucial for the enduring effectiveness of AMS programs. Looking ahead, their contributions will be instrumental in achieving the best possible patient outcomes and managing healthcare resources effectively as we transition into the post-pandemic world.[30, 32]

For the post-pandemic era, it is recommended that pharmacists continue to play a pivotal role in AMS. They should leverage the experience gained during the pandemic to further strengthen AMS programs. This could involve maintaining the use of technology for remote stewardship activities, enhancing data analytics for better decision-making, and continuing education on AMS practices to accommodate new and re-emerging pathogens. Additionally, there should be an emphasis on resilience in AMS programs to prepare for future public health emergencies, ensuring that AMS activities can withstand the pressures of increased healthcare demands. Pharmacists should also advocate for policies that support sustained funding and resources for AMS initiatives, emphasizing the long-term benefits of antimicrobial optimization on patient outcomes and healthcare costs.[19, 30, 33]

## 8. Strengths and limitations

To investigate the AMS implementation BP and DP in acute care settings. There were some limitations associated with this review at the methodology level since non-English articles were excluded, which may introduce language bias because some pieces were excluded on that basis. The studies included in this review were primarily located in developed countries with more advanced healthcare systems than other countries. In this study, the analysis was focused exclusively on core and supplemental strategies and measures of AMS implementation in adult patients. There are numerous studies in the literature on AMS practices, focusing on antibiotic use, consumption, and resistant bacteria. However, these were excluded from the analysis.

## 9. Conclusions

Worldwide, pharmacists provide essential frontline care to COVID-19 patients in hospitals and acute care settings. The complexity of diagnosing and treating COVID-19 patients with bacterial infections in the hospital and AMS implementation require a multi-disciplinary team of experts, which includes pharmacists. Pharmacists are still underutilised healthcare resources in the AMS implementation, and pharmacists must be considered antibiotic experts. Following the O'Neill review and findings in 2016, the number of deaths from AMR infections is estimated to reach 10 million annually due to the AMR crisis. Understanding the AMS strategies, such as formulary restriction, antibiotic review, and prospective audit with feedback, could help extend pharmacists' role in AMS implementation. In addition, the improvement of pharmacist AMS education and the development of antimicrobial guidelines will help pharmacists develop tactical AMS strategies to support member organisations in implementing the AMS and decreasing the AMR threat in the future. We hope that this list of contributions by pharmacists from five countries in this article could help to change this perspective.

Thus, the AMS pharmacist cooperates with the healthcare team to develop, review and update antimicrobial guidelines for preventing antimicrobial resistance in acute care settings. Hence, this reveals that the AMS pharmacists' roles extended beyond traditional duties.

A clinical pharmacist APS services should include:

- Support and alleviate the burden of emergency departments and intensive care units by supporting medical staff to develop antimicrobial guidelines and practice pathways.
- Achieving benefits in terms of reducing unnecessary use of antimicrobials and maintain the judicious use of antimicrobials.
- Better access to and use of surveillance data to monitor patients' clinical information and verify the ongoing treatment.
- Also, provides clinical advice to optimise antimicrobial prescription and use.
- Monitor compliance with antimicrobial treatment guidelines and strengthen collaboration between healthcare teams.
- Tackling antimicrobial resistance using antibiograms, revising the guidelines to minimise misuse, and ensuring the continued efficacy and safety of existing antimicrobials.

**Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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# Appendix 68.

Healthcare professionals’ knowledge, attitudes and perceptions towards antibiotic prescribing, antibiotic resistance and stewardship during the COVID-19 pandemic: A descriptive study at a secondary care setting in the UK.

Submitted to JAC-Antimicrobial Resistance Journal.

**Healthcare professionals' knowledge, attitudes and perceptions towards antibiotic prescribing, antibiotic resistance and stewardship during the COVID-19 pandemic: A descriptive study at a secondary care setting in the UK**


## ABSTRACT

### Background:

Antimicrobial resistance (AMR) is a major public health threat, potentially causing 10 million deaths annually by 2050. The WHO has emphasised the need for increased awareness and action against AMR, a challenge further intensified by the COVID-19 pandemic. The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) report 2023 indicated a rise in antibiotic use post-pandemic. Misuse of antimicrobials during this period has deepened the AMR crisis, making antimicrobial stewardship (AMS) a priority.

### Methods:

A cross-sectional survey was conducted at a secondary care setting, a UK NHS Foundation Trust. It targeted healthcare professionals (HCPs) to assess their knowledge, attitudes, and perceptions towards antibiotic prescribing, AMR, and AMS during the COVID-19 pandemic. The survey included 240 participants, predominantly pharmacists, doctors, and nurses, with data collected via an online platform.

### Results:

The median knowledge score among HCPs was 50.13%. While there was a strong agreement that AMR poses a public health issue, there were gaps in knowledge regarding AMS's impact on patient outcomes and appropriate antibiotic treatment durations. Attitudes towards AMS were positive, yet practice gaps were evident, particularly in compliance with local antimicrobial guidelines.

### Conclusion:

This study highlights the essential role of enhancing HCPs' awareness, knowledge, and practices in antibiotic prescribing. It emphasises the significant influence of the COVID-19 pandemic on AMR and AMS, stressing the necessity for robust AMS educational programs. Future efforts must focus on

innovative tools and resources to strengthen AMS and effectively combat AMR, ensuring patient safety in the evolving healthcare environment.

## INTRODUCTION

Antimicrobial resistance poses a significant global public health challenge, stemming from bacteria's capacity to resist the effects of antimicrobial agents, such as antibiotics. It is estimated that by 2050, AMR could be responsible for 10 million deaths annually.[1] Recognising the seriousness of this issue, the WHO has devised a comprehensive global action plan to tackle AMR. This plan highlighted the pressing need for increased awareness and joint efforts.[2] Effective utilisation of antibiotics in healthcare settings pivots on collaboration among all healthcare professionals. Such collaboration has proven effective; a study found that a concerted approach encompassing management, responsibility, drug experience, action tracking, education, and reporting reduced antibiotic use's relative risk by 34%.[3-4]

The COVID-19 pandemic, caused by SARS-CoV-2, has potentially exacerbated AMR. As of December 2023, approximately 773 million individuals were diagnosed with COVID-19, resulting in nearly 7 million deaths worldwide.[5] Evidence suggests that increased antimicrobial therapy during the pandemic could have augmented the incidence of resistant infections.[6] In 2022, the CDC reported a 15% surge in AMR-related hospital deaths for the preceding year, attributing this rise to the pandemic.[7] The widespread misuse and excessive use of antimicrobials during the pandemic in healthcare facilities and the broader community have further magnified this problem.[8] Such imprudent use has deepened the AMR crisis, yielding detrimental global effects.[9] The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) 2023 report highlighted that after the 2022 pandemic measures were lifted, there was a surge in priority pathogens and secondary care antibiotic usage. Yet, figures remained under those from 2018 due to an 11.8% decrease in outpatient prescriptions. Usage of anti-Clostridioides difficile agents increased by 70.2%, and fluctuations in the use of 'Access', 'Watch', and 'Reserve' antibiotics demonstrated evolving patterns in antibiotic stewardship.[10] The study on antibiotic use in 640 respiratory tract infection patients showed increased "Watch" category antibiotics use during the pandemic, underscoring the need for strong AMS and AWaRe classification application in prescriptions for patient safety and combating antibiotic misuse amid global health challenges.[11]

A robust understanding of bacterial resistance to antibiotics is crucial in combatting AMR, as a lack of knowledge can lead to misuse.[12] Antimicrobial stewardship (AMS) is an organisational approach that focuses on ensuring the right antimicrobial prescriptions and the best antibiotic usage practices, aiming to diminish AMR through specific policies and guidelines. [13] AMS emphasises judicious antibiotic use, which is crucial in the UK's AMR strategy, aligning with healthcare policy and clinical practice guidelines outlined by UK Health Security Agency (UKHSA).[14]

A comprehensive understanding of bacterial resistance to antibiotics, coupled with informed attitudes and perceptions, is essential for combating AMR. Misconceptions and erroneous attitudes can lead to antibiotic misuse. [12] Antimicrobial stewardship (AMS) employs an organisational approach, focusing on the correct prescription of antimicrobials and the best usage practices to mitigate AMR through well-founded policies and guidelines.[13] AMS, advocating for prudent antibiotic use based on accurate knowledge, appropriate attitudes, and perceptions, is pivotal to the UK's AMR strategy.[14] This aligns with the healthcare policy and clinical practice guidelines stipulated by the UK Health Security Agency (UKHSA).[15] Such an approach, underpinned by knowledge, attitudes, and perceptions, is fundamental to the progression of AMS and the protection of public health.

Knowledge, attitude, and practice (KAP) towards AMR and AMS among healthcare professionals (HCPs) are essential areas of exploration, given their role in prescribing antibiotics in acute care settings.[16] A 2020 study assessing the KAP of doctors regarding AMS found that approximately 56% recognised the term AMS. However, the study also reported that over 50% of the HCPs were unfamiliar with AMS.[17] A robust understanding of bacterial resistance to antimicrobials is pivotal in preventing AMR since deficient knowledge, attitudes, and perceptions can lead to improper usage.[14] The KAP concerning AMR among HCPs is especially vital, considering their influence on appropriate antibiotic prescriptions to patients. However, research examining HCPs' KAP during the COVID-19 pandemic is scarce, with only one study centred on nursing students.[16] Prior studies have yielded varied outcomes; some suggest a limited awareness of AMR among HCPs, while others report satisfactory knowledge levels.[17] Given the unprecedented challenges introduced by the pandemic, it's conceivable that the understanding of AMR among HCPs might have waned during this time. Addressing these uncertainties, this study seeks to explore the KAP of HCPs towards antibiotic prescribing, AMR, and AMS during the COVID-19 pandemic and identify the factors affecting AMS practices during the pandemic.[16, 18] The objectives of this study are to explore the knowledge, attitudes and perceptions of HCPs regarding antibiotic prescribing, and AMS practices during the COVID-19 pandemic, at one NHS Foundation Trust, a secondary care setting in the UK.

## METHODS

### Ethics

This research received ethical clearance from the Health Research Authority (HRA) with the reference number 22/EM/0161, as determined by the Research Ethics Committee (REC). The University of Hertfordshire (UH) ethics committee further approved the study protocol under the reference LMS/PGR/NHS/02975. The authors declare no conflicts of interest in relation to this study. Participants who responded to the survey implicitly gave their informed consent, agreeing to the use of their anonymised data for the purposes outlined in the survey.

### Study design and setting

This study utilised a cross-sectional design, employing a questionnaire survey to explore HCPs' knowledge, attitudes, and perceptions about antibiotic prescribing PP and DP. The research was executed through an online survey targeting doctors, nurses, and pharmacists at NHS Foundation Trust. Data collection was facilitated using the secure and UH-trusted platform Qualtrics XM (Qualtrics, 2015). The survey began on June 12, 2023, a Monday, and was completed by September 13, 2023, a Wednesday.

### Participants

Eligibility for participation in this study is determined by inclusion and exclusion. The Inclusion Criteria are as follows: (i) Participants must be HCPs, which includes professionals such as doctors, nurses, and pharmacists; (ii) Participants must be adults, with a minimum age of 25; and (iii) participants must be registered with their respective professional regulatory organisations: doctors with the General Medical Council (GMC), pharmacists with the General Pharmaceutical Council (GPhC), and nurses with the Nursing and Midwifery Council (NMC). All HCPs, regardless of their professional role as a doctors, nurses, or pharmacists, are ineligible to participate if they lack work experience at NHS Foundation Trust during the pandemic.

### Registration

This study has been officially registered with the ISRCTN registry. The ISRCTN registry is a primary registry acknowledged by the WHO and the International Committee of Medical Journal Editors (ICMJE), accepting all clinical research studies.[19] Moreover, it was registered in Octopus, the global primary research record.[20]

### Data collection tools and approach

A structured questionnaire comprising 12 closed and open-ended questions was developed. A literature review on behaviour change and antibiotic prescribing in UK healthcare settings and a behavioural analysis from PHE developed the questionnaire's design.[21] The survey, designed to align with the objectives of the study, can be found in Supplementary Documents S1 to S3. The survey comprises four sections: Respondent Demographics, Awareness and Knowledge about Antibiotic Prescribing and AMR, Perceptions and Attitudes towards Antibiotic Prescribing and AMS, and AMS Practices.

### Sample size

To ascertain an appropriate and accurate sample size, data on the total number of healthcare professionals was gathered: 206 pharmacists, 2,140 nurses, and 5,636 doctors, with a total headcount of 7,982. The survey sample size was calculated at 240, considering a 5% margin of error, 95% confidence interval, and an expected 20% response rate. The survey commenced from Monday, June 12, 2023, to Wednesday, September 13, 2023, using an online-based data collection method. The survey invitations, featuring a link and a unique barcode, were distributed online.

### Statistical methods

The main author collected, extracted and analysed the results. The responses from the participants were provided to the researcher as a completely anonymised set for analysis. A pilot test involving 20% of the sample (50 out of 240 respondents, later excluded from the main survey) evaluated the survey's effectiveness in addressing research questions and established its validity and reliability. This pilot also helped estimate the questionnaire's completion time, roughly 10 minutes. Post-pilot, the questionnaire was refined for clarity and relevance. Validity assessments included face validity by AMS pharmacists at the Trust and content validity by the Royal Pharmaceutical Society (RPS) research team.[22] Reliability was confirmed using Cronbach's Alpha on pilot responses, with excellent, good, and moderate reliability scores across various sections. The average score of 0.80 demonstrates high internal consistency.

### Patient and public involvement

The study protocol was submitted to the Citizens Senate, an organisation focused on patient care with a considerable representation of elderly individuals. They provided useful suggestions and comments.

### Data analysis

The survey results were analysed using descriptive statistics and IBM SPSS Statistics version 27.0 for Windows. [23] For data analysis, the study also utilised descriptive statistical techniques through Excel 2019 for Windows (www.microsoft.com, 2019).[24]

## RESULTS

A total of 240 HCPs responded to the survey, with results recorded online and subsequently analysed. Data was exported to an Excel sheet from the secure online platform, 'Qualtrics'.[25] The researcher organised and cleaned the data, providing codes for the 5-point Likert scale responses as follows: 0 for Strongly Disagree; 1 for Disagree; 2 for Neutral; 3 for Agree; and 4 for Strongly Agree.

### Healthcare professionals' demographic characteristics

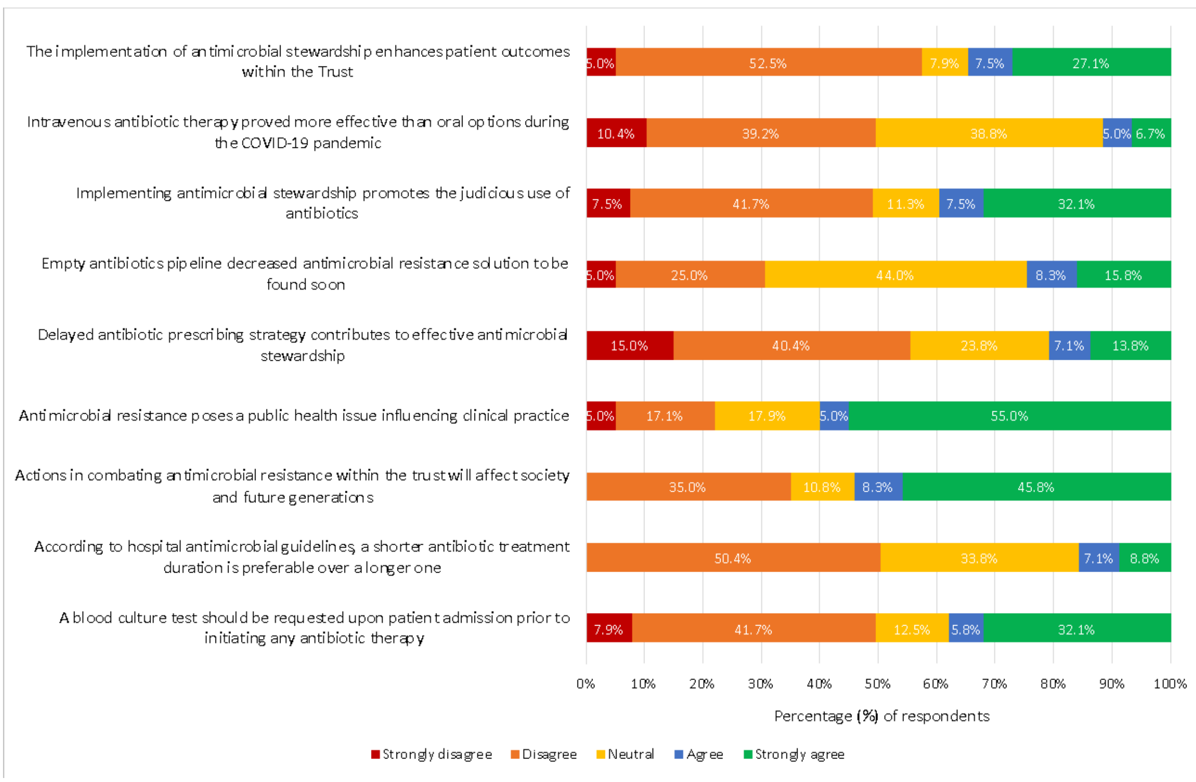
Most survey respondents were pharmacists (n=125, 52%), doctors (n=72, 30%), and nurses (n=43, 18%). Table 5.2 illustrates the breakdown of participants' age characteristics: most respondents (n=96, 40.0%) were between 32 and 41 years old. In regard to education, most participants held a postgraduate master's degree (n=163, 68.0%) or a postgraduate doctorate degree (n=43, 18.0%), while only a small percentage had an undergraduate degree (n=24, 10%). Regarding years of experience, those with 6-20 years were most represented among respondents (n=132, 55%). Table 5.2 provides a detailed breakdown of the HCPs' demographic characteristics. Most respondents were female (56%), and the predominant qualification was a pharmacist (52%). Concerning educational achievements, the majority of respondents held a postgraduate master's degree (68%). Regarding job banding, the majority were in band 7 (27%) (Table 1).

