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Abstract

Background

Medication errors are one of the leading causes of harm in healthcare. Review and analysis of errors have often emphasized their preventable nature, and potential for re-occurrence. In the past decade, research has focussed on estimating the scale of medication errors and prevention. Much of this work has been in secondary care, which is associated with high-risk procedures and the use of high-risk medicines. However, patients receive most of their healthcare needs in primary care. Of the few error studies conducted in primary care to date, most have focussed on estimating the incidence, describing the nature of individual parts of the medicines management system, and evaluating individual error-prevention strategies. Studying individual parts of the system does not provide a complete perspective and may further weaken the evidence and undermine interventions.

Aim and Objectives

This paper reviewed the existing literature on the incidence of medication errors in primary care across the entire medicines management system. The objectives were:

1. To appraise studies addressing medication error rates in primary care
 - a. To report error rates at each point of the system
 - b. To appraise the methods used to identify errors in the studies
 - c. To identify of the most susceptible points and patient groups
 - d. To compare error rates between healthcare settings, and
2. To identify studies on interventions to prevent medication errors in primary care.

Methods

A systematic search of the literature related to medication errors in primary care was performed in the following databases: PubMed (MEDLINE), International Pharmaceutical Abstracts (IPA), Embase, PsycINFO, PASCAL, Science Direct, Scopus, Web of Knowledge, and CINAHL PLUS from 1999 to November, 2012. Bibliographies of relevant publications were searched for additional studies.

Results

Thirty-three studies estimating the incidence of medication errors, and thirty-six studies evaluating the impact of error-prevention interventions in primary care were identified and reviewed. Studies stating definitions and methods used, and those measuring the impact of interventions were included. This review demonstrated that medication errors are common, and occur at every stage of the process, with error rates between < 1% and >90%, depending on the part of the system studied and the definitions and methods used. It was difficult to directly compare error rates between studies due to differing units of measurement and sampling methods. There is some evidence that the prescribing stage is the most susceptible, and that the elderly (over 65 years), and children (under 18 years) are

more likely to experience significant errors, although little research has focussed on these age groups. Individual interventions such as medication reconciliation or pharmacist-led interventions demonstrated marginal improvements in medication safety when implemented on their own but had more impact when jointly implemented. The overall safety and quality of the medication system could be improved by adopting a holistic approach to management and interventions.

Conclusion

Targeting the more susceptible population groups and the most dangerous aspects of the system may be a more effective approach to error management and prevention in primary care. Co-implementation of existing interventions at points within the system may offer time- and cost-effective options to improving medication safety in primary care.

Keywords: Medication error (and related terms) and primary care (and related terms); not secondary care (and related terms).

Introduction

Medical error and patient safety have been the subjects of discussions for government bodies, healthcare organizations, the media, researchers and patients in the past decade. The American Institute of Medicine (IOM) report, *“To err is human”*, describes the harmful, common, expensive and, importantly, the preventable nature of medical errors [1]. A UK Department of Health (DH) report, *“An organization with a memory: learning from adverse events in the NHS (National Health Service)”* [2], emphasises the importance of learning from errors based on their potential for reoccurrence. These government reports underscore the need for a paradigm shift in safety culture within healthcare teams and organisations, the role of teamwork, and active reporting. The USA, UK, World Health Organization and many developed countries including Australia and Denmark, have identified that priority needs to be given to improving patient safety and outcome [2-6].

Medication errors are one of the most common types of medical errors resulting in patient morbidity and mortality [7-10]. Much of the research conducted on medication safety has focussed on the secondary care setting because of its associated high-risk procedures such as blood transfusion, surgery and the potential for hospital-acquired infections [8]. However, a few studies have indicated that patient safety incidents in hospitals take their roots from primary care management [11].

The medicines management process differs between secondary and primary care owing to variations in practitioner, patient and process features with implications for error potential. For example, in secondary care, there is close co-working amongst healthcare professionals – doctors, nurses, pharmacists – and medication administrations and reviews occur in collaboration. In primary care however, patients come into contact with these health care professionals at different times and places, and mostly self-administer their own medicines. Patients may frequent multiple pharmacies in primary care presenting challenges for medicines reconciliation [12]. Medication monitoring in primary care is further complicated by relying on the patient to organise and book follow-up appointments [13]. A World Health Organization (WHO) body, World Alliance for Patient Safety, concludes that inadequate or inappropriate communication and coordination are major priorities for patient safety research in developed countries [14].