**Table 1.** Demographics characteristics of the survey respondents

| | | Count | % |
|---|---|---|---|
| Age | 25-31 years old | 58 | 24.0% |
| | 32-41 years old | 96 | 40.0% |
| | 42-51 years old | 36 | 15.0% |
| | 52-61 years old | 38 | 16.0% |
| | 62-75 years old | 12 | 5.0% |
| Educational achievement | Undergraduate degree | 24 | 10.0% |
| | Postgraduate degree (Diploma) | 10 | 4.0% |
| | Postgraduate degree (Master Degree) | 163 | 68.0% |
| | Postgraduate degree (Doctoral Degree) | 43 | 18.0% |
| Gender | Female | 134 | 54.0% |
| | Male | 89 | 35.9% |
| | Non-binary | 5 | 2.0% |
| | Prefer not to say | 12 | 4.8% |
| Professional background | Pharmacist | 125 | 52.0% |
| | Doctor | 72 | 30.0% |
| | Nurse | 43 | 18.0% |
| Job banding | Band 5 | 43 | 18.0% |
| | Band 6 | 58 | 24.0% |
| | Band 7 | 65 | 27.0% |
| | Band 8a | 22 | 9.0% |
| | Band 8b | 24 | 10.0% |
| | Band 8c | 10 | 4.0% |
| | Band 9 and more | 18 | 8.0% |
| Years of experience | ≤5 years | 48 | 20.0% |
| | ≥20 years | 60 | 25.0% |
| | 6-20 years | 132 | 55.0% |

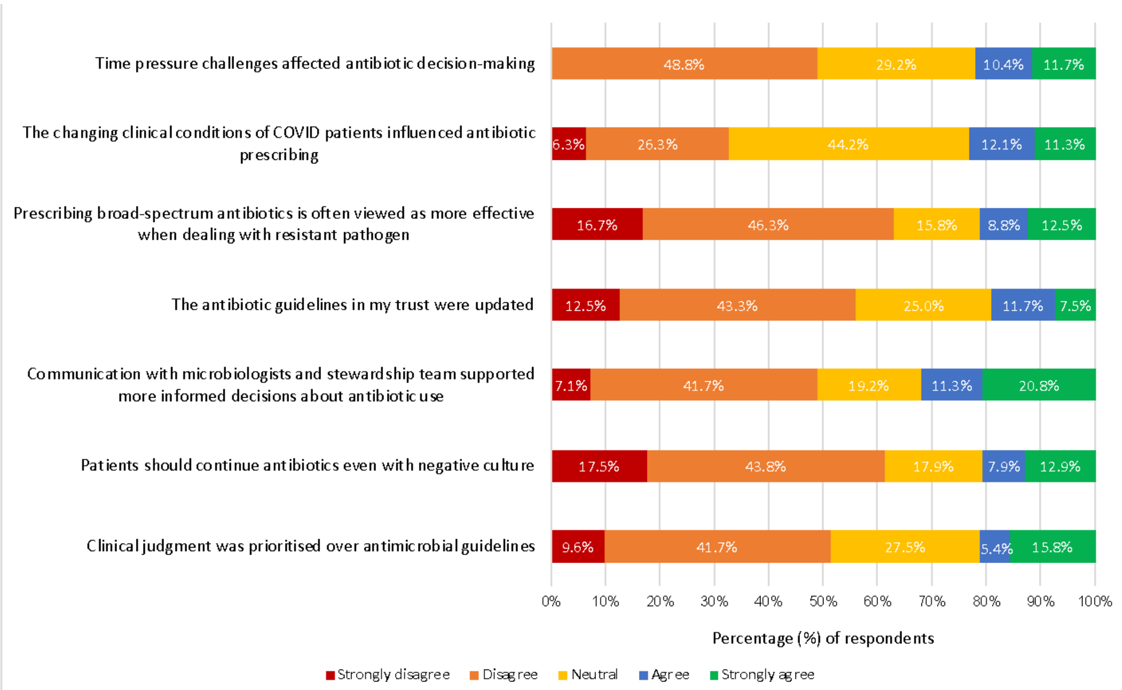
The median knowledge score of the study group was 50.13%. Regarding knowledge, most of the respondents reported that they strongly agree that antimicrobial resistance poses a public health issue influencing clinical practice (n=132, 55.0%). Additionally, most strongly agreed that Actions in combating antimicrobial resistance within the trust will affect society and future generations (n=110, 45.8%). Among participants, respondents expressed strong and equal agreement with the statements that implementing antimicrobial stewardship promotes the judicious use of antibiotics and that a blood culture test should be requested upon patient admission prior to initiating any antibiotic therapy (n=77, 32.1%). However, participants showed insufficient knowledge regarding the statements that 'the implementation of antimicrobial stewardship enhances patient outcomes within the Trust' (n=126, 52.5%). Additionally, respondents disagree with the statement, 'According to hospital antimicrobial guidelines, a shorter antibiotic treatment duration is preferable over a longer one' (n=121, 50.4%) (Figure 1).

**Figure 1.** Stacked bar chart for knowledge of healthcare professionals towards antibiotic prescribing, antimicrobial resistance, and stewardship during the COVID-19 pandemic.



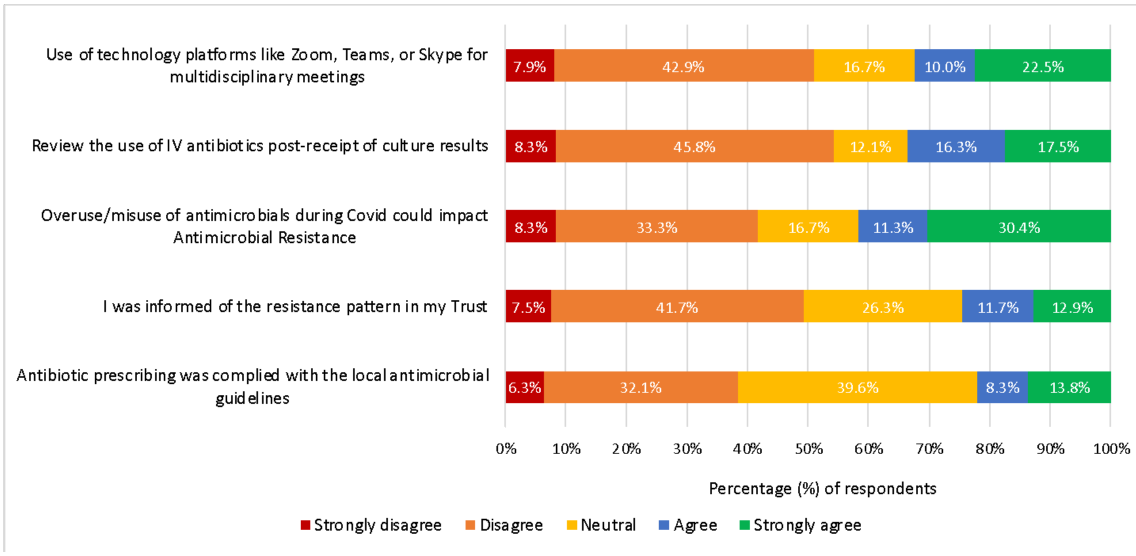
In terms of the participants' attitudes and perceptions, the median attitude score was 44.03%. Approximately 21% strongly agreed that communication with microbiologists and the stewardship team supported more informed decisions about antibiotic use, and 16% strongly agreed that clinical judgment was prioritised over antimicrobial guidelines. However, approximately 49% (n=117) disagreed with the statement, 'Time pressure challenges affected antibiotic decision-making,' and about 46% (n=111) disagreed with the statement, 'Prescribing broad-spectrum antibiotics is often viewed as more effective when dealing with a resistant pathogen' (Figure 2).

**Figure 2.** Stacked bar chart for attitude and perception of healthcare professionals towards antibiotic prescribing, antimicrobial resistance, and stewardship during the COVID-19 pandemic.




For practice, the median practice score was 45%. Approximately 42% of respondents strongly agreed and agreed with the statement, 'Overuse/misuse of antimicrobials during COVID could impact Antimicrobial Resistance' (n=100). Regarding the statement 'Review the use of IV antibiotics post-receipt of culture results,' it showed (n=81, 33.8%), and concerning 'Use of technology platforms, such as Zoom, Teams, or Skype for multidisciplinary meetings,' it showed (n=78, 32.5%). However, some respondents disagreed with the statement, 'Antibiotic prescribing complied with the local antimicrobial guidelines' (n=77, 32.1%) (Figure 3).

**Figure 3.** Stacked bar chart for the practice of healthcare professionals towards antibiotic prescribing, antimicrobial resistance, and stewardship during the COVID-19 pandemic.




## DISCUSSION

This survey questionnaire was conducted in one English NHS Foundation Trust and focuses on assessing HCPs' KAP towards antibiotic prescribing, AMR, and AMS during the COVID-19 pandemic. The study participants demonstrated good knowledge and practice; however, their attitude requires further improvement. Such findings highlight a deficiency in efficacious AMS educational and training programmes. Furthermore, this study identified certain HCPs who need to improve their knowledge and practice towards antibiotic prescribing, especially during the pandemic. The study provides vital insights into HCPs' knowledge and perceptions concerning antibiotic prescribing, AMR, and AMS during the COVID-19 pandemic, with a median knowledge score of 50.13%. Recently, a Saudi Arabian study reported a median knowledge score of 72.73% among primary healthcare workers on antibiotic use, contrasting with Pakistani clinicians in Lahore's public hospitals, who displayed significant knowledge gaps in AMR and AMS. Despite recognising AMR as a global issue, many lacked an understanding of appropriate antibiotic selection, with a call for more education highlighted.[26]

In Pakistan, clinicians' knowledge of Antimicrobial Stewardship (AMS) and Antimicrobial Resistance (AMR) was found to be relatively poor. This multi-centre, cross-sectional study in Lahore's public tertiary care hospitals surveyed 336 clinicians using a 45-question KAP questionnaire. While 92% acknowledged AMR as a global issue, only 66% correctly identified that colds and flu don't require antibiotics. About 68% were confident in their antimicrobial practices, yet 96% saw the need for more knowledge. The study revealed gaps in understanding the AM spectrum and appropriate drug choices, with a strong desire among clinicians for further education and training.[27]

In the UK, a survey of 2404 healthcare workers, primarily nurses, pharmacists, and doctors, revealed high awareness that antibiotics don’t work against viruses and have side effects. However, under 80% recognised the personal and transmission risks of antibiotic-resistant bacteria. While acknowledging a link between their prescribing and resistance spread, only 64% felt personally responsible for controlling it. Barriers included lack of resources and time and patient disinterest. Notably, 35% prescribed antibiotics in the past week due to patient deterioration fears, suggesting the need for multifaceted strategies to promote prudent antibiotic use.[28]

In this current study, participants exhibited good knowledge on only two questions related to knowledge, with >50% accuracy. Approximately 55% recognise AMR as a public health threat affecting clinical practice, aligning with findings from a Swiss study, emphasising the need for a multifaceted approach to tackle AMR globally. Additionally, about 46% agreed that actions to combat AMR within the trust will affect society and future generations, which aligns with the United Nations report.[4] Critical knowledge gaps, especially in antimicrobial stewardship and antibiotic guidelines, have been identified, emphasising the need for refined, targeted educational interventions. This corresponds with the ECDC study, where a survey of 18,365 healthcare workers across 30 EU/EEA countries showed substantial knowledge of antibiotic use but notable gaps in understanding the development and spread of resistance. Despite efforts to raise awareness, only a small percentage of healthcare workers supplied patients with resources on prudent antibiotic use. These findings highlight the pressing need for targeted antimicrobial stewardship interventions to change prescribing behaviours.[30] Findings from this study prompt consideration of potential barriers to effectively implementing AMS during health crises and highlight the necessity for continual exploration and support in this domain.

A mixed-methods study involving 383 healthcare professionals identified educational and systemic adherence gaps to AMS principles, exacerbated during the pandemic. Findings underscore the need for targeted training and resources. Notably, HCPs displayed positive attitudes towards enhancing communication for AMS implementation, addressing a critical gap in AMS functionality.[31] A small percentage of participants in the current study strongly agreed and agreed with the statement, 'Time pressure challenges affected antibiotic decision-making.' Additionally, 'Prescribing broad-spectrum antibiotics is often viewed as more effective. '

The research in Cambodia highlighted that routine habits and insufficient microbiological support drive inappropriate antibiotic use.[32] Additionally, in England, doctors under stress often favour broad-spectrum antibiotics, inadvertently fostering AMR.[33] Despite this, healthcare professionals show a readiness for improved AMS communication, indicating a need for diverse strategies to address AMS challenges across healthcare systems effectively. This suggests the importance of using varied approaches in addressing AMS barriers among HCPs.

For practice, interestingly, approximately 42% of respondents strongly concurred that antimicrobial overuse during COVID-19 could exacerbate AMR, aligning with a 2022 study that highlighted rampant unnecessary antibiotic prescriptions during the pandemic. In a systematic review adhering to PRISMA guidelines, from 970 studies, 130 were analysed, revealing that 78% of COVID-19 patients received antibiotics, with cephalosporins (30.1%) and azithromycin (26%) most commonly prescribed. Antibiotic use was indiscriminate across severity levels, with similar rates in severe (77.4%) and mild cases (76.8%). Only 11 studies reported secondary infections. The findings underline the overuse of antibiotics during COVID-19 due to the absence of a clear treatment strategy, emphasising the urgent need to uphold antimicrobial stewardship during viral pandemics.[34] Additionally, 34% of participants agreed with the statement, 'Review the use of IV antibiotics post-receipt of culture results.' A 2021 study highlighted the importance of antibiotic review. The AMS intervention enhanced early antibiotic review and stop rates but necessitated further optimisation, particularly in decision-tool utilisation.[35]

Regarding the statement "Use of technology platforms like Zoom, Teams, or Skype for multidisciplinary meetings," 33% of participants agreed, aligning with a UK study during the pandemic that acknowledged technology as a crucial facilitator for stewardship, e.g., virtual meetings and ward rounds.[36] The pandemic dissolved barriers, enhancing collaboration and necessitating innovative approaches, such as adapting AMS implementation for antibiotic review. The virtual use of technology is proposed as vital for managing future emergencies and AMR.[36] In this study, approximately 22% of respondents concurred that "Antibiotic prescribing complied with the local antimicrobial guidelines." While COVID-19 has influenced clinical judgment and antibiotic selection, adherence to the AMS toolkit from the PHE, "Start Smart, Then Focus," is pivotal, especially during crises, to uphold judicious antibiotic use as far as possible.[15] Furthermore, elevating awareness of antimicrobial guidelines is anticipated to positively influence AMS and resistance in the long term.

## STRENGTHS AND LIMITATIONS

The current study has several strengths. First, this study focused on the assessment of KAP of HCPs towards antibiotic prescribing, AMS and AMR, particularly during the COVID-19 pandemic. Second, the study represents the KAP of HCPs during COVID-19 who worked in acute care settings and who were first approached in any upcoming emergency crisis. Nevertheless, the study has a few limitations. First, the generalisability of the findings to all the HCPs in the UK is not possible because it covers only one Foundation Trust in England. Second, the respondents were HCPs who currently worked in the Trust. Some of them have left the Trust since the pandemic. However, it provided an overview of the situation during the pandemic, which could help in providing insights regarding antibiotic prescribing during the crisis, how AMS was affected and actions that could be taken to establish an ongoing advocating AMS program, which would be beneficial to stand by in any upcoming emergency situation. Preparing educational and training resources that can help increase awareness regarding AMS and facilitate its implementation in the crisis would help promote the judicious use of antibiotics, decrease the AMR, and protect patients' lives.

## CONCLUSION

This pivotal study emphasises the urgent necessity of boosting awareness, knowledge, and the implementation of effective practices among healthcare professionals in the realm of antibiotic prescribing. It reveals the profound impact of COVID-19 on antimicrobial resistance (AMR) and antimicrobial stewardship (AMS), spotlighting the dire need for comprehensive AMS education and training programs. Analysing responses from 240 diverse healthcare professionals, predominantly pharmacists, the study reveals a median knowledge score of 50.13% and a spectrum of attitudes and practices toward AMS. These critical insights highlight the far-reaching implications of diminished AMS activities on AMR. The study advocates for the deployment of innovative tools, the provision of educational resources, and the enhancement of awareness and collaborative efforts. This approach is essential to strengthen AMS, combat AMR effectively, and safeguard patient health in today's challenging healthcare landscape.

## FUNDING

None

## TRANSPARENCY DECLARATIONS

Nothing to declare.

## AUTHOR CONTRIBUTIONS

All authors, RAE, NU, and ZA, were integral to formulating the research question, designing the study, and executing the study protocol. RAE and ZA were responsible for reviewing the literature and preparing the survey, while RAE also managed its distribution. RAE took the lead on data extraction, formal analysis, investigation, methodology, validation, visualisation, and the drafting of the original manuscript. NU and ZA provided supervision, contributed to the visualisation, and engaged in the review and editing of the manuscript. All authors conducted critical revisions and gave their final approval for the manuscript to be published.

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**SUPPLEMENTARY DATA**

Documents S1 to S3 are available as Supplementary data at JAC Online.