Medication error studies evaluate whether a medicine is correctly handled within the medicines management system, which comprises of prescribing, transcribing, dispensing, administration and monitoring stages [9, 10, 15]. An Adverse Drug Event (ADE) is said to occur when patient harm is caused by the use of medication – a preventable ADE therefore may occur as a result of a medication error [9, 16]. The specific rates of medication errors (and preventable ADEs) are unknown; most errors in medication go unnoticed. Of those identified, few result in patient harm [17]. For instance, of a prescribing error rate of 1.5% detected in 36,200 medication orders in a UK hospital, *only* 0.4% orders contained a serious error [18]. In a recent UK primary care study, 4.9% prescriptions contained a prescribing or

monitoring error when the medical records of 1,200 patients from 15 general practices were reviewed [19]; of these, 1 in 550 (or 0.18%) of all prescriptions was judged to contain a severe error. In a UK study of 55 care homes, although 69.5% of all residents had one or more errors, the mean potential harm from errors in prescribing, monitoring, administration and dispensing were 2.6, 3.7, 2.1 and 2.0 (0 = no harm; 10 = death) respectively [20]. These seemingly 'low' values of actual harm are better understood when interpreted in terms of the high volumes of prescriptions issued daily within any healthcare system. Even more so, associated patient morbidity and mortality is simply unquantifiable.

The preventable nature of medication errors, and the potential for re-occurrence are perhaps their most important characteristics. These attributes underpin medication safety concepts such as error reporting and learning, and the development and implementation of prevention strategies, as errors are often the results of the systems that produce them [21]. A few studies have estimated the preventability of medication errors in primary care [22-30]. In the UK, approximately 5% admissions to secondary care have taken their roots from preventable drug-related problems at an estimated cost of over £750 million per year to the NHS [7]. A healthcare system, with safety and quality at its heart, is therefore expected to capture errors, and most importantly, prevent re-occurrence.

System thinking has underpinned successful investigations into sub-optimal patient care – the events of the Bristol Royal Infirmary in the UK sparked an investigation, which focussed on evaluations of the system rather than the events in isolation [10]. Most error studies focus on individual points within the medicines management system, instead of adopting critical and holistic evaluations of the whole system of the use of medicines [8]. Similarly, interventions have often concentrated on improving individual parts of the system. For instance, automation in hospital pharmacies has aimed at improving the dispensing process [31], – even though other parts of the system may also benefit from some form of automation . This individualistic approach fails to recognise that errors are indeed the results of the systems that produce them and does not provide information on the relationship between the units that make up the system [21, 32].

To date, there have been few systematic reviews to appraise the safety of the entire medication use system in primary care across healthcare systems.

Aim of review

This paper reviewed the existing literature on the incidence of medication errors in primary care across the entire medicines management system. The objectives were:

2. To appraise studies addressing medication error rates in primary care
 - a. To report error rates at each point of the system
 - b. To appraise the methods used to identify errors in the studies
 - c. To identify of the most susceptible points and patient groups
 - d. To compare error rates between healthcare settings, and
2. To identify studies on interventions to prevent medication errors in primary care.

Methods

Data sources

Electronic databases of MEDLINE, International Pharmaceutical Abstracts (IPA), Embase, PsycINFO, PASCAL (searched together on Wolters Kluwer/OVID SP platform in the British Library, BL), Science Direct, Scopus, Web of Knowledge and CINAHL PLUS were searched. The choice of databases was based on the BL resources in Medicine and Healthcare, University of Hertfordshire Medicines-related database recommendations, and relevant publications. Reference lists of retrieved articles and relevant review articles were checked manually for further relevant studies.

Search terms and strategy

An initial scoping review retrieved 2,530 hits after removal of 450 duplicates. Following screening of the first 350, over 200 articles were secondary care-related studies; subsequently, a revised search strategy excluded secondary care terms. Furthermore, the term “adverse drug event” was used as a medication error search term. This returned over 10,000 additional results. The first 300 articles were related to the harm due to drug use. However, this review aimed to identify failures in the medication use process in order to provide an overview of the overall reliability, efficiency and safety.

The search strategy, tailored for each database, therefore included two concepts, medication error and primary care, and excluded a third, secondary care (see [Table 1](#)). “Medication error” was used as MeSH term and keyword. A hand search of key journals, which included International Journal of Pharmacy Practice (IJPP), Quality and Safety in Healthcare, and Pharmacy World and Science, was also performed.