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**Supplementary 1.** Survey questionnaire exploring HCPs KAP towards antibiotic prescribing, AMS and AMR. here is the link to the survey: https://herts.eu.qualtrics.com/jfe/form/SV_1ZKfYklqov5KjIO

**Supplementary 2.** Information Sheet for Healthcare Professional Participants.

**Supplementary 3.** Survey Participation Invitation Letter for Healthcare Professionals.

# Appendix 69. Brief Report

Evaluation of COVID-19 Impact on Antimicrobial Stewardship in a UK Acute Care Setting.

Submitted to JAC-Antimicrobial Resistance.

# Brief Report: Evaluation of COVID-19 Impact on Antimicrobial Stewardship in a UK Acute Care Setting


## Abstract

A research project was conducted at a UK acute care setting, from March 2021 to September 2023. It comprises three sequential studies: a systematic review identifying key antimicrobial stewardship (AMS) strategies, a patient record review highlighting shifts in antibiotic prescribing, and a healthcare professional survey. Our data showed the essential role of multidisciplinary teams (93%), increased inappropriate antibiotic prescribing from 16% to 20%, and significant pandemic-induced disruptions in AMS activities. Our research emphasizes the urgent need for strategic adaptations in AMS to address healthcare challenges, aimed at reducing the threat of antimicrobial resistance and preserving patient lives.



## Keywords

Antimicrobial Stewardship, Antibiotic Prescribing, COVID-19 Impact, Acute Care Settings, Antimicrobial Resistance


## Introduction

Investigating Antimicrobial Stewardship (AMS) prior to and during the COVID-19 pandemic is crucial for responsible antibiotic use and combating Antimicrobial Resistance (AMR) in secondary care settings [1, 2]. The pandemic has significantly altered healthcare practices, emphasizing the need for robust AMS strategies. From 12 March 2021 to 20 September 2023, our research offers an in-depth analysis of AMS and antibiotic prescribing through three sequential studies: a systematic literature review, a retrospective examination of patient records, and a prospective survey questionnaire. This project, undertaken at an English NHS Foundation Trust, addresses the escalating AMR crisis [1] – a global health concern leading to treatment failures and impacting patient safety [2]. By emphasizing AMS as a pivotal response to AMR, this research focuses on the critical aspects of antibiotic management – selection, dosing, and administration [3]. It acknowledges the added complexities introduced by COVID-19 to the ongoing AMR challenge [4], underlining the urgent need for collaborative efforts. This study not only enhances the academic understanding of AMS during a global health emergency but also guides future strategies for antibiotic use, AMS implementation and AMR mitigation in healthcare settings.

**Materials and Methods**

This research project encompassed three sequential studies, each pivotal in examining AMS and antibiotic prescribing in acute care settings during the COVID-19 pandemic. Initially, a comprehensive systematic literature review, registered with PROSPERO [5], analyzed global AMS strategies and measures spanning two decades, from 2000 to 2021, both prior to and during the pandemic [6]. Subsequently, a retrospective study was conducted at Bedfordshire Hospitals NHS Foundation Trust, focusing on assessing antibiotic prescribing patterns. In this phase, 640 patient records were analyzed, focusing on particular demographics, using a validated data extraction tool. This tool was developed based on the literature review and the "Start Smart, Then Focus" AMS Toolkit provided by Public Health England. [7]. Before undertaking the patient records review study, a pilot extraction involving 80 patient records was performed to ensure the validity and reliability of the data extraction tool. Given that AMS is a strategic approach to ensure the prudent use of antibiotics, a comprehensive evaluation of the impact of COVID-19 on AMS necessitates an immediate investigation into healthcare professionals' knowledge, attitudes, and perceptions regarding antibiotic prescribing during the pandemic. The final phase was a prospective survey targeting 240 healthcare professionals. This survey was designed to explore their knowledge, attitudes, and perceptions towards antibiotic prescribing, AMR, and AMS practices during the pandemic. Before launching the survey study, a pilot involving 50 participants was carried out to validate and confirm the reliability of the survey questionnaire. The data collected were analyzed using descriptive statistics in IBM SPSS, ensuring both reliability and validity of the survey. The insights from the survey have significantly contributed to the existing body of knowledge on AMS.

This research project is registered in the ISRCTN registry, and its findings are published in Octopus [8, 9]. Involvement of the public and patients was ensured by consulting with the Citizens Senate, which helped align the study with patient care concerns, ensuring its relevance and responsiveness.

**Figure 1.** Description of research methods, this research project consists of THREE sequential studies

**A Systematic literature review**

**A systematic literature review** of studies on antimicrobial stewardship (AMS) implementation has been conducted to investigate AMS strategies in acute care settings over the past 20 years. This review encompasses research conducted in acute care settings both prior to pandemic (PD) and during the COVID-19 pandemic (DP) on a global scale. The systematic literature review was registered with [PROSPERO] (registration number CRD42021242388) (York.ac.uk, 2022). The study has been successfully published in the PMC (PubMed Central) Journal.

**A retrospective study**

**A retrospective study** was undertaken at Bedfordshire Hospitals NHS Foundation Trust to assess antibiotic prescription patterns and AMS implementation before and during the COVID-19 pandemic. The study used medical records from adults aged 25+, pregnant women, and immunocompromised patients admitted in 2019 and 2020 with certain respiratory conditions. Exclusions included short A&E stays, non-prescription of antibiotics, and children. In total, 640 records (320 annually) were examined, each taking around 45 minutes. Data collection spanned 8 distinct periods, including four each from pre-pandemic and pandemic times. The review employed the PHE 'Start Smart - Then Focus' toolkit for validation.

**A prospective survey study**

**A prospective survey study** was conducted among healthcare professionals to gauge their understanding and perspectives on antibiotic prescription, AMR, and AMS during the COVID-19 era. The questionnaire was crafted from the PHE's report on secondary care hospital antibiotic prescriptions. The Royal Pharmaceutical Society and AMS pharmacists at the Trust validated the survey content. It targeted 240 healthcare professionals, specifically doctors, nurses, and pharmacists aged 25+. These professionals had to be registered with bodies like the GMC, GPhC, or NMC. Those lacking pandemic-era experience at the Trust were excluded. The chosen sample size ensured robust data collection for thorough analysis.

**Results**

In the initial phase of the study, a comprehensive systematic literature review was conducted, retrieving 8,763 articles from various databases. From these, 13 full-text articles were selected based on the inclusion criteria for the review. The studies focused on AMS implementation, categorizing strategies into core and supplemental, along with AMS measures like BP and DP. This phase underscored the vital need for effective AMS, especially during the COVID-19 pandemic. The review highlighted the importance of a multidisciplinary team approach in AMS, evident in 93% of the reviewed studies. Prospective audits and feedback were prominent in 92% of the studies. Additionally, 77% included quality improvement initiatives, while antibiotic reviews, AMS education, and guideline implementation were featured in 69% of the studies, underlining their significance in AMS strategies and measures

[6]. Tailoring AMS interventions to local resources and executing proactive audits and reviews were especially effective during the pandemic. Implementing guidelines, establishing clinical pathways, and launching educational programs emerged as critical for the success of AMS [6].

The second phase of this research project entailed a detailed review of 640 patient records, focusing on antibiotic prescribing patterns for respiratory tract infections (RTIs), including pneumonia, during the years 2019 and 2020 at a UK acute care setting, NHS Foundation Trust. This phase, guided by the WHO's AWaRe classification, aimed to assess the pandemic's impact on antibiotic prescribing and AMS [10]. A significant portion of the study's participants, primarily aged 66-85 years, accounted for 48.8% in 2019 and 46.3% in 2020. Community-Acquired Pneumonia (CAP) was the most common diagnosis, affecting around 39.4% of patients prior to pandemic and 42.5% during the pandemic. The timing of antibiotic reviews post-admission usually occurred within 48-72 hours, with no notable difference between 2019 and 2020. However, the pandemic saw significant shifts in AMS interventions, such as 'Continue Antibiotics' and 'De-escalation', indicating changes in clinical decision-making. The usage of amoxicillin/clavulanic acid increased slightly, whereas azithromycin prescriptions rose substantially, reflecting a shift in prescribing trends. Despite these changes, the consumption of some antibiotics remained consistent [7].

In terms of evaluating the five rights of antibiotic safety, as defined by the Institute for Healthcare Improvement (IHI), this phase of the study also revealed an increase in inappropriate antibiotic prescribing without proper indication, rising from 16% in 2019 to 20% in 2020 [11]. Inappropriate routes of administration increased slightly, while inappropriate drug choice remained stable. Interestingly, inappropriate dosing rose, but inappropriate duration decreased slightly [12]. In terms of AMS participation, the involvement of pharmacists increased slightly, while that of physician decreased. However, combined collaboration among healthcare professionals showed a significant increase. These findings emphasize the evolving nature of antibiotic use during the pandemic and the critical role of robust AMS measures [12]. This phase reinforces the importance of integrating the AWaRe classification into prescribing decisions for enhancing patient safety and mitigating antibiotic misuse [7].

The last phase, this cross-sectional study, carried out between June and October 2023 within the same acute care setting, involved surveying 240 healthcare professionals (HCPs). The survey comprised 12 close-ended questions, developed based on the Public Health England (PHE) literature review focusing on behaviour change and antibiotic prescribing [13]. The survey results revealed that the majority of respondents were pharmacists (52%), with doctors (30%) and nurses (18%) following. The most represented age group was 32-41 years (40%), and a significant 86% of participants held postgraduate degrees. The findings showed a median knowledge score of 50.13%, indicating a moderate level of understanding regarding AMS and antibiotic prescribing practices. The study also highlighted the impact of COVID-19 on AMS activities, with notable disruptions in stewardship education (81.3%), ward rounds (74.6%), and audit feedback (70.0%). Interestingly, only a small percentage (15.8%) observed a positive impact on multidisciplinary team meetings. For comprehensive results, please refer to Supplement Report 1.

Recommendations

This research project underscores the urgent necessity to address the escalating misuse of antibiotics, a situation exacerbated by the COVID-19 pandemic. Key recommendations include the formation of multidisciplinary AMS committees in each healthcare Trust and the regular update of local antibiotic guidelines informed by ongoing surveillance. It is crucial to conduct regular AMS ward rounds, enhance professional training, and establish connections across different healthcare settings. Further, integrating AMS measures into electronic systems and promoting AMS research are essential steps.

From an academic standpoint, embedding AMS in the curricula of both undergraduate and postgraduate healthcare disciplines is vital. This should be complemented by interprofessional education and dedicated AMS-focused registration programs. In clinical practice, appointing AMS leads, conducting frequent antibiotic reviews, and improving documentation practices are imperative. Aligning local antibiotic policies with updated guidelines and ensuring their accessibility are also critical.

Key research outputs include the development of an AMS Roadmap, a Dynamic Dashboard, and a comprehensive training program, all of which contribute significantly to the efficacy and implementation of AMS. These tools are particularly useful for adapting AMS strategies to overcome challenges posed by the pandemic. In the post-pandemic landscape, the role of pharmacists in AMS is highlighted as increasingly important. For detailed recommendations, refer to Supplement Report 1.

Future research directions should focus on assessing both the short-term and long-term impacts of AMS on a global scale, particularly in terms of clinical, economic, and resistance outcomes. This involves evaluating the effectiveness of AMS programs after their implementation, continuously updating antimicrobial medicine guidelines, and expanding surveys to capture diverse perspectives on antibiotic use.

**Conclusion**

This comprehensive study, encompassing a literature review, patient record analysis, and a healthcare professional survey, highlights the critical aspects of antimicrobial stewardship (AMS) during the COVID-19 pandemic. Key findings include the necessity of a multidisciplinary team approach in AMS (93%), the importance of audits and feedback (92%), and the role of quality improvement initiatives (77%). The review of 640 patient records at an NHS Foundation Trust revealed significant shifts in antibiotic prescribing, with a rise in inappropriate prescribing from 16% in 2019 to 20% in 2020. The survey of 240 healthcare professionals showed a moderate understanding of AMS (average score: 50.13%) and highlighted the pandemic's disruptive impact on AMS activities. These results underscore the need for robust AMS measures, tailored interventions, and continuous education to enhance patient safety and mitigate antibiotic misuse. The study advocates for strategic, multidisciplinary approaches in AMS to effectively manage antimicrobial resistance in the evolving healthcare landscape.

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**Potential conflicts of interest.** All authors: no reported conflicts.

**Author contributions.** RE: Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft. NU: Supervision, Visualization, Writing – review & editing. ZA: Supervision, Visualization, Writing – review & editing.

**Patient consent.** The retrospective study did not require informed consent due to its nature.

**Ethics approval.** Ethical approval for this study was granted by the Health Research Authority (HRA), with the Research Ethics Committee (REC) assigning reference number 22/EM/0161. In compliance with this approval, the study protocol underwent review and received approval from the University of Hertfordshire (UH) ethics committee under the reference LMS/PGR/NHS/02975.

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# Appendix 70.

Maximising Survey Participation: Novel Distribution Strategies in Survey Questionnaire Research Study Exploring Antimicrobial Stewardship and Prescribing During COVID-19 Pandemic at a Secondary Care Setting in England.

Submitted to BMJ Global Health.

# Maximising Survey Participation: Novel Distribution Strategies in Survey Questionnaire Research Study Exploring Antimicrobial Stewardship and Prescribing During COVID-19 Pandemic at a Secondary Care Setting in England

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**Summary Box**

- This communication addresses the global health challenge of Antimicrobial Resistance (AMR), exacerbated by the COVID-19 pandemic, emphasising the need for comprehensive research on antimicrobial stewardship and prescribing practices.
- Multidisciplinary collaboration: Conducted at an NHS Foundation Trust, this research project exemplifies the significance of collaborative efforts between academia and healthcare institutions for evidence-based research in addressing AMR.
- The survey questionnaire study employed eye-catching, professionally designed posters featuring QR codes to attract healthcare professionals' attention and encourage survey participation.
- The inclusion of QR codes in poster designs provided a quick and easy way for healthcare professionals to access and complete the survey directly.
- The research strategically utilised digital channels, such as group emails and newsletters, to distribute the survey effectively among healthcare professionals.
- The combination of visual appeal and technological convenience in the survey distribution approach aimed to maximise engagement and response rates in secondary care settings.
- By using both traditional and modern dissemination methods, the study ensured that the survey was easily accessible to a broad audience of healthcare professionals, enhancing the overall participation rate.

**Introduction: The Global Impact of Antimicrobial Resistance and the COVID-19 Pandemic**

Antimicrobial resistance (AMR) is a critical global health issue, with over 1.2 million deaths in the previous year.[1] In 2016, the O'Neill[1] review highlighted an impending silent pandemic, foreseeing a staggering 10 million yearly deaths due to AMR by 2050, amounting to one death every three seconds.[2] This startling projection underscores the pressing need for coordinated action, innovation, and collaboration to stave off this looming public health disaster.[3] In 2019, the World Health Organization (WHO) categorised AMR among the top ten global public health threats necessitating immediate intervention.[4] Antimicrobial stewardship, an organisational strategy advocating judicious antibiotic use, is pivotal to the UK's Five-Year Antimicrobial Resistance Strategy.[5] The World Health Organisation (WHO) reported that the COVID-19 pandemic caused over 6 million deaths, therefore amplifying the AMR health crisis.[6 7] In secondary care settings, the easing of pandemic restrictions and the return to pre-pandemic health activity levels led to a significant increase in both priority pathogen rates and antibiotic prescribing behaviours.[8 9] This highlighted the need for an in-depth understanding of how the pandemic influenced antibiotic prescribing and antimicrobial stewardship (AMS).[10] Antimicrobial stewardship, an organisational strategy advocating judicious antibiotic use.[11 12] In order to tackle this concern, a two-phase doctoral research project was initiated to explore antimicrobial prescription practices and AMS at an NHS Foundation Trust located in the East of England. The project aimed to investigate the period prior-to-the-pandemic (PD) as well as the period during-the-pandemic (DP).

**Patient and Public Involvement**

Patient and public involvement played a crucial role in this study. The study was shared with representatives from the Citizens Senate. Their valuable input and feedback were sought and incorporated into the study.

**Registration**

This study has been officially registered with the ISRCTN registry. The ISRCTN registry is a primary registry acknowledged by the WHO and the International Committee of Medical Journal Editors (ICMJE), accepting all clinical research studies.[13] Moreover, it was registered in Octopus, the global primary research record.[14]

**Two-Phase Doctoral Research Project in Antimicrobial Prescribing and Antimicrobial Stewardship**

The commencement of the research project took place subsequent to obtaining the essential ethical approvals from the HRA. The first phase involved an extensive case note review of 640 patients from 2019 and 2020, taking about 45 minutes per case to gather relevant information. The results offered valuable insights into antibiotic prescribing and AMS implementation PD and DP. The second phase used a survey questionnaire to explore healthcare professionals' perceptions, attitudes, and knowledge concerning antibiotic prescription practices PD and DP. This phase started after receiving the Trust's ethics approval with the confirmation of Capacity and Capability (C&C), an anonymous online survey circulated among doctors, nurses, and pharmacists within the Trust. The survey commenced on Monday, June 12, 2023, and concluded on Wednesday, September 13, 2023. Hosted on the secure Qualtrics platform, the survey was distributed electronically alongside an invitation letter, a Participant Information Sheet (PIS),[13] and a professionally designed poster. The sample size for the survey was determined to be 240, with a margin of error of 5%, a confidence interval of 95%, and an anticipated response rate of 20%.

**Innovative Poster Design for Engaging Healthcare Professionals**

To secure approval from the Health Research Authority (HRA), it's vital to create engaging materials for healthcare professionals. Accordingly, the primary author developed a healthcare-oriented poster, which was included in the ethics application. The poster designed for Bedfordshire Hospitals NHS Foundation Trust serves as a dynamic and compelling invitation to participate in a survey about antibiotic prescribing and AMS practices during the COVID-19 pandemic. Featuring eye-catching colours, strong typography, and relevant graphics like QR codes and medical imagery, it aims to involve doctors, pharmacists, and nurses. The poster clearly outlines its goals, offers user-friendly access, and its ethical approval enhances credibility. Effectively blending visual and content elements, it communicates its purpose to the target audience, making it an effective tool for promoting participation and facilitating the research study. See Figure 1 for the professional poster aimed at healthcare professionals within the Trust.