Selection criteria

Studies conducted in any country between January 1999 and November 2012 and reported in English, were included. Studies, which reported the frequency of errors in the medicines management process, and interventions to prevent errors, were included. All definitions of error such as inappropriate prescribing, prescribing-, dispensing-, administration- and monitoring- errors, irrational drug use, hazardous prescribing, drug interactions, were included. Studies estimating error rates of one medication or therapeutic group, and those that did not report the method used for collecting error data or evaluating interventions were excluded.

The first author (JGO) screened all titles and abstracts to determine whether the article met the inclusion criteria and should be retrieved. Another reviewer (MG) screened a random 5% sample to check the reliability of the screening. JGO then read and extracted data from the articles included in this review.

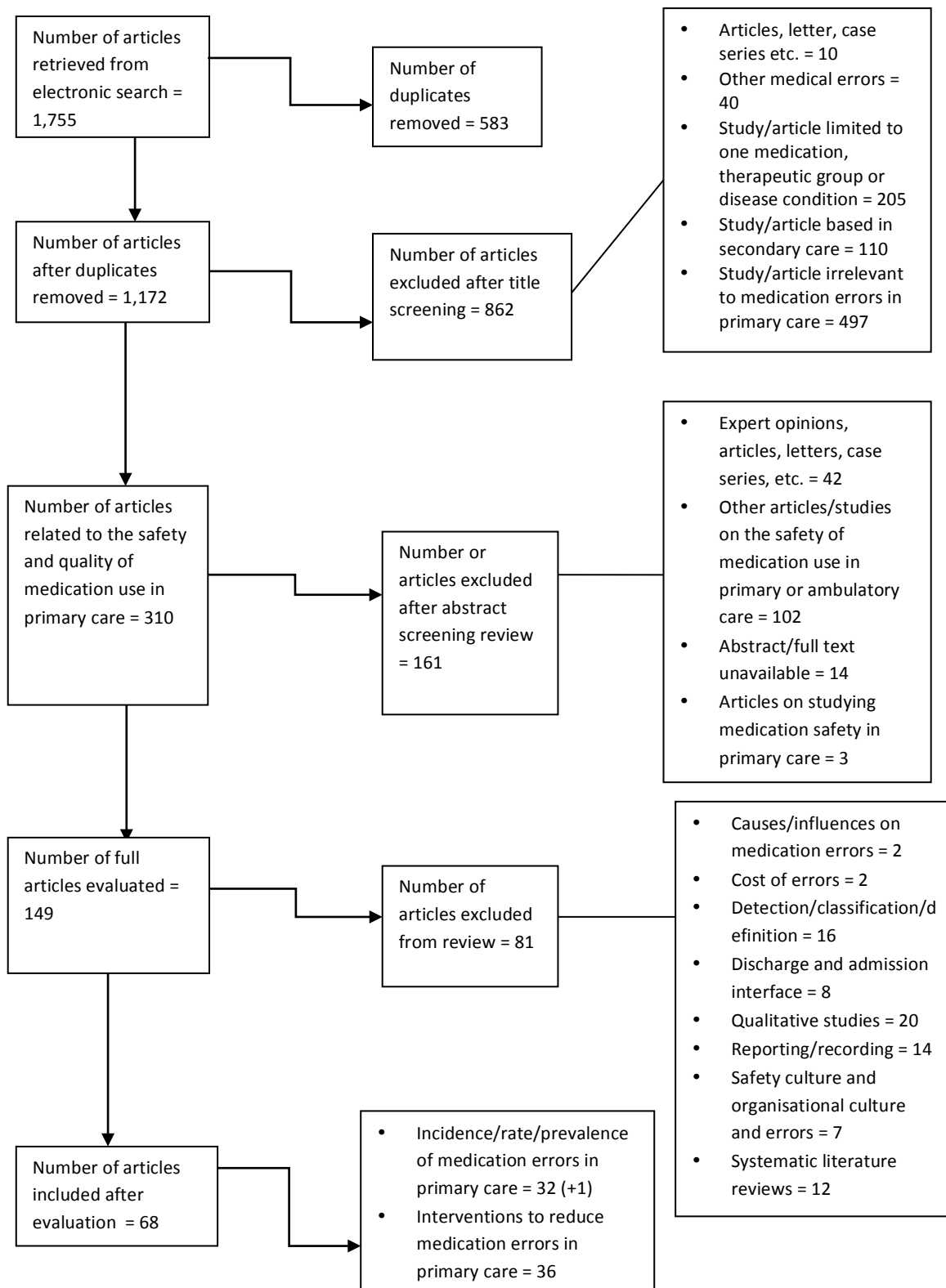
Process of data extraction

Search results were exported to Endnote X5 (Thomson Reuters). Duplicates were removed. Article titles and abstracts were initially reviewed for relevance followed by actual article review to clarify any ambiguities. Information from incidence studies was extracted onto a pro-forma showing primary author, year of publication, study design and setting, sample size, error type, error definitions and reported error rates (Table 2). Intervention studies were grouped into broad categories (Table 3).

Table 1: Search terms

Medication error terms		Primary healthcare terms		Secondary care-terms
Medication error, prescribing error, dispensing error, medication administration error, transcription error, drug error, drug mishap, medication mistake, medication mishap, dispensing mistake, prescribing mistake, wrong drug, wrong dose, incorrect drug, incorrect dose, drug death.	And	Primary care, primary healthcare, general practice, family practice, patient admission, patient discharge, continuity of patient care, doctors' office, ambulatory care, surgery.	Not	Secondary care, secondary healthcare, inpatient, hospital, ward, emergency department.

Figure 1: Flow chart of titles screening



Results

The output of the search process is shown in Figure 1. Thirty-two studies, which estimated the incidence of medication errors in primary care were identified; a manual search retrieved one additional study [19]. Thus, thirty-three studies were identified and reviewed (Table 2)

Table 2 (sheet 1): Summary of studies reviewed on the incidence of medication errors in primary care (see table in separate excel spreadsheet document submitted along side the main manuscript)

Incidence of medication errors in primary care

Of the studies reviewed, twelve were conducted in the USA, ten in the UK, two in Bahrain, one each in Malaysia, Italy, Germany, Saudi Arabia, Denmark, Spain, India, Australia and Ireland between 1995 and 2013, and published between 1999 and 2012. Prescribing error rates were comparable across countries in some instances – Bahrain – 7.7% prescriptions [33]; UK 7.5% & 5% prescriptions [19, 34]; USA 7.6% & 11% prescriptions [12, 35]; India 6.1% items [36] and Ireland 6.2% prescriptions [37].

Table 2 (sheet 2): Country distribution of studies (see table in separate excel spreadsheet document submitted along side the main manuscript)

Of the studies reviewed, nine were conducted in primary care centres (general practices). Ten of the studies were conducted in the community pharmacy setting, ranging from one to 1,146 pharmacies [26, 28, 29, 38-44]. Two studies were conducted in care facilities – aged care [45], and nursing or residential homes [20]. Two studies each estimated medication error rates in elderly patients [24, 45] and paediatrics [44, 46]. One study was conducted in the primary care setting of a university [47].

The parts of the medication management system studied were sometimes apparent from the article title, aims or objectives; other times, they were inferred from the methods reported or the results presented. The part of the medication system studied comprised the prescribing stage (26 studies) [12, 19, 20, 22-29, 33-38, 42, 44, 46-52], transcription (4 studies) [26, 29, 43, 46], dispensing (10 studies) [20, 26-28, 39-43, 45], monitoring (8

studies) [19, 20, 23, 24, 26, 27, 46, 50] and administration(10 studies) [20, 23-25, 27, 28, 42, 46, 53, 54].

Table 2 (sheet 3): Number of studies at each stage of the medication management system in primary care (see table in separate excel spreadsheet document submitted along side the main manuscript)

The studies used differing methods to collect error data. These methods were either retrospective or prospective and varied with the part of the medicines management system being studied:

Studies, which evaluated prescribing or monitoring errors, used one of these methods: patient clinical record reviews [12, 19, 20, 22-24, 46-50], prescription audits [12, 22, 28, 29, 33-38, 42, 44, 46, 49], incident reports reviews [26, 27, 40], patient surveys or interviews [12, 23, 46], and claims reviews [52].

There were important variations even within methods; for instance, retrospective prescription reviews were conducted by reviewing patient medical records [19], through pharmacists' screening and intervention [28], or researchers' screening and/or observations [22, 44].