**Figure 1.** Professional A4 Poster for Healthcare Professionals: Distributed Across All Wards and Departments of Bedfordshire Hospitals NHS Foundation Trust, Including Luton and Dunstable Hospital and Bedfordshire Hospital.

NHS Bedfordshire Hospitals NHS Foundation Trust

THRIVE: Teamwork, Honesty & openness, Respect, Inclusivity, Valuing people, Excellence

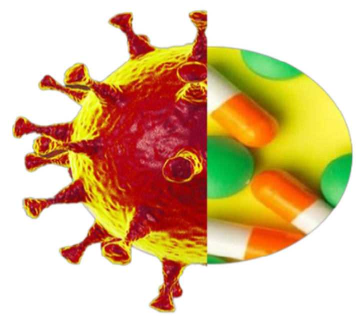
University of Hertfordshire UH

**Call for Participants for Survey Questionnaire Study!**

**Investigating Attitudes of Doctors, Nurses, and Pharmacists Towards Antibiotic Prescribing Before and During the COVID-19 Pandemic at Bedfordshire Hospitals NHS Trust**

- Looking for doctors, pharmacists, and nurses working in Bedfordshire Hospitals NHS Foundation Trust.

- This survey questionnaire aims to explore the attitudes and perceptions of healthcare professionals towards Antibiotic prescribing and Antimicrobial Stewardship (AMS) practices, both before and during the COVID-19 pandemic.



- If you are interested in participating in the survey, kindly capture an image of the **QR Code** provided.

- For any additional queries regarding this study, Rasha Abdelsalam Elshenawy is available for contact.


REC Reference: 22/EM/0161 - East Midlands Leicester South Research Ethics Committee

Version 2 – Date: 24/05/2023

Thank you!
Rasha Abdelsalam Elshenawy
On behalf of the research team

Contact Details Work Number: 07393530537 Email: Rasha.Elshenawy@ldh.nhs.uk

### Innovative Survey Dissemination Strategies in Healthcare Settings

Innovative approaches were employed to enhance the survey's visibility and participation. A prominently displayed QR code was developed on posters to facilitate direct access and completion of the survey. The poster was designed using attractive elements and pertinent information on the survey study, which were disseminated widely within the healthcare environment and strategically positioned in high-visibility areas in the wards. The survey was shared with the 'Communication Team' within the Trust to distribute the survey digitally via weekly newsletters and group emails. Moreover, the timing for sending group emails was also carefully considered. The preferred slots were selected as 8-9 am in the morning, prior to the commencement of a busy day, lunch break between 12-1 pm, and finally, at the day's end from 5-6 pm. Novel and innovative dissemination strategies were employed, leveraging effective communication and coordination with ward managers and matrons to facilitate the widespread physical dissemination of the survey within the wards.

### Innovative Survey Dissemination Strategies in Healthcare Settings

Novel distribution strategies, spearheaded by the research pharmacist in collaboration with ward managers, sisters in charge, and matrons, were employed to enhance the visibility of the survey within the wards. These multi-disciplinary efforts, highlighting the vital role of pharmacists, led to an encouraging interest among the staff, who were keen to complete the survey when it was introduced. Survey posters were strategically displayed in nurses' stations, staff rooms, on medicine trolleys, and near main workstations. To ensure doctors' awareness, posters were also placed in the Multidisciplinary rooms (MDT), close to doctors' desktops and on notice boards within the rooms. Moreover, the survey was placed in the medicine room and on IV antibiotics cabinets in clean rooms and treatment rooms, further extending its visibility.

### Multidisciplinary Collaboration for Survey Distribution in Wards

The R&D department recommended two poster sizes for broad dissemination: A4-sized for ward displays and A5 for medicine trolleys. The A5 posters, aimed at healthcare staff, were placed in key areas, such as nurses' stations, lounges, workstations, and notice boards in Bedfordshire Hospitals NHS Foundation Trust's Luton & Dunstable Hospital and Bedfordshire Hospital. See Supplements 1-3 for various sizes of the poster.

### Combining Technology and Traditional Methods for Survey Visibility

To encourage survey participation, 50 A4-sized survey posters were printed and distributed across all wards and departments by the primary author. Additionally, the poster image served as an email header to promote the survey link, and a QR code was shared in the Trust's newsletter and group emails, successfully reaching healthcare professionals in Bedfordshire. The AMS pharmacists within the Trust took the initiative to disseminate the survey electronically amongst all pharmacists. This strategy was intended to enhance responses and motivate them to participate in the survey. Employing contemporary technology alongside traditional distribution techniques, enriched by previously introduced innovative ideas, significantly enhanced the survey's visibility within the Trust. Maximising survey responses through these novel comprehensive hospital-wide distribution strategies highlighted the significance of improved antibiotic prescribing in battling AMR. They heightened awareness among healthcare professionals about their essential role in this global crisis. The pharmacy department played a pivotal role, prominently displaying the poster on the primary pharmacy board, clinical board, antimicrobial stewardship board, and even in the pharmacy's kitchen area. A chronological order of survey distribution at Bedfordshire Hospitals NHS Foundation Trust (Both L&D and Bedford hospitals) is given in Table 1.

**Table 1.** Chronological order of the survey distribution among HCPs at the Trust.

| Date | Survey Activity |
|---|---|
| **12th June 2023** | ● A visit was made to the L&D hospital to ensure the distribution of the invitation package by the R&D and AMS pharmacist, who sent an invitation email to the HCPs to invite them to participate in the survey initially.<br>● The researcher had a meeting with the R&D department to discuss the survey distribution, poster design, and suitable printing sizes.<br>● The R&D recommended printing two sizes: an A4-sized poster to be displayed in the wards and an A5 poster to be displayed on medicine trolleys.<br>● Additionally, they recommended using laminated posters to avoid contamination within the wards.<br>● Finally, they suggested designing another size for the poster to be used as a header in the invitation emails. They also recommended that the researcher distribute the survey and discuss the purpose of the survey with the staff in the wards to encourage responses. |
| **19th June 2023** | ● To promote survey responses, the researcher printed 50 A4-sized survey posters and requested that ward managers and the head of department distribute them in L&D hospital.<br>● The researcher attended the AMS round, discussing ways to distribute the survey within the Trust successfully with the AMS lead, microbiology consultant, and AMS pharmacists.<br>● Doctors, nurses, and pharmacists were approached by researchers, who explained the survey's purpose and target population as a strategy to increase recruitment and distribution. A week later, an increase in the responses was recorded.<br>● Survey posters were placed and displayed in several strategic locations in L&D hospital, such as nurses' stations, staff rooms, main halls, notice boards, and medicine trolleys in the bays.<br>● One ward manager proposed placing the survey poster on the computer desk in the nurses' station.<br>● Another sister in charge shared the poster within the nurses' WhatsApp group. A different ward manager forwarded the survey link to doctors and nurses using group emails.<br>● The pharmacy cooperated by displaying the survey on the Antimicrobial Stewardship Clinical Board, the main notice board, and the digital pharmacy screen and by sending it to all pharmacists via email. |
| **22nd June 2023** | ● The AMS pharmacist at Bedford Hospital sent the in-survey invitation package to the pharmacists, while the R&D sent the invitation package to the doctors and nurses using group emails.<br>● The researchers printed 50 copies of A4 and A5 posters and requested that the ward managers and head of department distribute them in the hospital.<br>● The survey posters were placed and displayed in various strategic locations, such as MDT rooms, staff rooms, treatment rooms, doctor rooms, main halls, notice boards, nurses' stations, medicine trolleys in ward bays, and clean rooms at Bedford Hospital.<br>● One ward manager suggested placing the survey poster as a mouse pad for the main desktop computers in the wards.<br>● Another sister in charge placed the poster in front of the desktop computer and on the counter. |
| **7th July 2023** | ● The communication team within the Trust sent the survey invitation package in the weekly newsletter, 'The Week,' to all HCPs within both hospitals. |

| | |
|---|---|
| **21st July 2023** | • After two weeks, the communication team within the Trust re-sent the survey invitation package in the weekly newsletter 'The Week' to all HCPs within both hospitals. |
| **29th July 2023** | • The R&D department resent the survey invitation package to the doctors, pharmacists, and nurses using the group emails. |
| **16th August 2023** | • There was no increase in responses, possibly due to the summer holidays.<br>• The researcher met with the supervisors to discuss methods to encourage survey responses.<br>• They recommended waiting until September, when people return from summer holidays, and then resending the survey link. |
| **6th September 2023** | • The researcher sent an email to the R&D and AMS pharmacists at both hospitals, as well as the AMS lead, requesting the re-circulation of the survey packages and suggesting the addition of a sense of urgency to the invitation email.<br>• The researcher drafted a message with an urgent tone to be used for survey dissemination.<br>• The researcher sent an email to the Communication Team within the Trust, requesting the inclusion of the survey links in the weekly newsletter 'The Week' and proposed using an attractive title: 'A Vital Call to Action'. |
| **13th September 2023** | • As the number of responses decreased, the researcher communicated with the AMS pharmacist and the AMS lead in the Trust, suggesting they circulate the survey via the Trust's WhatsApp groups for pharmacists, doctors, and nurses. |
| **15th September 2023** | • The data collection period has ended. |

The combination of traditional methods, technological dissemination, and varied poster sizes, along with newsletter circulation, significantly enhanced survey responses. While initially low, consistent exposure to posters in wards and on medicine trolleys increased engagement. Critical to this success was the distribution of the survey via weekly newsletters, group emails, and WhatsApp groups by the Trust Communication Team, R&D and AMS team. Timely reminders to health professional leaders like ward managers, matrons, and AMS leads were pivotal in quickly reaching the target response rate. Additionally, the personal approach of the primary investigator explaining the survey during poster placement in wards, and demonstrating QR code access, markedly improved compliance and participation among healthcare professionals. For the comprehensive poster titled "Maximising Survey Participation in AMR Research: Novel Distribution Strategies," please refer to Supplement 4.

### Final Report Circulation and Dissemination of Insights

Upon completing the survey analysis, the primary author prepared and circulated the final report, encompassing key findings, to healthcare professionals at the Foundation Trust via the weekly newsletter and group emails. In alignment with World Antibiotic Awareness Week (WAAW), insights from this research were shared on Springer Nature Community, offering an evaluation of antimicrobial stewardship in the context of COVID-19 and its role in combating antimicrobial resistance within the United Nations (UN) Sustainable Development Goals framework. Special gratitude is extended to the AMS team at the Bedfordshire Hospitals NHS Foundation Trust and the University of Hertfordshire for their unwavering support. Their commitment has greatly contributed to the research and the global battle against AMR. The Final report of this research project has been submitted successfully to the HRA website.[15] Appreciation is also due to the antimicrobial stewardship pharmacists at the Trust for their collaborative efforts in AMR research and to the Trust's R&D department for their invaluable support in the PhD project on antimicrobial stewardship during the pandemic.[16]

**Conclusion**

A multidisciplinary team approach is vital for conducting consistent and integrated research projects. The collaboration between academic institutions and NHS trusts is key in conducting evidence-based research to tackle AMR, deepening our understanding of AMS and prescribing practices. Consistently distributing this survey questionnaires enhances response rates and heightens healthcare professionals' awareness of AMR and AMS. Employing both traditional and digital methods for survey distribution ensures comprehensive and integrated responses. Such collaborative efforts are instrumental in translating AMR awareness into action, thereby promoting judicious antibiotic use and sustaining AMS implementation. Moreover, lessons learned from the COVID-19 pandemic regarding its impact on antibiotic prescribing, AMS, and AMR provide actionable insights. These novel survey distribution strategies are crucial for maintaining effective AMS practices, addressing the AMR challenge, ensuring sustained AMS implementation, and preparing for future health emergencies.

**Ethical Approval**

Ethical approval for this study was granted by the Health Research Authority (HRA), with the Research Ethics Committee (REC) assigning reference number 22/EM/0161. In compliance with this approval, the study protocol underwent review and received approval from the University of Hertfordshire (UH) ethics committee under the reference LMS/PGR/NHS/02975. The authors have no conflicts of interest to disclose.

**Financial support**

Not applicable.

**Competing Interests**

The authors declare no competing interests.

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# Appendix 71.

SWOT Analysis and Insights into the Health Research Authority Approval Process for COVID-19 Antimicrobial Stewardship Research in UK Secondary Care: Advocating Think Ethics (Preprint).

# SWOT Analysis and Insights into the Health Research Authority Approval Process for COVID-19 Antimicrobial Stewardship Research in UK Secondary Care: Advocating Think Ethics

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**Abstract:**

This article explores the Health Research Authority's (HRA) approval process for a research project on antimicrobial stewardship (AMS) conducted at an English NHS Foundation Trust during the COVID-19 pandemic. The project, involving a retrospective review of patient records and a survey of healthcare professionals, faced the intimidating task of navigating the Integrated Research Application System (IRAS). The streamlined HRA process, incorporating a thorough review by the NHS Research Ethics Committee (REC) and regulatory checks, efficiently replaced the need for multiple reviews across NHS organisations. Obtaining HRA approval required strict adherence to confidentiality requirements and thorough documentation submission, including research protocols and participant information sheets. The REC's evaluation process covered both full committee reviews and proportionate reviews, each with specific timeframes. This methodical approach ensured the protection of participant rights and dignity. Post-approval, the project could not commence until all regulatory approvals were in place, necessitating effective project management skills and strategic communication. The study yielded valuable insights into AMS practices prior to and during the pandemic, highlighting shifts in antibiotic prescribing patterns and the impact of COVID-19 on these practices. Notably, the study revealed the importance of robust AMS to ensure appropriate use and combat antimicrobial resistance. Reflecting on this journey, key lessons include the importance of public and patient involvement, the effectiveness of engaging materials for participant recruitment, the benefits of registering research for global collaboration, and the necessity of addressing feedback constructively. These experiences have significantly contributed to the authors' professional growth, enhancing research skills and reinforcing the importance of ethical considerations and clear communication in research projects. This article offers a comprehensive view of the HRA approval process and its implications for future research projects, particularly in the field of AMS and antimicrobial resistance, which is a global health threat.

**Introduction:**

The journey in securing Health Research Authority (HRA) approval for a research project at One English NHS Foundation Trust was a defining experience in my academic career (1). This project comprised two studies: a retrospective review of NHS patient records and a prospective survey questionnaire of healthcare professionals at the Trust. Navigating the application process via the Integrated Research Application System (IRAS) was initially daunting, but the system's user-friendly design, which included auto-population of relevant fields and an average completion length of about 20 pages, made it manageable (2). This article's objective is to delve into the lessons learned from navigating the HRA ethical application process, coupled with a reflective analysis using the SWOT model. The project entailed a retrospective review of NHS patient records and a forward-looking survey among healthcare professionals, offering profound insights. These experiences are integral to the 'Think Ethics' initiative, advocating the value of strategic evaluation in the realm of research.

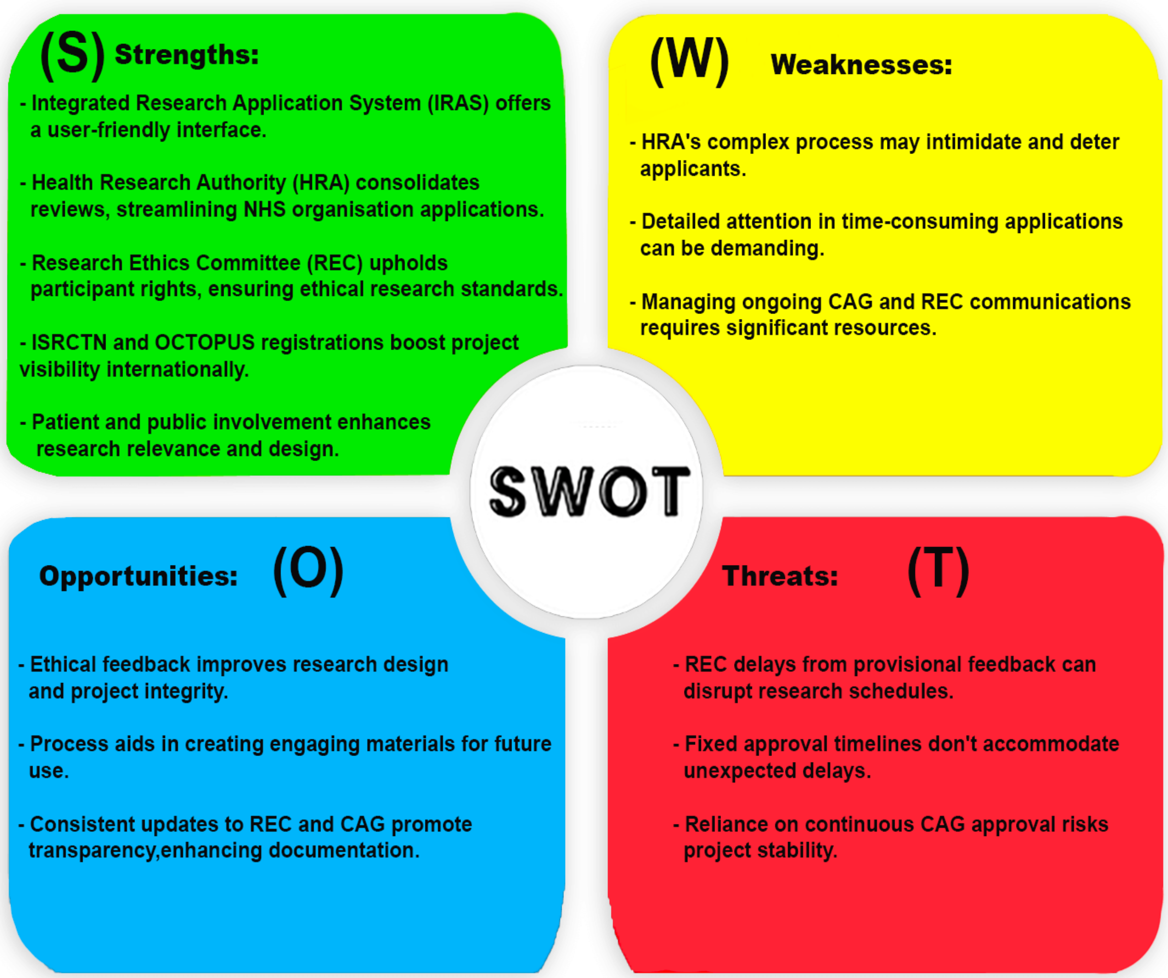
**Methods:**

In this study, the Health Research Authority (HRA) approval process was meticulously followed, involving an extensive review by the NHS Research Ethics Committee (REC) and regulatory compliance and governance checks by HRA staff. This procedure replaced the necessity for multiple reviews by various NHS organisations, thus streamlining the focus of their study delivery capabilities (3). Central to gaining HRA approval, especially due to the requirement of accessing confidential patient information without consent, was a stringent adherence to the Confidentiality Advisory Group (CAG) application guidelines. This involved submitting a cover letter, a signed application form, the research protocol, data protection registration, and a Caldicott Guardian endorsement, with the approval contingent on both HRA and REC endorsements. The REC application played a vital role in ensuring the protection of participant rights and dignity. This necessitated a comprehensive submission of documents through the Integrated Research Application System (IRAS), including the research protocol and participant information sheets. The REC's evaluation process encompassed either full committee reviews or streamlined proportionate reviews, each with a designated timeframe. The process for booking a REC meeting via IRAS was clearly guided and straightforward. Following the booking, the REC Manager assessed the application's validity and issued a validation letter. The REC meeting provided a platform to address any ethical concerns with the committee directly (4-6). Additionally, the SWOT analysis was employed to provide a reflective analysis of the various aspects of this process, enhancing our understanding of the practical dynamics involved in securing HRA approval.

**Results**

After receiving the REC's favourable opinion, it was crucial not to start the research until all regulatory approvals were in place. The study had to commence within 12 months of approval, and any significant amendments required re-approval.  The SWOT analysis of the Health Research Authority (HRA) Approval Process for the Antimicrobial Stewardship NHS Research Project revealed distinct strengths, weaknesses, opportunities, and threats. Strengths included the user-friendly IRAS interface, HRA's consolidation of reviews, REC's upholding of ethical standards, and the visibility boost from ISRCTN and OCTOPUS registrations (7, 8). Weaknesses were identified as the intimidating complexity of the HRA process, the demanding nature of detailed applications, and the resource-heavy management of CAG and REC communications. Opportunities emerged from ethical feedback enhancing research design, while threats involved REC delays potentially disrupting schedules and the risks associated with continuous CAG approval reliance. The streamlined ethical approval process facilitated the development of robust studies, such as the descriptive study on the WHO AWaRe classification for antibiotic stewardship in addressing antimicrobial resistance at an English NHS Foundation Trust before and during the COVID-19 pandemic (10). Another pivotal study evaluated the 'Five Rights' of antibiotic safety at the same NHS Foundation Trust during the aforementioned periods (11). Furthermore, research findings have been shared in a poster presentation at the Royal Pharmaceutical Society and subsequently published in the International Journal of Pharmacy Practice (12). Further work includes an ongoing publication titled "Start Smart, Then Focus: Antimicrobial Stewardship Practice at One NHS Foundation Trust in England Before and During the COVID-19 Pandemic" (13), along with other forthcoming articles.

**Figure 1.** SWOT Analysis of the HRA Approval Process for the Antimicrobial Stewardship NHS Research Project.



**Discussion:**

The SWOT analysis advocates the HRA's pivotal role during the COVID-19 pandemic, facilitating the research project approvals essential for rapid vaccine development and other medical interventions. Despite strengths like the user-friendly IRAS and the efficient review consolidation, the complexity of the HRA process and the intensive resource demands for CAG and REC communications are areas that could benefit from the new ways of working, as suggested by the public involvement. Committee feedback highlights the value of diverse perspectives and structured discussions, which aligns with identified opportunities for enhancing research design through ethical feedback. Addressing the consistency of information and improving discussion frameworks could further streamline the ethics review process, potentially mitigating the threats posed by delays and continuous approval dependencies. The study gathers insights from 151 UK Research Ethics Committee members, evaluating the effectiveness of ethics reviews for rapid COVID-19 medical interventions. Emphasising the importance of diverse input and structured discussions, it identifies the need for more consistent information and clear guidance on key issues as areas for improvement (9).

**Conclusion:**

The HRA application process, guided by the 'Think Ethics' principle, was an enlightening journey that enhanced our research skills and project management capabilities. It advocated the necessity of extensive preparation, ethical consideration, and clear communication in research. These experiences have substantially contributed to my professional development and the quality and integrity of my research project. The lessons learned are outlined below:

1. Understanding ethics requirements, such as public and patient involvement, enriches research by ensuring relevance, enhancing study design, improving materials for clarity, and fostering ethical standards that resonate with participant needs and perspectives.
2. Developing attracting materials proved crucial for enhancing participant involvement. For instance, the strategic use of a healthcare poster significantly encouraged survey participation. Placing this poster in key areas, such as wards and staff rooms, effectively reached healthcare professionals, thereby encouraging a higher response rate to the survey.
3. Registering research in ISRCTN and OCTOPUS increases visibility, promotes transparency, aligns with international standards like WHO criteria, and facilitates global collaboration in clinical research (7).
4. Efficient project management requires effective organisation, prioritisation, and budgeting of research activities.

5. Responding to provisional or unfavourable feedback, although challenging, is essential for research enhancement. This includes a thorough review of committee comments and addressing concerns in a detailed response. Initially, this process seemed daunting, but it soon became evident how vital it was for upholding the integrity of the research.
6. Responses to the REC needed to be concise, clear, and well-referenced, addressing all requested changes.
7. Regular communication with the CAG to manage the Annual Review and Closure Form ensures timely support and the conclusion of the study. Keeping the REC updated about research progress and submitting the final report is critical for providing valuable feedback and sharing research outcomes.
8. The SWOT analysis of the HRA Approval Process, as detailed in Figure 1, evaluates internal (Strengths and Weaknesses) and external (Opportunities and Threats) factors impacting the success and integrity of this NHS research project.

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# Appendix 72.

How Pharmacists Can Contribute to Effective Antimicrobial Reviews: Best practice principles and practical advice for structuring antimicrobial reviews and effective stewardship practices.

Published in Pharmaceutical Journal, February 2024.

# How Pharmacists Can Contribute to Effective Antimicrobial Reviews

*Best practice principles and practical advice for structuring antimicrobial reviews and effective stewardship practices.*

By: Rasha Abdelsalam Elshenawy

After reading this article, you should be able to:

- Understand the role of essential antimicrobial stewardship tools and frameworks to improve antibiotic prescribing;
- Structure an antimicrobial review effectively, covering all relevant details;
- Personalise the antimicrobial review to ensure patient-centred care and effective antimicrobial stewardship practices;
- Develop skills for effective antimicrobial review and stewardship practices to mitigate antimicrobial resistance threat.

Antimicrobial resistance (AMR) significantly impacts global public health, having been linked to approximately 4.95 million deaths in 2019 [1]. This resistance strains healthcare systems and carries considerable economic implications. A key factor driving antimicrobial resistance is the consumption of antibiotics, with higher usage promoting resistance both at population and individual patient levels [1]. Although antibiotic use varies widely between and within healthcare systems, antimicrobial reviews provide crucial opportunities to optimise antibiotic prescribing and reduce the misuse of antibiotics. Strategies to reduce overuse in hospitals hinge on prescribers making informed decisions to discontinue unnecessary antibiotic medicines. However, there is limited evidence on how to best support these critical decisions. The aim of antibiotic reviews is to decrease the misuse of antibiotics by encouraging appropriate decisions at clinical antibiotic reviews and to promote the effective use of these medications to address the challenge of AMR [2].

Antimicrobial stewardship (AMS) aims to minimise resistance by ensuring that antibiotics are prescribed only when clinically indicated and that narrow-spectrum agents are used whenever appropriate [3]. Within the UK, a number of tools and policies have been developed to provide best-practice guidance on AMS. The Antimicrobial Prescribing and Stewardship (APS) competency framework, originally released in 2013 and revised as of August 2023, acts as an integral guide within England to enhance the calibre of antimicrobial treatment and stewardship, thus mitigating the risks associated with inadequate antimicrobial usage. It is in accord with England's Code of Practice for AMR, the UK's 20-year vision for AMR, and the 5-year action plan for AMR [4]. The framework is designed to support prescribers in various care settings, advancing their proficiency in antimicrobial prescription and stewardship practices. Emphasising patient-centred care and judicious decision-making, the framework's goal is to curtail the development of AMR and improve the management of infections, ensuring improved patient safety and quality of care [4]. A study at NHS Foundation Trust examined antibiotic prescribing trends for RTIs during 2019-2020, highlighting shifts and reinforcing antibiotic review and AMS practices in addressing AMR [5].

The "Start Smart Then Focus" toolkit, first published in 2011 and most recently updated in September 2023, provides clinicians and healthcare leaders within England's inpatient settings with a robust framework for AMS. It aims to mitigate AMR and uphold patient care standards through evidence-led protocols. The resource guides initial, judicious antimicrobial application, followed by a critical review and refinement of treatment, secured in clinical data and diagnostic insights. Additionally, it sets out best practice components for antimicrobial prescribing and comprehensive stewardship programmes, advocating the importance of regular audits, education, and delineated responsibilities across the healthcare team. Compliance with the toolkit's directives is crucial to meet the regulatory requirements of England's healthcare system, ultimately contributing to the national efforts to reduce the risk of AMR while safeguarding the quality of care for patients with infection [6].

In response, the antimicrobial review kit (ARK) was developed as an intervention designed to facilitate multifaceted behaviour change to reduce antibiotic use in acute general medical inpatients safely. The antibiotic review kit created a structured process that would promote optimised prescribing and provide timely opportunities for prescription review where appropriate optimisation decisions could be made [7]. Effective antibiotic review is crucial to enhance audits. It is important that initial prescriptions comply with local antimicrobial guidelines and are subject to review within 72 hours or later after the initial prescription to maintain robust antimicrobial stewardship and optimise antibiotic utilisation [7]. Although the ARK intervention was initially developed for acute hospitals, the underlying principles apply equally to pharmacists working across all sectors [8]. This article will provide practical tips and advice on how clinical antibiotic reviews can be effectively conducted.

## Best practice for effective antibiotic review and effective antimicrobial stewardship

The following information summarises key criteria of best practice with regard to safe and effective antimicrobial prescribing and advice on how to effectively structure an antibiotic review. These principles should be followed at each stage of the prescribing process, and the review stage can be used to create a safety net and evaluate their implementation [6].

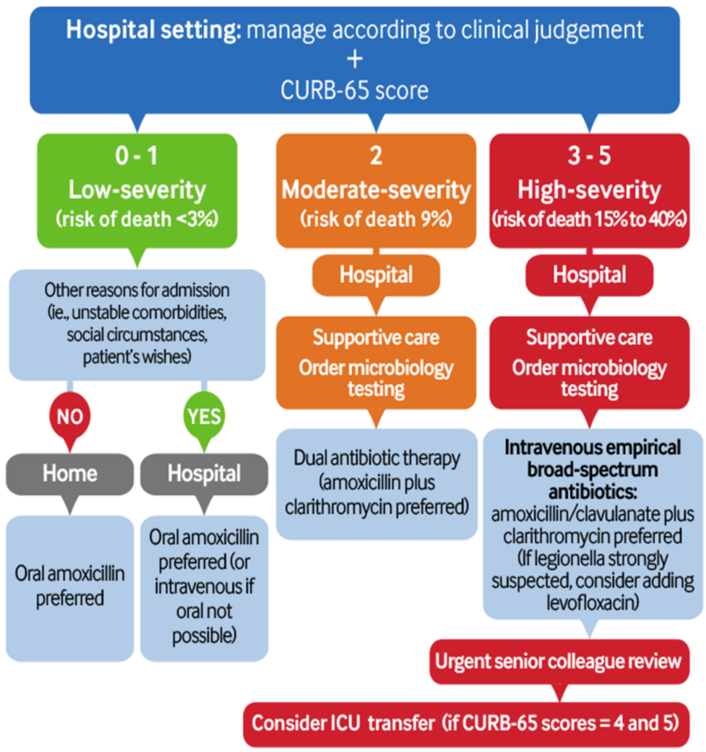
**Initial Assessment:** This is conducted at the time of the 'Initial Antibiotic Prescription'. Prescribers should begin with the "Start Smart" principle by verifying the presence of infection through patient history, clinical signs, laboratory results, and imaging. Confirm the primary diagnosis, any healthcare-associated risk factors, and whether the patient is immunocompromised or in need of emergency antibiotics for sepsis. It is essential to differentiate between empirical antibiotics and pathogen-directed antibiotic medicine [6,9]. Empirical therapy is based on the prescriber's initial impression of the most likely cause of the infection and initial diagnosis based on the local antimicrobial guidelines. It should be informed by an assessment based on the history, symptoms, main diagnosis and the severity of the infection.

In community-acquired pneumonia (CAP), for example, a number of evidence-based tools have been developed to optimise empirical antibiotic therapy, with the CURB-65 tool used as a good example for risk assessment [10].

> The CURB-65 tool [9] uses a scoring system that includes five prognostic indicators, each contributing one point: **C**onfusion, **U**rea levels above 7 mmol/litre, **R**espiratory rate over 30 breaths per minute, **B**lood

pressure under 90mmHg systolic or 60mmHg diastolic, and **A**ge 65 or older. In adults, CAP severity assessment involves clinical judgment supported by mortality risk scores like CURB65. A score of 0 or 1 indicates low severity, 2 points to moderate severity, and a score between 3 and 5 reflects high severity [11]. The CURB-65 risk assessment framework for community-acquired pneumonia is shown below.

**Figure 1.** Risk assessment and management of community-acquired pneumonia [11].




**Allergy Status:** Accurately determining a patient's penicillin allergy is vital, as over 90% of those labelled as allergic are not [12]. This mislabelling often leads to the use of less effective, second-line antimicrobials, increasing costs and adverse outcomes. Healthcare providers should audit the documentation of penicillin allergy status and its source [6].

**Diagnostic tests including microscopy, culture and sensitivity:** Utilising microscopy, culture, and sensitivity tests aids in the appropriate selection of antimicrobials, especially in cases of treatment failure. Actions taken following these diagnostic test results should be audited [6].

**Choice of antimicrobial agent(s):** Use the "Then Focus" approach within 48-72 hours of initial prescription to review the patient's response to the initial empirical therapy and laboratory data [6]. Choose antimicrobials based on both empirical evidence and culture results, tailoring the choice to the patient's specific needs. Ensure adherence to the five rights (5Rs) of antibiotic safety, including the right patient, drug, dose, time, and duration, in accordance with local antibiotic guidelines [13]. Selecting the appropriate antimicrobial therapy is crucial to avoid healthcare-associated infections (HCAIs), AMR, and unnecessary drug exposure. This choice should adhere to local guidelines and include auditing the dose and route of administration [6].

Identify the likely pathogens through culture data and match them against the pharmacology of available antimicrobials, taking into account the site of infection and penetration efficacy of the drugs [6].

**Person-Centred Care:** Being person-centred means individualising care for each patient, ensuring the safe prescription of antibiotics, and taking into account necessary dosage adjustments, pharmacokinetics, and pharmacodynamics [14]. The role of pharmacy in delivering person-centred care is pivotal. Pharmacists need to be recognised as part of the multidisciplinary team that can support people with infections and other comorbidities, such as kidney and liver diseases or immunocompromised patients in any setting [9,15].

Antibiotic side effects (e.g., tendon rupture with fluoroquinolones, kidney issues with aminoglycosides) should be explained to patients with consideration given to their level of health literacy and the most appropriate means of communication for the individual.

Dose adjustments or changes in medication should be considered when necessary, such as renal dose adjustments for vancomycin and meropenem. Potential drug interactions should also be discussed with the patient, including drug-drug, drug-food, and drug-disease, such as erythromycin and statins, which can interact, increasing statin side effects, and dairy products, which can inhibit the absorption of tetracycline antibiotics.

**Total Duration of Antimicrobial Therapy:** Treatment should not exceed 5-7 days (including both IV and oral) unless specific guidelines or specialists recommend otherwise [6]. Shorter antimicrobial courses have been shown to be equally effective for uncomplicated infections and reduce adverse effects and resistance pressure [16]. Auditing compliance with local guidelines for the total duration of therapy for each type of infection is recommended [6,16].

**Documentation:** Record the diagnosis with certainty, the antibiotics used, and the review date. Documentation should be thorough to facilitate clear communication and continuity of care. A review date or expected duration on antimicrobial prescriptions should be documented to prevent indefinite treatment and reduce AMR risk [6,17].

**Interprofessional Collaboration:** Communicate effectively with the healthcare team, including prescribers, about antibiotic therapy choices and changes based on microbiology results and patient clinical conditions [4,6].

**Patient education:** Engage in shared decision-making with the patient, ensuring they understand the rationale for the use of antimicrobials. Educate patients and healthcare professionals on the appropriate use of antibiotics at every opportunity [17]. Provide counselling on the use of antibiotics as prescribed and the implications of AMR and repeat these messages at the review stage. Use evidence-based resources to support education and encourage prudent antibiotic use [18,19].