Dispensing errors were evaluated using one of these methods: direct observations of dispensing activities [39], retrospective examination of dispensed medicines [20, 41, 43, 45], incident reporting [27], and review of self-reported incidents and 'near misses' [26, 28, 40, 42].

It was sometimes difficult to interpret the methods used to detect and evaluate administration errors; of those clearly stated, the methods used were direct observation [20], retrospective review of administration data [27] or patient records [24, 53], barcode systems [54], patient surveys and/or self-reports [23, 42, 46].

Three studies used more than one method to evaluate medication errors – in one study, prescriptions and clinical records were reviewed to evaluate prescribing errors [22]; in another, patient surveys and medical record review were both used to study monitoring errors [20]; and finally one study used, medical record reviews and healthcare professional interviews to detect and evaluate prescribing and monitoring errors [19].

Of the studies reviewed, only a few studies stated the error definition used (Table 2). Two studies, which used the same definitions of prescribing and monitoring errors, had common authors [19, 20].

Varying denominators were used to calculate and determine error rates. As such, the units of expression varied between studies. Studies reviewed expressed error rates as: a percentage of – total prescriptions [12, 19, 22, 26, 29, 33, 35, 37, 41, 44, 46], patients [19, 23, 45-47, 50], items/packs [34, 36, 37, 39, 40, 43, 49, 52, 54], opportunities for errors [20], total errors [27, 28], and in patient/person years [24, 48].

The highest error rates were recorded for the prescribing stage as follows: for paediatric patients – 90.5% of prescriptions (Bahrain) [44] and 74% of prescriptions (USA) [46], for elderly patients – 8.3% of opportunities for error [20], and when all errors (including administrative errors such as illegibility with hand-written prescriptions) were recorded [44].

The lowest error rates were recorded as follows: for incident report reviews – 23/10,000 prescriptions (prescribing error; Denmark) [55], for dispensing error rates – 1.4/10,000 prescriptions (Denmark) [55]; 0.08% and 3.3% items and 3.99/10,000 items (UK) [39, 40, 43], and in studies, which focussed on a specific prescribing category – 0.2% total items (Italy, interactions) [52]; 0.7% patients (USA, interactions) [50].

Interventions to reduce medication errors in primary care

Thirty-six studies evaluating interventions to prevent errors in primary care were reviewed – computerisation including provider order entry systems (CPOE), electronic prescribing, clinical decision support/clinical alerts and electronic health records [12, 13, 56-66], personal digital assistants (PDAs) [67], educational outreach and prescribing support [14, 63, 68-74], formularies [68, 69], pharmacist-led interventions [64, 69, 75-77], barcode systems [78], medication reconciliation and patient engagement [79-82], quality management strategies [83] (Table 3)

Previous systematic reviews and meta-analysis of interventions to prevent medication errors in primary care in the existing literature have demonstrated a weakness in the evidence of effectiveness interventions [84-87]. Most interventions have been individually implemented and evaluated.

Table 3: Interventions to reduce medication errors in primary care

Interventions	References ¹
1. Computerisation/electronic interventions:	
• Computerised physician/provider order entry (with or without clinical decision support, CDS e.g. monitoring alerts)	Gandhi et al, 2005; 2002[12, 13]; Devine et al, 2010[59]; Palen et al, 2006[88]; Tamblyn et al, 2008[66] ² , Gandhi et al, 2005
• Electronic Health Record (EHR), electronic prescribing, and electronic transfer of prescriptions	Abramson et al, 2011[56]; Devine et al, 2010 [59]; Boockvar et al, 2010[57]; Moniz et al, 2011[62]; Nemeth et al, 2010[63]
• Personal digital assistance with clinical decision support	Berner et al, 2006[58]; Dallenbach et al, 2007[67]
• EHR with weight-based prescribing (CDS)	Ginzburg et al, 2009 [89]
• CPOE with retrospective medication profiling	Glassman et al, 2007 [90] ³
• Community pharmacy Patient Medication Record (PMR) with drug interaction software/other alerts	Hazlet et al, 2001 [60]; Humphries et al, 2007[61]; Raebel et al, 2007 [64]
• Authentication at the point of dispensing (stand-alone, PMR-linked and electronic transfer of prescriptions (ETP)-linked)	Franklin and O’Grady, 2007[43]
• Pharmacy computer system with dispensing support (medication alert/verification)	Norden-Hagg et al, 2010 [91]; Raebel et al, 2007 [64]
• Computer-assisted feedback between healthcare professionals	Avery et al, 2012 [69]

¹ Studies demonstrating marginal impact (see footnotes 3 and 4 below) were included to reinforce the need for optimisation of interventions

² There was a significant reduction in therapeutic duplication problems in the computer-triggered group (odds ratio 0.55; p = 0.02) and no effect on prevalence of prescribing problems at follow-up.