## Possible outcome of the antimicrobial review

Evidence indicates that a 'review and revise' approach reduces mortality risks [6]. Once the antimicrobial review has been completed, there will be five potential outcomes: **C**ease, **A**mend, **R**efer, **E**xtend, or **S**witch for effective treatment management [6, 20]. This is referred to by the mnemonic 'CARES' which is explained further below [6,21].

- **Cease:**

- Stop antimicrobial treatment if no infection is present to prevent harm and resistance.

- Evidence [6] supports ending treatment early if no infection signs are found, improving survival rates.

- Strategies should focus on reducing unnecessary antimicrobial use to prevent resistance escalation.

- **Amend:**

- Amend antimicrobial prescriptions, ideally choosing a narrower spectrum agent or a broader one if necessary, to ensure effective and proportionate treatment [6].

- Change prescriptions to narrower agents when possible to enhance both effectiveness and safety [6].

- A recent study emphasised the significance of the 'De-escalation' AMS strategy, or changing to narrower antibiotics, during emergencies like the COVID-19 pandemic [9].

- **Refer:**

- Direct suitable patients to non-ward-based services or virtual wards for continued care. These services have been shown to be safe and effective and can lead to high patient satisfaction [6].

- Referrals to non-ward based services can enable an early switch from IV to oral antimicrobials, aligning with UK best practice guidelines [22].

- **Extend:**

- Continue antimicrobials only when clinically necessary, with a documented review or stop date.

- Shorter courses are often as effective as longer ones [15] and reduce the risk of developing resistance.

- Unnecessary extended antibiotics can lead to increased resistance and adverse effects [23].

- **Switch:**

- IV-to-oral Switch (IVOS) criteria are pivotal to enhance patient recovery and reduce risks [6,22].

- Studies confirm early IVOS is as effective as prolonged IV treatment [6].

- Benefits include reductions in infection risk, healthcare costs, and environmental impact.

## Case-Based Learning

### Patient Case 1

D.L. is a 44-year-old woman who attended A&E in June with a sudden onset of cough, lethargy, and fever with chills over the past four days. She lives in Indiana with her partner and maintains a healthy lifestyle, running 25 miles a week as part of a running club. She hasn't travelled recently and works from home. Her vital signs show a respiratory rate of 32 breaths per minute, blood pressure at 124/71 mm Hg, heart rate at 98 beats per minute, and oxygen saturation of 93% while breathing room air. Her WBC is elevated at 19 x $10^3$ cells/mm$^3$, and she has a fever of 102.1°F (38.9°C). Her BUN level is 17 mg/dL. She is conscious and alert. Chest X-ray shows a consolidation in the left lower lobe of her lung. She has been admitted to the hospital for pneumonia treatment.

1. Which of the following is D.L.'s CURB-65 score?

A. 1.

B. 2.

C. 3.

D. 4.

Answer: B

The CURB-65 score can be used to assess a patient's risk of mortality related to pneumonia and to make hospital admission decisions. One point is assigned for each of the five criteria the patient meets; they are then summed for the final CURB-65 score. The patient is not confused (0 pt), and BUN is no greater than 19 mg/dL (0 pt); the patient's respiratory rate is greater than 30 breaths/minute (1 pt), she has a blood pressure greater than 90/60 mm Hg (0 pt), and she is younger than 65 (0 pt). Therefore, her CURB-65 score is 1 (Answer B is

correct; Answers A, C, and D are incorrect).

## Patient Case 2

The patient received Amoxicillin orally. On day 5 of hospitalisation, D.L has improved. Her current vital signs are a respiratory rate of 18 breaths/minute, blood pressure of 112/70 mm Hg, and heart rate of 70 beats/minute. Her SaO2 is 98% on room air. Her last fever was 73 hours ago, and her WBC is 12 x 103 cells/mm3. D.L. is being discharged today.

Which is most appropriate for her?

A. Discontinue antibiotic therapy.

B. Continue antibiotic therapy for two more days with azithromycin orally at discharge.

C. Continue antibiotic therapy for two more days with ceftriaxone orally at discharge.

D. Continue antibiotic therapy for two more days with levofloxacin orally at discharge.

Answer: A

This patient has been afebrile for more than 48–72 hours, is saturating well on room air, is normotensive, and has a normal heart rate and respiratory rate. She has no signs of clinical instability. Given this, it is safe to discontinue antibiotic therapy now (Answer A). Answers B–D are incorrect because she does not require additional therapy, given her clinical stability. If she did require additional therapy, levofloxacin would be suboptimal, given the risk of tendon rupture and other adverse effects, and azithromycin would be suboptimal as well, given the high risk of S. pneumoniae resistance and lack of concern for atypical pathogens in this case.

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# Appendix 73.

Longer Versus Shorter Antibiotic Duration for Respiratory Infections Before and During the COVID-19 Pandemic at a Secondary Care Setting in the UK: To Fight Antimicrobial Resistance.

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**Longer Versus Shorter Antibiotic Duration for Respiratory Infections Prior to and During the COVID-19 Pandemic at a Secondary Care Setting in the UK: To Fight Antimicrobial Resistance**

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**Abstract**

As antimicrobial resistance (AMR) escalates globally, examining antibiotic treatment durations for respiratory infections becomes increasingly pertinent, especially in the context of the COVID-19 pandemic. This retrospective study at a UK secondary care setting compares shorter (≤5 days) versus longer (6-7 days and >8 days) antibiotic durations among 640 adult patients treated for respiratory infections in 2019 and 2020. The study utilises local antimicrobial guidelines and clinical evidence to assess the appropriateness of prescribing practices. Findings indicate that shorter antibiotic courses are as effective as longer ones, particularly for COPD infective exacerbation, HAP and COVID pneumonia. However, a shorter duration shows a significant difference in treatment outcomes in CAP and 'Unspecific' respiratory tract infections (RTIs). The research supports the mantra that "Shorter Is Better" and aligns with global initiatives to combat AMR by advocating for evidence-based, tailored antibiotic therapies. Despite its insights, the study acknowledges limitations such as its focus on an adult population and the exclusion of pediatric cases. The results highlight the need for continuous research to adapt antibiotic prescribing practices to evolving healthcare challenges.

**Keywords**

Antimicrobial resistance; Antibiotic duration; Antibiotics; Respiratory tract infections; COVID-19 pandemic; Antimicrobial stewardship; antibiotic prescribing.

**1. Introduction**

In the face of rising antimicrobial resistance (AMR), the global health landscape is rapidly changing [1]. This resistance threatens the efficacy of conventional treatments such as antibiotics, chemotherapy, and various pharmaceuticals. Recognising the severity of AMR, the World Health Organisation (WHO) has classified it among the ten global threats to health worldwide, calling for the prudent use of antibiotics [2]. To address this crisis, the development of novel strategies and the reinforcement of existing treatments are at the forefront of scientific research [2]. With infectious diseases becoming more prevalent and pathogens increasingly outpacing current treatments, the necessity for diverse approaches in combating AMR has never been more crucial [3].

In response to this crisis, Antimicrobial Stewardship (AMS) initiatives have become crucial, promoting the responsible use of antibiotics to mitigate the risks associated with AMR [4]. The importance of AMS programs is highlighted by the rapid spread of AMR, which complicates the management of infectious diseases [5]. This increase in resistance leads to longer hospital stays, spiralling healthcare costs, and a rise in mortality rates, highlighting the urgent need for effective AMS measures [6]. Implementing AMS strategies, such as 'IV-to-Oral Switch', 'Discontinuing Antibiotics', and 'De-escalation', was essential to ensure the effective enactment of AMS [7]. The development of new AMS strategies was critical, especially in the context of the COVID-19 pandemic, which influenced antibiotic prescribing practices and exacerbated the misuse of antibiotics [8]. Integrating this new AMS strategy, refining existing practices, and enacting robust preventive measures can enhance our defences against infectious diseases and more effectively tackle the escalating issue of AMR [5].

Recent evidence suggests that short-course antibiotic therapy can be as effective as longer courses, prompting a re-evaluation of prescribing practices to mitigate the emergence of AMR [9,10,11]. This shift towards shorter courses is supported by studies demonstrating comparable outcomes between short and long therapies, marking a significant change in clinical practice standards [12]. In the UK, efforts to reduce antibiotic resistance include addressing antibiotic over-prescribing, where substantial evidence indicates that reducing antibiotic use could lower or stabilise resistance levels [13]. This involves starting treatments only when necessary, selecting appropriate drugs, and avoiding unnecessarily long treatment durations. However, less attention has been paid to minimising prolonged treatment durations as a strategy to control antibiotic overuse in primary care [6]. Additionally, the side effects associated with antibiotic use, such as diarrhoea, rash, and candidiasis, highlight the importance of minimising treatment duration to reduce the risk of adverse outcomes, including Clostridium difficile infections [14]. Recent guidelines and studies advocate for shorter antibiotic courses for common infections, suggesting that such practices can effectively clear infections while minimising the selection and spread of resistant bacteria [15]. The principle of administering the minimum effective duration of antibiotic therapy to reduce AMR risk and drug toxicity is a cornerstone of AMS, with evidence from randomised controlled trials supporting short courses for lower respiratory tract infections [12]. However, the optimal duration of antibiotic therapy for pleural infection remains unclear, with limited high-quality evidence available [16].

This study aims to compare the effectiveness and appropriateness of shorter versus longer antibiotic treatment durations for respiratory tract infections in adults during 2019 and 2020. It categorises the antibiotic treatments into three durations: shorter duration (5 days or fewer), longer duration (6-7 days), and (over 8 days). Additionally, the study explores factors that might justify a more prolonged course of antibiotic therapy. This research contributes to bridging gaps in the existing literature by offering a comparative analysis of antibiotic treatment durations at a secondary care setting, NHS Foundation Trust, in 2019 (prior to the COVID-19 pandemic) and in 2020 during the pandemic.

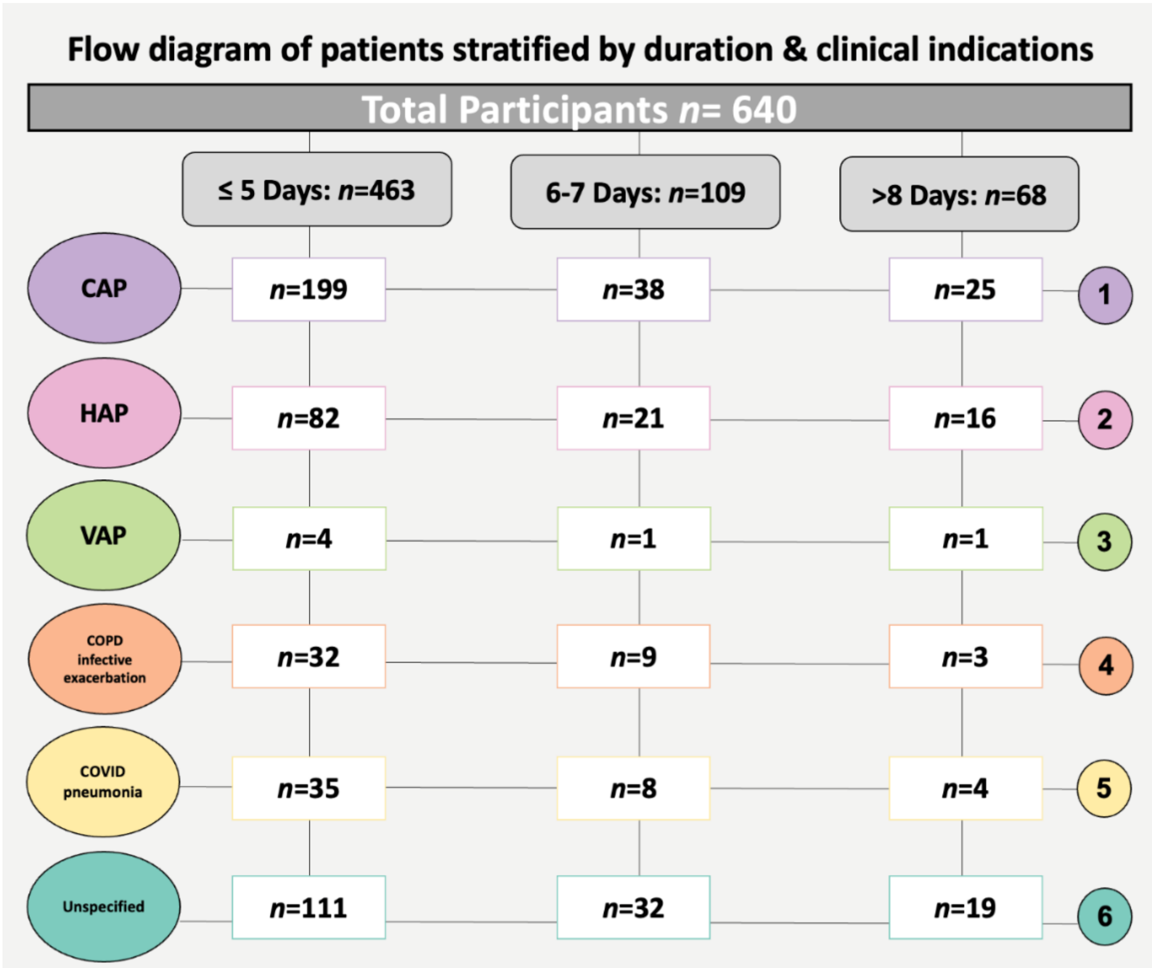
## 2. Results

### 2.1. Categorising Antibiotic Treatment Durations: Shorter and Longer

The flow chart presents the categorisation of 640 patients based on antibiotic treatment duration and respiratory diagnoses, with durations segmented into 'Shorter Duration' (≤5 days) and 'Longer Duration' (6-7 days and >8 days). This categorisation is derived from local antimicrobial guidelines, a review of the literature, and the clinical relevance of antibiotic duration practices. Of total 640 patients, admitted in 2019 and 2020, there was 463 patients received antibiotics for ≤5 days, 109 for 6-7 days, and 68 for periods exceeding 8 days.  Based on the information extracted from patients' medical records, primary diagnoses were categorised by specific respiratory infections. These include community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), chronic obstructive pulmonary disease (COPD) infective exacerbation without pneumonia, and COVID-19 pneumonia. Alongside these, indeterminate diagnoses such as upper respiratory tract infections (URTIs), lower respiratory tract infections (LRTIs), or pneumonia were grouped under the 'Unspecified' category for respiratory tract infections (RTIs).

In the CAP category, treatment durations were as follows: 199 patients received antibiotics for ≤5 days, 38 for 6-7 days, and 25 for periods exceeding 8 days, illustrating the variation in treatment lengths for different respiratory conditions. For HAP, 82 patients were treated for ≤5 days, 21 for 6-7 days, and 16 for more than 8 days. Regarding COPD exacerbations and COVID pneumonia, 32 and 35 patients, respectively, were treated for a shorter duration of ≤5 days. For patients with 'Unspecified' RTIs, 111 received a shorter treatment course of ≤5 days.

**Figure 1.** Flow diagram for extracting a representative sample of 640 patient medical records from 2019 and 2020, stratified by duration and clinical indications.




CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus.

### 2.2. Clinical and Demographic Characteristics

Table 1 represents the patient characteristics and clinical features of 640 patients hospitalised prior to and during the COVID-19 pandemic across 2019 and 2020, categorised by antibiotic treatment duration: ≤5 days, 6-7 days, and >8 days. Regarding age, the median values are relatively consistent across the categories, recorded as 79, 80, and 79.5 for the ≤5 days, 6-7 days, and >8 days groups, respectively. No significant differences were observed in white blood cells (WBCs) or C-reactive protein (CRP), with p-values of 0.3 and 0.7, accordingly. Length of stay (LOS) demonstrated significant differences, correlating longer stays with antibiotic use exceeding 8 days, as indicated by a *p-Value* of <0.01.

**Table 1.** Patient characteristics and clinical features by antibiotic treatment duration for 2019 and 2020 admissions (n=640).

| | **Duration of antibiotic use** | | | ***p*-Value** |
|---|---|---|---|---|
| | **≤ 5 Days** | **6-7 Days** | **> 8 Days** | |
| | ***n* (%)** | ***n* (%)** | ***n* (%)** | |
| Age (Median, IQR) | 79 (21) | 80 (17) | 79.5 (19) | 0.8 |
| WBCs (Median, IQR) | 34.1 (123) | 46 (131) | 16.5 (117) | 0.3 |
| CRP (Median, IQR) | 76 (206) | 91 (291) | 103.5 (240) | 0.7 |
| LOS (Median, IQR) | 8 (10) | 9 (10) | 15 (17) | **<0.01** |

WBCs, white blood cells; CRP, C-reactive protein; LOS, length of stay.

In Table 2, it was found in 2019 and 2020, most of the patients 237 (73.6%) had shorter appropriate antibiotic courses of ≤5 days in 2019 and 226 (71.1%) in 2020. No significant difference was observed in antibiotic duration based on year, gender, outcomes (discharge or death), allergies or clinical characteristics, such as hypertension (HTN), heart failure (HF), diabetes mellitus (DM), and asthma. Most of the study population, 384 (82.9%), were discharged with shorter antibiotic courses of ≤5 days, with no significant difference between the three categories.

**Table 2.** Demographic and clinical characteristics of patients admitted prior to and during the COVID-19 pandemic in 2019 and 2020 (*n*=640).

| | | | **Duration of antibiotic use** | | | ***p*-Value** |
|---|---|---|---|---|---|---|
| | | | **≤ 5 Days** ***n*=463** | **6-7 Days** ***n*=109** | **> 8 Days** ***n*=68** | |
| | | | ***n* (%)** | ***n* (%)** | ***n* (%)** | |
| Demographic characteristics | Year | 2019 | 237 (51.2) | 53 (48.6) | 32 (47.1) | 0.3 |
| | | 2020 | 226 (48.8) | 56 (51.4) | 36 (52.9) | |
| | Gender | Male | 227 (49) | 60 (55) | 34 (50) | 0.6 |
| | | Female | 236 (51) | 49 (45) | 34 (50) | |
| | | Discharged | 384 (82.9) | 97 (89) | 61 (89.7) | 0.9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Patient Outcomes | Died | 79 (17.1) | 12 (11) | 7 (10.3) | |
| | Allergy | | 36 (7.8) | 11 (10.1) | 6 (8.82) | 0.6 |
| Clinical characteristics | Indication | CAP | 199 (43) | 38 (34.9) | 25 (36.8) | 0.9 |
| | | HAP | 82 (17.7) | 21 (19.3) | 16 (23.5) | 0.7 |
| | | VAP | 4 (0.9) | 1 (0.9) | 1 (1.5) | - |
| | | COPD infective exacerbation | 32 (6.9) | 9 (8.3) | 3 (4.4) | 0.6 |
| | | COVID pneumonia | 35 (7.6) | 8 (7.3) | 4 (5.9) | 0.6 |
| | | Unspecified | 111 (24) | 32 (29.4) | 19 (27.9) | 0.4 |
| | Comorbidities | Hypertension (HPN) | 212 (45.8) | 47 (43.1) | 32 (47) | 0.5 |
| | | Heart failure (HF) | 63 (13.6) | 24 (22) | 8 (11.8) | 0.3 |
| | | Hypercholesterolemia | 69 (14.9) | 17 (15.6) | 12 (17.6) | 0.3 |
| | | Diabetes mellitus (DM) | 79 (17.1) | 22 (20.1) | 18 (26.5) | 0.6 |
| | | Asthma | 41 (8.9) | 11 (10.1) | 4 (5.9) | 0.1 |
| | Chest X-rays | Pneumonia | 66 (14.3) | 16 (14.5) | 11 (16.2) | 0.3 |
| | | No pneumonia | 107 (23.1) | 22 (20.1) | 18 (26.5) | |

CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus; HPN, hypertension; HF, heart failure; and DM, diabetes mellitus. The P-value is significant if less than 0.5.

### 2.3. Most Frequent Prescribed Antibiotics for Respiratory Infections

Table 3 outlines the most commonly prescribed antibiotics for patients with RTIs in a UK secondary care setting over two years, 2019 and 2020. The antibiotics are categorised by the duration of their administration: ≤5 days, 6-7 days, and >8 days. Amoxicillin/clavulanic acid was the most frequently prescribed antibiotic, with 283 (61.1%) of prescriptions for ≤5 days. Additionally, levofloxacin accounted for 50 (10.8%) of its use within the shorter duration category of ≤5 days. There was no significant difference in the durations for most of the prescribed antibiotics, except for metronidazole and piperacillin/tazobactam, which had p-values of 0.01 and 0.007, respectively.

**Table 3**. Most frequent antibiotics were used for patients with respiratory tract infections in 2019 and 2020.

| Antibiotic | Duration Category | | | *p-Value* |
|---|---|---|---|---|
| | **≤ 5 Days** **_n_=463** | **6-7 Days** **_n_=109** | **> 8 Days** **_n_=68** | |
| | *n* (%) | *n* (%) | *n* (%) | |
| Amoxicillin | 16 (3.5) | 4 (3.7) | 1 (1.5) | - |
| Amoxicillin/Clavulanic Acid | 283 (61.1) | 61 (56) | 36 (52.9) | - |
| Azithromycin | 5 (1.1) | 0 (0) | 2 (2.9) | - |
| Benzylpenicillin | 3 (0.6) | 1 (0.9) | 1 (1.5) | - |
| Ceftazidime | 6 (1.3) | 1 (0.9) | 2 (2.9) | - |
| Ciprofloxacin | 11 (2.4) | 2 (1.8) | 4 (5.9) | - |
| Clarithromycin | 23 (5) | 7 (6.4) | 2 (2.9) | - |
| Levofloxacin | 50 (10.8) | 6 (5.5) | 3 (4.4) | - |
| Metronidazole | 4 (0.9) | 1 (0.9) | 4 (5.9) | **0.01** |
| Piperacillin/Tazobactam | 53 (11.4) | 22 (20.2) | 12 (17.6) | **0.007** |

### 2.4. Shorter Versus Longer Antibiotic Courses in Respiratory Infections

A key finding of this study was the assessment of the appropriateness of initial or empirical antibiotic prescribing according to local guidelines. Appropriate prescribing was evaluated by comparing the prescriptions with local antimicrobial guidelines for both PP and DP periods (BSAC Stewardship, 2018. The study focused on analysing the differences between shorter and longer courses of appropriate antibiotic therapy for various RTIs. For instance, with CAP, local guidelines recommended an antibiotic treatment duration ranging from 5 days (shorter duration) to longer durations of 6-7 days and >8 days. Similarly, in cases of COPD infective exacerbation, a shorter antibiotic course of ≤5 days was assessed against longer durations of 6-7 days and >8 days.

Table 4 presents a comparison of appropriate antibiotic prescribing: shorter versus longer durations of antibiotic treatment prior to and during the COVID-19 pandemic in 2019 and 2020. For conditions, such as HAP, VAP, COPD infective exacerbation, and COVID-19 pneumonia, a 'Shorter Duration' of ≤5 days was shown to be as effective as 'Longer Durations' of 6-7 days and >8 days. There was no significant difference in the appropriateness of shorter versus longer antibiotic durations among the three RTI categories, with the exceptions of CAP, which showed a p-value of 0.02, and 'Unspecified' RTIs, which had a p-value of 0.07.

Furthermore, the majority of patients were appropriately prescribed antibiotics for shorter durations of ≤5 days, representing 164 (35.4%) of the cases. There is no significant difference was observed in the appropriateness of shorter versus longer durations of antibiotic prescribing across the three categories in the overall study population. COVID-19 and VAP cases are fewer in number, with varied appropriateness across durations. The data presented in the table suggests a move towards prescribing shorter courses of antibiotics, a change that aligns with current efforts to fight antimicrobial resistance. This shift becomes particularly notable in the management of patients with COVID-19.

**Table 4.** Characteristics between short versus long antibiotic course treatment groups and appropriateness of antibiotics. Significant p-value is <0.05.

| Indication (n, %) | | Duration of antibiotic use | | | *p-Value* |
|---|---|---|---|---|---|
| | | **≤ 5 Days** ***n*=463** | **6-7 Days** ***n*=109** | **> 8 Days** ***n*=68** | |
| | | *n (%)* | *n (%)* | *n (%)* | |
| Appropriateness of antibiotics | CAP (262, 40.9%) | 84 (18.1) | 25 (22.9) | 14 (20.6) | **0.02** |
| | HAP (119, 18.6%) | 45 (9.7) | 11 (10.1) | 7 (10.3) | 0.7 |
| | VAP (6, 0.9%) | 3 (0.6) | 1 (0.9) | 1 (1.5) | 0.6 |
| | COPD infective exacerbation (44, 6.9%) | 17 (3.7) | 5 (4.6) | 1 (1.5) | 0.6 |
| | COVID pneumonia (47, 7.3%) | 8 (1.7) | 1 (0.9) | 1 (1.5) | 0.4 |
| | Unspecified (162, 25.3%) | 7 (1.5) | 2 (1.8) | 0 (0) | **0.07** |
| | Overall (640, 100%) | 164 (35.4) | 45 (41.3) | 24 (35.3) | 0.5 |

CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus.

**3. Discussion**

This study provides valuable insights into the challenges and adjustments in antimicrobial stewardship during an unprecedented global health crisis. This, in turn, informs future strategies and policy modifications in combating AMR and managing global health emergencies. The historical 7-day for antibiotic therapy, has been long challenged, especially for pneumonia treatments. Studies have revealed that short-course treatments (3-5 days) are just as effective for community-acquired pneumonia, and ≤8 days are sufficient for nosocomial pneumonia, compared to the conventional 7-10 or 10-15 days. This not only counters the misconception that prolonged treatment prevents resistance but highlights that longer treatments may increase resistance emergence. The Antibiotic Mantra, "Shorter Is Better," advocates for therapy durations tailored to the patient's response, shifting from the outdated practice of fixed, extended courses to a more evidence-based, patient-specific approach [17]. In this study, for patients with CAP, 199 patients were treated for shorter duration ≤5 days, 38 for 6-7 days, and 25 for more than 8 days. A statistically significant difference was observed across the three duration categories, with CAP showing a p-value of 0.02. However, in the case of Hospital-Acquired Pneumonia (HAP), there was no significant difference between the three categories, with a p-value of 0.7.

In 2018, Public Health Ontario (PHO) launched the "Shorter is Smarter" initiative, highlighting the critical need to reduce the duration of antibiotic therapy in long-term care settings. This initiative sheds light on the concept of selective pressure, where antibiotic use can eliminate susceptible bacteria and allow resistant strains to multiply. Advocating for shorter courses of antibiotics, it demonstrates their effectiveness compared to longer durations for treating conditions like pneumonia. These shorter courses, ranging from 5 to 6 days as opposed to the traditional 7 to 14 days, aim to decrease resistance and side effects. Supported by studies on common infections among both hospitalized and ambulatory long-term care patients, this strategy encourages minimizing antibiotic use to reduce harm [18].

In confronting antibiotic resistance, prescribing fewer antibiotics is crucial. A 7-day treatment, a vestige of Constantine the Great's decree, lacks evidence for modern medicine. Over 45 RCTs now affirm that shorter courses are as effective for various infections, including pneumonia. For instance, 3–5-day treatments for community-acquired pneumonia and ≤8 days for nosocomial pneumonia are proven effective. Each additional day of antibiotics raises adverse effects by 5%, compelling the medical community to embrace the "shorter is better" approach for better outcomes and less resistance [10].

In 2021, a study examining short versus long antibiotic courses for treating infections revealed no difference in effectiveness but found that longer durations were linked to more hospital admissions due to complications. Research on 4 million cases in England indicated prescriptions of 8-15 days had higher risks compared to shorter treatments. The findings support the use of brief courses in combating antimicrobial resistance and suggest a shift in clinical guidelines towards shorter antibiotic durations [11].

In 2023, a study conducted in the UK, evaluated antibiotic use in patients with RTIs, using WHO AWaRe classification. Notably, it observed a slight increase in the use of amoxicillin/clavulanic acid and a substantial rise in azithromycin prescriptions, highlighting shifts in prescribing trends. Despite these changes, some antibiotics displayed steady consumption rates. These findings highlight the importance of understanding antibiotic use patterns during the AMR threat. The increase in the usage of "Watch" category antibiotics during the pandemic emphasises the urgency of robust AMS measures. The research confirms that incorporating the AWaRe classification in prescribing decisions is crucial for patient safety and combating antibiotic misuse. This study provides essential insights into the changing landscape of antibiotic prescribing during a global health crisis, reinforcing the necessity for ongoing AMS vigilance to effectively address AMR challenges [19]. This study revealed that amoxicillin/clavulanic acid was the antibiotic most commonly prescribed, accounting for 283 (61.1%) of prescriptions lasting ≤5 days. For the majority of antibiotics prescribed, the duration did not significantly vary, with the exceptions being metronidazole and piperacillin/tazobactam, which showed significant differences with p-values of 0.01 and 0.007, respectively. In 2023, another study in Japan showed that a shorter treatment duration (3–5 days) likely offers the best balance of effectiveness and treatment burden for managing Community-Acquired Pneumonia (CAP) in adults who have achieved clinical stability. Nevertheless, the limited number of studies considered and the overall moderate to high risk of bias could affect the reliability of these findings. Additional research focusing on this shorter duration of treatment is necessary [20].

A study conducted in the USA at an academic children's hospital from January 2017 to May 2020 evaluated antibiotic treatment durations for culture-negative sepsis in pediatric ICU patients. It revealed that a short course (≤7 days) resulted in lower mortality and shorter hospital stays compared to a long course (>7 days), with no significant difference in 30-day mortality or Multidrug-resistant organisms (MDRO) acquisition. These findings suggest the potential efficacy of shorter antibiotic therapies, emphasising the need for further extensive research to validate these results and inform future sepsis treatment protocols [21]. Implementing antimicrobial stewardship and focusing on antibiotic safety are crucial steps in combating antibiotic resistance, an issue highlighted by numerous studies and initiatives [22]. By adopting these new AMS strategies, emphasising shorter durations of antibiotics, enhancing our current guidelines, and implementing effective disease prevention measures, we can bolster our safeguards against infections and more effectively address the rising challenge of AMR. This approach ensures the safe and judicious use of antibiotics, contributing to better health outcomes.

*3.1. Strengths and Limitations*

This study offers pivotal insights into optimising antibiotic therapy durations, particularly underlining the efficacy of shorter antibiotic duration. For example, it finds that ≤5-days antibiotic courses for COPD infective exacerbation and COVID pneumonia are just as effective as longer ones, challenging the traditional 7-10 days regimens and suggesting a shift towards more tailored, patient-specific approaches. Additionally, the "Shorter is Smarter" initiative by Public Health Ontario and findings from multiple RCTs support the move to shorter courses, aiming to reduce antibiotic resistance and adverse effects. This discussion synthesises evidence from around the globe, including significant research from the UK, USA, and Japan, reinforcing the mantra "shorter is better" for antibiotics. Such insights are pivotal for evolving AMS strategies and adapting to the nuances of managing infections during health crises, emphasising the need for ongoing research to refine antibiotic use and enhance patient care.

However, it faces certain limitations. The focus on an adult population, excluding individuals under 25 and children, restricts its demographic applicability. Additionally, its emphasis on RTIs limits the scope of findings. The brief duration of the study and the evolving nature of SARS-CoV-2 could also impact the results. While the findings offer valuable insights into antibiotic use during a pivotal time of the COVID-19 pandemic in 2020, they should be interpreted with these limitations in mind, highlighting the need for continuous research to understand healthcare professionals' antibiotic prescribing practices during pandemic conditions. Our results emphasise the significance of accurate diagnoses and the application of severity scoring tools for guiding appropriate antibiotic usage, key for managing AMR. Furthermore, the study corroborates the efficacy of shorter antibiotic courses, in line with local guidelines and clinical evidence, a strategy that should be integrated into emergency planning while maintaining adherence to best practices.

## 4. Methods

### *4.1. Study Design and Setting*

This cross-sectional retrospective study aimed to estimate the prevalence of appropriate antibiotic prescribing among shorter and longer durations of antibiotics in adult patients aged 25 years and above who were admitted to a secondary care setting in the UK, between 1 August 2021 and 28 February 2023. Serving approximately 400,000 people, this secondary-care provider is equipped with about 742 beds. The study's findings were reported in line with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.

### *4.2. Participants*

To optimise participant diversity, this investigation adopted a stratified sampling methodology for the selection of medical records. The cohort encompassed adults aged 25 years and above, including pregnant women and individuals with compromised immune systems who were admitted to the Trust during the years 2019 and 2020. The focus was particularly on those administered antibiotics for RTIs, covering instances of pneumonia across both years and extending to COVID-19 in 2020. Exclusion criteria were established for individuals who had a stay of less than 48–72 hours in the accident and emergency (A&E) department, those not administered antibiotics, and paediatric patients. The research protocol underwent evaluation and received input from the Citizens' Senate, an entity championing patient care with substantial representation of the elderly demographic. The protocol's registration was completed with the ISRCTN registry, a database recognised by the World WHO and the International Committee of Medical Journal Editors (ICMJE) for all clinical research endeavours [23]. Detailed criteria for participant inclusion are accessible in the protocol published on the ISRCTN platform. Additionally, the investigation was documented in Octopus, a comprehensive global repository for primary research records [24].

*4.3. Data Sources and Variables*

The primary author (RA) extracted data from the electronic medical records of patients within the Trust. These data included age, sex, allergies, indications for treatment, comorbidities, CRP levels, WBC count, chest X-ray results, and the duration of antibiotic treatment, categorised as shorter duration (≤3 days) and longer duration (6-7 days and >8 days). Additionally, the LOS and patient outcomes, whether discharged or deceased, were also recorded.

Patient selection was based on electronic health record (EHR) entries identified by their respective ICD-10 codes for RTIs. This covered a range of conditions, encompassing both specific and indeterminate diagnoses. Specific conditions included CAP, COPD infective exacerbation, HAP, and VAP. In 2020, the selection criteria were expanded to include cases of COVID-19 pneumonia. Additionally, indeterminate diagnoses such as URTIs, LRTIs, and pneumonia were categorised as 'Unspecific' RTIs. The primary diagnosis of RTIs in these records played a crucial role in determining the initial or empirical antibiotic prescribed to the patients.

The study's sample size was meticulously calculated based on Public Health England's estimation that 20% of all antibiotics prescribed in the UK might be inappropriate [25]. Utilizing Minitab statistical software, the sample size was determined by considering the overall population size, a 10% margin of error, and a 95% confidence interval. Data collection covered medical records from both prior to and during the COVID-19 pandemic, specifically spanning the years 2019 and 2020. A total of 640 medical records were analysed, with data from each year systematically sampled to ensure representativeness and to create a solid dataset for examining antibiotic prescribing trends.