³ Marginal improvements in ADE preventability was reported (16% in the Usual Care group and 17% in the Provider Feedback group had an associated warning; 95% CI for the difference, -7 to 5%; p = 0.79)

Interventions	References ¹
<ul style="list-style-type: none"> Pharmacy system improvement strategies 	
<p>2. Educational support, prescribing support and management:</p>	
<ul style="list-style-type: none"> Academic detailing and educational outreach, Pharmacological profiling of patients, use of formulary/drug lists 	<p>Ahmad et al, 2006 [68]; Avery et al, 2012 [19]; Bregnhøj et al, 2009 [70]; Lafata et al, 2007 [72]; Lopez-Picaso et al, 2011 [73]; Nemeth et al, 2010 [63]; Stefanovic et al, 2011 [74]</p>
<p>3. Pharmacy or Pharmacist-led interventions</p>	
<ul style="list-style-type: none"> Collaborations between pharmacists and prescribers (general practice) 	<p>Avery et al, 2012 [19]; Braund et al, 2010 [76]; Buurma et al, 2004 [77]; Humphries et al, 2007 [61]; Raebel et al, 2007[64]; Bregnhøj et al, 2009 [70]</p>
<ul style="list-style-type: none"> Collaborations amongst healthcare providers (e.g. from other healthcare setting) 	<p>Booij et al, 2003 [75]</p>
<ul style="list-style-type: none"> Clinical Pharmacy Services 	<p>Sorensen et al, 2009 [92]</p>
<ul style="list-style-type: none"> Pharmacy-led bar code medication administration systems 	<p>Wild et al, 2009 [78]</p>
<p>4. Medication reconciliation: medication reviews and medication monitoring</p>	<p>Bernstein et al, 2007 [79]; Varkey et al, 2007 [82]</p>
<p>5. Quality management strategies</p>	<p>Singh et al, 2012 [83]</p>

Discussion

This review of the literature demonstrated that safety and quality issues currently exist at each stage of the medication management system, the prescribing stage being the most susceptible point. There is some evidence that children and the elderly are the more susceptible patient groups. Error rates ranged between <1% and 90% depending on the error definition, methods used, and on the patient population being studied. Direct comparison across settings was difficult due to variation in methodology, definitions and units of measurements. However, when error rates were expressed with a common denominator, rates were comparable between countries. Collaborations between practice and research may provide cost-effective options to interventions to prevent errors and improve patient outcomes [8].

This review has tried to present a holistic view of the safety of the medication use pathway in primary care across different healthcare settings, and has evaluated a broad range of error types. By doing so, the susceptible points in the medicines use process, and the most vulnerable patient populations were identified. The results are applicable across a range of healthcare settings, and provide opportunities for stakeholders to influence practice and policies in a strategic, scientific manner.

One of the limitations of this review is the exclusion of the term “adverse drug event” from the medication error terms, which may have meant that relevant articles were not identified. Furthermore, previous research show that patient safety incidents in hospitals take their roots from primary care management – in the UK, 6.5% admissions to hospital were related to adverse drug reactions in a study of 18,820 patients that were admitted to hospital [11]. Valuable insight may have been obtained from studying the admission-discharge interface. However, due to the varying nature of the primary-secondary care interface across countries, studies at the admission-discharge interface were not included. Lastly, studies included in this review were not of the same level of evidence; the aim was to provide an estimate of the incidence of medication errors in primary care. As such, limiting the studies to the same evidence levels would have precluded the international insight, which has been hopefully provided.

Most of the studies reviewed were actually conducted in community pharmacies, not within general practices [26, 28, 29, 38-44] following patients’ receipt of their prescriptions from general practices – even though the studies are often described as “primary health centres”, [33-37, 44], they may be better described as community-based.

The number of sites and the duration of observation were highly variable; one study was actually done in one community pharmacy [29]. The absolute number of patients and/or prescription items is of significance based on the opportunities for errors. Only two studies [19, 43] reported a systematic and scientific determination of sample size. The sampling period is also an important variable. Study periods need to consider the effect of seasonal

variations on prescription volumes and types, and hence error rates. As such, prescription reviews conducted over a one-week period as reported in some of the studies reviewed [33, 42, 44] are not necessarily representative of day-to-day practice.

Although some of the studies suggest that older and younger patients are more likely to experience a clinically significant medication error than the rest of the population [19, 20, 25, 93], only two studies each, focussed on elderly patients [24, 45] and children [44, 46]. With an aging population, co-morbidities, polypharmacy [47], contact with multiple providers [47, 94], care transitions [20] are on the increase. The need for weight-based therapeutic interventions in children [93, 95] and lack of readily available proprietary medicines in strengths suitable for paediatric dosing often necessitating titration, have long influenced medication safety in the paediatric setting. Moreover, the elderly and children use primary healthcare more than the rest of the population with implications for medication safety in the face of the ever-pressured healthcare system. There is therefore an urgent need for more research into medication safety amongst these patient populations.

Previous researchers have identified the prescribing and administration stages as the most dangerous stages of the medicines management system [15]. Twenty-six of the thirty-three studies reviewed evaluated the prescribing stage in keeping with this finding. There is some suggestion in the existing literature that errors occur when patients take their medicines, and that there is a need to prioritize processes at the patient end of the system for interventions [8]. This review showed that there is a shortage of studies at the 'patient end of the system,' because of the obvious difficulties. Nonetheless, there is substantial evidence in practice that many patients may not be using their medicines as directed resulting in therapeutic failure and hospital admissions [96-98]. Research and practice must therefore overcome the challenges of evaluating medication administration quality and safety in primary care to improve patient health outcomes.

Although the use of varying error definitions by researchers in determining error rates has been previously identified [8, 99-101], this review has confirmed that this problem still exists. This is reflected in the wide range (<1% - >90%) of error rates reported. Such variance in definitions and data capture could lead to erroneous evaluations of the system causes of error. Attempts to develop common definitions for practice and research have been made [43, 95, 101], and although more studies and practice in secondary care are adopting the use of these definitions [102], there is still significant variation among the studies reviewed. One study [19] adapted a definition developed in secondary care for use in primary care but due to differences in the medication handling system between both settings, this approach may be burdensome, difficult to interpret, and result in loss of important data. There is a need for a primary care practitioner-led definition of a prescribing error, where the highest error rates are recorded.

This review has also demonstrated that error rates varied with the method of identification. For example, the highest error rate of 90.5% prescriptions, [44] was recorded in Bahrain

following the audit of paper prescriptions issued for paediatric patients from 20 primary health care centres. Although all errors, including illegibility were captured, this figure excluded 'minor errors of omission'. When paper prescriptions were reviewed in a prospective cohort study in the US, 94% of all medication errors (74% prescriptions) recorded were at the prescribing or ordering stage [46]. While it may be argued that systems, which produce minor errors like incomplete prescriptions are also able to produce major errors that lead to patient harm [21], defences within the system would intercept some 'minor' errors such as illegibility; for example, a clinical check on a prescription prior to dispensing by a pharmacist is a major "defence process". Conversely, in healthcare systems where pharmacists' roles are circumvented (such as in a dispensing practice) or otherwise undeveloped (as in most developing countries), there is a breakdown in this defence.

A high prescribing error rate of 8.3% opportunities for error or 39% of all patients was also recorded in a study of elderly patients in residential and care homes [20]. The methods used to record medication errors were robust, comprising patient interviews, note reviews, practice observations and dispensed items examination. This was possible because all elements of the methods were applicable on the same sites. Incomparably with other studies, the dispensing error rate in this study was higher than both the prescribing and administration error rates reported in the same study. In the healthcare setting in this study, general practitioners and community pharmacists manage home patients' prescribing and dispensing activities. These patients also have carers who provide their intermediate healthcare needs, including medication administration. The challenge with this arrangement is that vulnerable patients who need healthcare the most do not have ample opportunities to interact directly with their practitioners and pharmacists. The use of cassette type monitored dosage systems appear to be a practical solution for dispensing their medication but the study demonstrated that the incidence of dispensing errors is highest with this type of delivery system. Should nursing and residential homes be viewed and treated like subsets of secondary care? This is a policy issue that should be thoroughly evaluated.