In this NHS Foundation Trust, the initiation of empirical antibiotic treatment is based on an initial, tentative diagnosis at the time of patient admission. The primary author meticulously evaluated the alignment of the chosen empirical antibiotic treatments with the local antibiotic guidelines to ascertain their appropriateness. These local guidelines serve as a gold standard, detailing the criteria for selecting empirical antibiotics, encompassing considerations for the type of infection, patient-specific factors, and local resistance patterns. The assessment process involves a thorough review of the antibiotics prescribed and examining aspects such as the type of antibiotic and prescribed duration. This review extends beyond the initial diagnosis and is dynamically adapted based on the patient's clinical response, results from microbiological testing, and additional diagnostic procedures, as chest X-ray findings. This method ensures that the antibiotic therapy aligns not only with the preliminary diagnosis but also remains responsive to the evolving clinical scenario and diagnostic insights, thus optimising patient care whilst adhering to antimicrobial stewardship practices.

A data extraction tool was employed to obtain the necessary data from patients' medical records. The data extraction tool was prepared in order to obtain the necessary information from the patient's medical records. The AMS data extraction tool was prepared, encompassing demographic information, primary diagnosis, investigations, and patient outcomes. The extraction process took approximately 45 min per patient's medical record for the primary author to gather the required data.

The primary author reviewed the literature and the UKHSA's AMS Toolkit to develop the data extraction tool [9]. The authors discussed, recognised, and agreed to the elements within the tool. A pilot study was conducted to provide an initial overview of the data and to evaluate the feasibility of the data extraction tool in addressing the research questions. To validate the tool, two independent authors separately extracted data from 1% of the sample (four patient records). An agreement rate of 80% or higher was used as a measure of the tool's validity. Additionally, to assess the tool's reliability, both authors independently extracted data from another 1% of the sample (four records). Inter-rater reliability was determined by comparing the percentage agreement in data extracted independently. Any disagreements were resolved through discussion.

### *4.4. Statistical Methods*

Descriptive analyses were conducted. Data on categorical or binary variables were presented as numbers (n) and proportions (%). Initial data, including age, gender, allergies, indications, comorbidities, duration, WBC count, CRP levels, and chest X-ray results, were described using numbers (n) and percentages (%) and further analysed. The Chi-square test was utilised for categorical variables, and the Kruskal-Wallis test was applied to numerical variables. The appropriateness of prescribed antibiotics among different indications across the three duration categories was also analysed using the Chi-square test. This study compared the appropriateness of prescribed antibiotics for RTIs in adult patients admitted in 2019 and 2020 to a secondary care setting across three antibiotic duration categories: shorter duration (≤5 days) and longer duration (6-7 days and >8 days). For more advanced statistical analysis, IBM SPSS Statistics version 22.0, RStudio version 2022, and R version 4.2.2 were used [26,27].

**5. Conclusions**

This study critically evaluates the impact of shorter versus longer antibiotic durations on RTIs prior to and during the COVID-19 pandemic in a UK secondary care setting, addressing the urgent challenge of AMR. With AMR emerging as a challenging threat to global health, the necessity for effective AMS initiatives has become more apparent, prompting a re-evaluation of antibiotic prescribing practices. Through a comprehensive analysis of 640 patient records from 2019 and 2020, this research highlights significant findings: shorter antibiotic courses (≤5 days) for conditions as COPD exacerbation, COVID pneumonia and HAP demonstrate comparable efficacy to traditional longer courses, challenging longstanding clinical norms and supporting the "Shorter Is Better" mantra. Notably, the study reveals no significant difference in treatment outcomes between shorter and longer durations for most RTIs, except for CAP, where shorter treatments were notably effective. These insights are instrumental in refining AMS strategies, particularly in light of the COVID-19 pandemic's impact on antibiotic usage patterns. This research emphasises the importance of tailored, evidence-based antibiotic therapy to combat AMR, advocating for a shift towards shorter treatment durations aligned with local guidelines and clinical evidence. This approach promises to optimise patient care while combating the AMR crisis, marking a pivotal step forward in infectious disease management.

**6. Author Contributions**

R.A.E. was responsible for the data collection, while the study's framework and inception were a joint effort by R.A.E., N.U., and Z.A. The literature review was conducted by R.A.E. under the guidance of N.U. and Z.A., who also supervised the extraction of data from electronic patient records. The dataset was compiled by R.A.E., with rigorous oversight from N.U. and Z.A. in the data verification, access, and analysis processes. The initial manuscript draft was penned by R.A.E., refined through the input of N.U. and Z.A. All the co-authors were actively involved in interpreting the data, and collaboratively editing and approving the manuscript, ensuring collective agreement before submission. Z.A. serves as the guarantor for the research content. Data anonymisation and secure storage were managed using the University of Hertfordshire's protected systems, where R.A.E. also conducted the data analysis. The final manuscript has been reviewed and consented to by all authors.

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**Institutional Review Board Statement**

Ethical approval for this study was granted by the Health Research Authority (HRA), with the Research Ethics Committee (REC) assigning reference number 22/EM/0161. In compliance with this approval, the study protocol underwent review and received approval from the University of Hertfordshire (UH) Ethics Committee under the reference LMS/PGR/NHS/02975.

**Informed Consent Statement**

Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement**

The datasets presented in this article are not readily available, according to the institution's policy. Requests to access the datasets should be directed to r.a.elshenawy@herts.ac.uk.

**Conflicts of Interest**

The authors declare no conflicts of interest.

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# Appendix 74.

Maximising Survey Participation: Novel Distribution Strategies in Survey Questionnaire Research Study Exploring Antimicrobial Stewardship and Prescribing During COVID-19 Pandemic at a Secondary Care Setting in England.

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# Novel survey distribution methods: impact on antimicrobial resistance research outcomes

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### *Introduction*

Antimicrobial resistance (AMR) caused over 1.2 million deaths in 2019.[1] AMR poses a significant global health crisis, with predictions of 10 million deaths per year by 2050.[2] Recognized by the WHO as a top public health threat, AMR poses significant challenges, exacerbated by the COVID-19 pandemic.[3,4] Antibiotic resistance research is paramount for understanding prescribing behaviours, AMR and antimicrobial stewardship (AMS), aiming to improve antibiotic prescribing practices and combat the threat of AMR effectively.[5] Survey studies offer a valuable avenue for antimicrobial research, providing insights into prescribing behaviours, attitudes towards AMR, and the effectiveness of AMS practices.[6] The field of antibiotic prescribing has encountered challenges in survey participation, which is evident at both local and national levels.[7] Recruiting healthcare professionals to respond to surveys on antibiotic prescribing presents unique challenges due to their demanding schedules, the complex nature of antibiotic prescribing and the urgent need to address AMR.[8] Therefore, innovative survey distribution methods are essential to enhance participation rates, gather comprehensive data and inform evidence-based interventions to mitigate the threat of AMR effectively.[9]

A research project was undertaken at one of the National Health Service (NHS) Foundation Trusts. A prospective survey questionnaire was conducted to investigate the perceptions, attitudes and knowledge of 240 healthcare professionals regarding antibiotic prescription practices during the pandemic. The survey was initiated on 12 June 2023, and concluded on 13 September 2023. The survey was administered using Qualtrics and distributed electronically, accompanied by an invitation letter, participant information sheet[10] and professional poster. Ethical approval for this study was obtained from the Health Research Authority (HRA), with the Research Ethics Committee assigning reference number 22/EM/0161. In accordance with this approval, the study protocol underwent review and was approved by the University of Hertfordshire ethics committee under reference LMS/PGR/NHS/02975. Patient and public involvement were integral to this study, with representatives from the Citizens Senate being engaged. Their valuable input and feedback were integrated into the study's design and execution. Additionally, this study has been registered with the ISRCTN registry and Octopus, the global primary research record, ensuring transparency and accountability in research dissemination and reporting.[10,11]

The aim of this article is to evaluate the impact of using novel hybrid survey distribution methods, integrating traditional and digital strategies, in enhancing participation and achieving the target response for AMR/AMS research outcomes.

The objectives were as follows:

(i) To evaluate the effectiveness of novel survey dissemination strategies in healthcare settings;
(ii) To explore the potential for applying innovative survey distribution strategies across various areas related to AMR/AMS research;
(iii) To highlight the role of collaborative, multidisciplinary approaches in conducting impactful survey research to address public health challenges and enhance AMS efforts;
(iv) To identify key insights and recommendations to inform future AMR/AMS research initiatives based on the findings.

### *Methods*

To secure the HRA's ethical approval,[12] preparing attractive materials was crucial, including a visually attractive poster aimed at boosting respondent engagement. Specifically designed for healthcare professionals, this poster incorporated attractive colours, bold typography, QR codes and medical imagery. Such elements effectively captured the attention of doctors and nurses, encouraging their participation in a survey focusing on antibiotic prescribing and AMS practices during COVID-19. The poster's clear objectives and user-friendly layout further heightened its effectiveness as a tool for research participation (Figure 1).

Innovative strategies significantly enhanced visibility and participation in a healthcare survey. QR code-enabled posters, designed with key survey information, were placed in high-visibility areas, such as nurses' stations and staff rooms, ensuring easy access. The survey's digital distribution, through weekly e-newsletters and group e-mails from the Trust's Communication Team, was carefully timed to maximize engagement during optimal periods, such as early mornings, lunch hours and evenings. This multifaceted approach combined physical poster placement with effective digital dissemination, leveraging both traditional and modern methods. The R&D department's advice on poster sizes also played a crucial role, ensuring widespread and effective visibility across key hospital areas. This innovative mix of physical and digital strategies effectively increased survey participation among healthcare professionals in the wards, emphasizing the importance of varied and accessible distribution methods. To enhance survey participation, 50 A4-sized laminated posters were printed and strategically placed in hospital wards and departments. This was supported by digital dissemination through group e-mails and e-newsletters featuring QR codes, as shown in Figures S1–S3 (available as Supplementary data at *JAC-AMR* Online). The mix of traditional and digital methods significantly increased healthcare professionals' involvement, boosting response rates and AMR awareness. Table S1


**Figure 1.** Professional poster for healthcare professionals within the Trust.

outlines a systematic distribution plan for a survey targeting healthcare professionals within a Trust. The approach includes targeted e-mails, strategic placement of posters, and digital distribution via newsletters and WhatsApp groups. This is designed to enhance participation rates in a study focused on antibiotic prescribing behaviours and AMS during the COVID-19 pandemic (see Supplementary data for details).

### Results

The high or improved participation in the survey was determined through a comprehensive analysis of various key indicators and outcomes resulting from the innovative survey dissemination methods implemented in this research project. Firstly, the response rate was monitored by comparing the number of responses received with the total number of surveys distributed over a specified period. Within a 3 month period, the objective of attaining the required sample size of 240 participants was successfully met, exceeding the response rate observed in preceding surveys or comparable questionnaires that did not incorporate innovative dissemination strategies. This achievement signifies an elevated level of participation, as highlighted by the R&D department. Secondly, qualitative feedback gathered from participants provided valuable insights into their experience with the survey dissemination methods. Positive feedback regarding ease of access, user-friendly design and the effectiveness of communication channels supported the notion of improved participation.

Additionally, feedback from key stakeholders within the Trust, such as R&D directors and AMS leads, contributed to assessing engagement levels. Lastly, quantitative data on dissemination metrics, including the number of posters distributed (200 copies), frequency of digital distribution through group e-mails and electronic newsletters (e-newsletter), and the use of QR codes, offered tangible evidence of the reach and effectiveness of the distribution methods. These novel survey dissemination methods successfully sustained participation rates and improved the overall outcomes of antimicrobial survey research.

### *Discussion*

The research on AMR highlights the need for innovative survey distribution methods to address the AMR global health crisis effectively. Traditional and digital methods were combined to enhance participation rates among healthcare professionals. Visually appealing posters with QR codes were strategically placed in hospitals, complemented by digital dissemination through e-mails and e-newsletters. This multifaceted approach facilitated the achievement of the required responses within a 3 month period, in contrast to the response rates of previous surveys conducted within the same NHS Foundation Trust. Interestingly, the systematic review by Meyer *et al.*[13] explores the variance in response rates for patient and healthcare professional surveys within surgery, revealing that factors such as survey type, follow-up methods, geographical location and respondent category significantly influence participation rates, with an average response of 70% for patient surveys and 53% for doctor surveys. The 2023 GP Patient Survey, conducted by NHS England and Ipsos, reveals insights into primary care service experiences, with a 28.6% response rate from 760000 participants out of 2.65 million queried.[14] However, there is a scarcity of data on survey participation rates in antibiotic prescribing, both locally and nationally.[13,14] The innovative dissemination strategies presented in this article are pivotal, as they demonstrate a significant impact on AMR research outcomes by effectively engaging healthcare professionals—a key step in tackling AMR.

Effective survey distribution is crucial for reaching target audiences, securing higher response rates, and obtaining quality data. Pros include improved engagement through diverse methods, such as e-mail, social media and short message service texts, which can be tailored to specific audiences and geographical locations. Cons include the potential for low response rates if methods are not well chosen, data privacy concerns and the risk of surveys being perceived as spam. Balancing the selection of distribution methods against research project goals and audience preferences is essential for research success.[15]

In this article, the lead author (RAE) has developed a dissemination plan before initiating the survey distribution. This involved assessing various dissemination methods and considering their pros and cons in collaboration with the R&D team at the Foundation Trust. The most effective means of dissemination were chosen based on available resources and optimal communication strategies with the target healthcare professionals. Novel methods were employed, including the strategic placement of posters in hospital wards and on notice boards. QR codes were used to streamline dissemination, and there was a collaborative effort with the Trust's Communication Team to distribute the survey through weekly e-newsletters and group e-mails.

Although traditional methods are capable of obtaining the necessary responses, they may face challenges in doing so and could result in significant delays in survey feedback, analysis and outcomes. Additionally, these methods sometimes struggle to engage a busy demographic effectively. Therefore, especially in the post-pandemic era, it is imperative to adopt innovative approaches, as detailed in the manuscript. These are essential for enhancing response rates, expediting survey responses and results, gathering complete data, promoting AMR research, and making a significant contribution to the global effort against AMR.[15,16]

As presented in this article, the use of traditional methods, such as sending reminder e-mails, was effective in encouraging responses and helped to increase survey participation. Qualitative feedback emphasized the effectiveness of these methods in facilitating participation. The combination of traditional and digital methods in disseminating the survey was also one of the important factors in achieving the required number of responses. This mixed approach offers benefits for resource-limited settings as it can be customized to fit each healthcare environment. Additionally, it encourages innovative thinking to reach the target survey participants and boost response rates effectively. Such engagement is invaluable in surveillance studies and other research related to AMR, a global health issue that requires urgent attention and continuous research to address and offer practical solutions to the AMR challenge.[17] Furthermore, these innovative approaches to survey dissemination may be applied to a wide array of survey studies, extending well beyond the domain of antimicrobial resistance.[17] They prompt the integration of creative, outside-the-box strategies that are tailored to engage the intended audience effectively. Such methods enable the adaptation of survey distribution to align seamlessly with the specific context of the healthcare environment, the distinctive characteristics of the survey itself and the available resources, thereby fostering a more impactful research engagement.[18] Adapting these methods to fit the local context allows for the overcoming of barriers, ensuring effective communication and participation even where resources are scarce. This therefore extends the potential impact of AMR research to mitigate the AMR challenge and save patient lives.[18]

Following the survey analysis, the lead author also disseminated the final report to healthcare professionals at the Foundation Trust and shared research insights on Springer Nature Community,[19] aligning with World Antibiotic Awareness Week.[20] This effort highlighted the role of AMS against AMR, reflecting the United Nations' Sustainable Development Goals.[19]

### *Conclusion*

This article has emphasized the impact of novel dissemination strategies in AMR/AMS research, demonstrating their effectiveness in enhancing participation and awareness among healthcare professionals. The strategic integration of hybrid methods—comprising traditional elements such as eye-catching posters with QR codes, and modern strategies like targeted e-mail campaigns—has effectively met participant targets, showcasing a viable solution to the challenge of engaging the busy medical community. This multifaceted approach not only shows the efficacy of these hybrid strategies in achieving the target survey responses but also highlights the potential of these methods to be applied broadly across various research domains beyond AMR. The findings advocate for a collaborative and multidisciplinary approach to conducting impactful antimicrobial research, emphasizing the urgent need for innovative, 'outside-the-box' methods in AMR/AMS research, particularly in the post-pandemic era. Although the surveys may not always be the most effective standalone research method, the innovative hybrid distribution strategies discussed could improve and complement other research methods. These strategies could significantly enhance AMR/AMS research, highlighting the need for creative, multidisciplinary approaches. This collaborative approach seeks to strengthen and sustain efforts that significantly support public health, ultimately aiming to save lives globally.

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## Transparency declarations

All authors declare no conflicts of interest.

## Data availability

All data extraction forms, statistical analytic codes and any other materials used in the review are available on reasonable request.

## Supplementary data

Figures S1 to S3 and Table S1 are available as Supplementary data at *JAC-AMR* Online.

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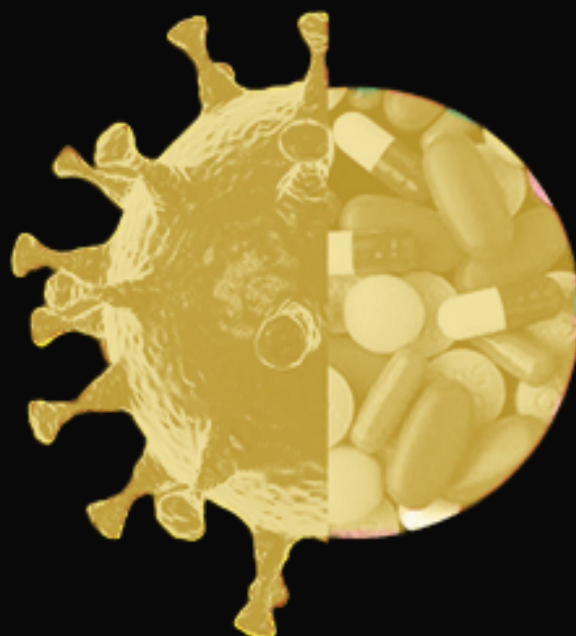

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