The lowest error rates were from data captured from incident reports – prescribing error study in Denmark (23/10,000 prescriptions/0.23% prescriptions) [55], and in a US study [27]. This is in keeping with the literature. Although incident reporting is very useful for organizational error learning, and provides valuable feedback to practitioners [103], research has shown that they can grossly underestimate error rates [103, 104]. In the study in Denmark, community pharmacists documented prescription errors they had intercepted. Although community pharmacists are a practical source of data, and perform important error interceptions [105, 106], under-reporting remains a risk when pharmacy owners or managers collect study data themselves as evident in the lower rates reported in such studies [26-29, 38-40, 42]. In addition, when error rates are determined solely by recording pharmacists' prescription interventions, the lack of access to patients' medical histories at

the time of data collection may become a barrier to adequate evaluation of the safety and quality of prescribing.

Review of patient medical or clinical notes in general practices is perceived as a rigorous method for collecting prescribing error data [104]. This is reflected in this review – studies, which included an element of case note reviews reported consistently higher rates of errors even across countries, when compared to the use of incident reports and review of pharmacists' interventions (Table 2, sheet 1). However, notable issues around patient confidentiality, informed consent, and ethical provisions preclude access to patient medical records and prolong study duration. The gold standard is the use of a mix of methods for data collection [104], as a study showed no overlap when five methods were used [107]. Studies, which used a mix of methods to evaluate the safety and quality of the medication system provided pertinent information such as, causes of prescribing errors, clinical significance of errors, patient harm, and resultant hospital admission[19, 20, 46, 53].

Dispensing error rates were consistently low across countries. A UK study where researchers directly observed dispensed items found higher rates than those studies where incident reporting and review of 'near misses' were used, emphasising the issue of under-reporting. The additional checks incorporated in the dispensing process impact accuracy. On another hand, the potential for detecting dispensing errors by patients is low when compared to the detection of prescribing errors by pharmacists and other healthcare professionals.

It can be difficult to compare error rates when they are expressed in varying units: as percentage of – prescriptions or items [12, 19, 22, 33, 44], packs/doses prescribed, dispensed or administered [40, 45], multiples of items or packs [39, 52], opportunities for errors[20], total number of patients recruited to the study [47], and in patient or person years[24, 48]. The use of varying denominators can also lead to variation in reported percentages. Based on the large volumes of prescription items used in primary care, error rates expressed as a percentage of total prescriptions or items will make easier interpretation.

It is interesting to note that when comparable denominators were used, there is much consistency in prescribing error rates across countries – Bahrain – 7.7% [33]; UK 7.5% & 5% [19, 34]; USA 7.6% & 11% [12, 35]; India 6.1% items [36] and Ireland 6.2% items [37].

Optimising interventions to prevent medication errors in primary care

Error-prevention strategies help to improve patient health outcomes, and reduce healthcare costs associated with drug-related harm [108]. During the last decade, strategies to prevent error occurrence have been directed at secondary care [31]. Attention is now being paid to methods for improving medication safety in primary care (Table 2). Interventions have been mostly implemented to individual parts of the medicines management system, without important collaborations between research and practice. Implementing interventions in an isolated manner may provide minimal effects as observed in previous studies [66, 90].

Healthcare is a complex system with an overarching aim of improving patient health outcomes. Isolated, spontaneous reactions to serious critical incidents without rigorous evaluations of the interactions between various units of the system only yield multiplicity of similar interventions with slight and ineffective modifications. Indeed, a systematic review and meta-analysis of interventions in primary care demonstrated the weakness of the evidence for effectiveness of interventions aimed at reducing hospital admissions or preventable drug related morbidity [87].

With an aging population, availability of innovative but more expensive therapeutic agents, and tight healthcare budgets, optimising existing interventions becomes necessary. In the recently published Pharmacist-led Information Technology Complex Intervention (PINCER) Study, simple feedback plus PINCER (an educational outreach and dedicated support) in general practice, patients in the intervention group were significantly less likely to have experienced a range of medication errors [69]. This intervention demonstrated the benefit of collaborative interventions to improve the safety of medication use in primary care, and ultimately improve patient health outcomes.

Conclusion

This review has provided an international perspective on the safety of medication use in primary care across the medication management system. Targeting the more susceptible population groups and the most dangerous aspects of the system may be more effective to error prevention in primary care. Collaborative implementation of existing interventions may offer time- and cost-effective options to improving medication safety and patients' health outcome in primary care.

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