Title of the article:

"The clinical and financial implications of a decade of prostate biopsies in the NHS: analysis of Hospital Episode Statistics (HES) data 2008-2019"

Concise title- Analysis of the Hospital Episode Statistics (HES) Dataset for the last decade of Prostate Biopsies

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Conflict of interest

Mr. Jim Adshead – Clinical advisor for the light point medical and receives expenses for mentoring robot with the NHS

Mr. Rick Popert - Reports honoraria for teaching and training paid as personal fees from BXTAccelyon, grants from NHS Innovation Accelerator, personal fees from BK Ultrasound, personal fees from Health Care of America (HCA), personal fees from 3D Biopsy, personal fees from American Urological Association, outside the submitted work.

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Abstract

Objective

To evaluate the clinical and financial implications of a decade of prostate biopsies in the United Kingdom National health Service (NHS) through the transrectal (TR) and transperineal (TP) route. In the current antibiotic resistant era, TR biopsies of the prostate have alarmingly high infectious complications and readmissions. The TP route is a credible step to minimise these events, however the data comparing the two approaches has not been consolidated.

Methods

This is an evaluation of TR versus TP biopsy approach in the context of 28 days post procedure complications and readmissions, with secondary evaluation of burden of expenditure in NHS hospitals over the entire decade (2008-2019) by evaluating national Hospital Episode Statistics (HES) data.

Results

In this data set of 486,467 prostate biopsies (387,879 TR and 98,588 TP), rates for infection and sepsis were higher for the TR compared to the TP cohort (0.53% vs 0.31% p <0.001 CI 99%). Rates of sepsis have more than doubled for TR biopsies in the last two years compared to the previous decade (1.12% Vs 0.53%). Infective complications were the main reasons for readmissions in the TR cohort; whereas urinary retention was the predominant reason for readmission in the TP cohort. Over the last decade, non-elective readmissions (NEL) seem higher for the TP group, however in the last two years these have reduced compared to the TR group (3.54%

Vs 3.74%). The cost estimates for NEL re-admissions for the entire decade were £33,589,527 and £7,179,926 respectively for TR and TP cohorts ($p < 0.001$). Estimated costs per patient re-admission were £2,225 and £1,758 in the TR and TP groups ($p < 0.001$).

Conclusions

Evaluation of nearly half a million prostate biopsies in the NHS over the entire decade gives sufficient evidence for the distinct advantages of the TP route over the TR route in terms of reduced infections and burden of expenditure. In addition there is a potential for saving both in upstream and downstream costs if performed under a local anaesthetic.

Funding-Intuitive Surgical provided a research grant to access HES data via Harvey Walsh

Introduction

As prostate cancer incidence and prevalence rise every decade, the scope for the diagnosis and treatment is expanding every year. The age standardised incidence rate for prostate cancer between 1993 and 2016 has rocketed by the tune of 41%, amounting to 47,740 new cases of prostate cancer being diagnosed in the United Kingdom (UK) in 2014-2016 [1]. This contributes to 13% of all cancers detected during these years [2]. Needless to say that the predictions for incidence rates are alarming with an estimated 12% increase between 2014 and 2035, translating to around 233 cases of prostate cancer per 100,000 males by 2035 [3]. To date biopsy stands as the gold standard for diagnosis and the advances have paved the way from initial finger guided sextant biopsies to magnetic resonance imaging (MRI) guided fusion biopsies through the transrectal (TR) or transperineal (TP) route in the last few years. However, these biopsies come with morbidity in terms of complications, not only including infections, but also hospital readmissions amounting to a burden on healthcare resources [4 - 11]. Worldwide literature shows worrying rates of infections and readmissions after needle biopsy of the prostate with a recent increase in the rates of infective complications especially through the transrectal route which after all transgresses the faecally contaminated rectal wall [4 - 6, 8 -10]. To clarify this issue in the UK, we interrogated prostate biopsies (TR and TP) performed over a decade in National Health Service (NHS) hospitals with a

specific focus on healthcare utilisation and secondary costs involved in readmissions.

Methods

We used widely available national Hospital Episode Statistics (HES) data which contains information on inpatient admissions, outpatient appointments and accident and emergency (A and E) attendances for all UK NHS Clinical Commissioning Groups (CCGs) [12]. We accessed HES data via a licensed intermediary Harvey Walsh using a research grant from Intuitive Surgical. The HES data is collected during patients' interaction with the healthcare system as part of the commissioning data set (CDS). Once processed by NHS digital it can then be used for both clinical and non-clinical purposes such as research or planning health services. The HES data encompasses patients treated within the NHS including private patients treated in NHS hospitals, patients residing outside of England, and the details of care delivered by treatment centres. The data contains information on patient demographics, diagnosis and treatment and is managed by the NHS Health and Social Care Information Centre with more than 12 million new records added annually. It is available routinely and the data is pseudonymised precluding the need for ethical approval. This data has been entered on real time basis avoiding any recall bias and is subject to quality control. Each "episode" represents an inpatient admission period during which they are assigned a diagnosis coded for in the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), for their admission [13]. Each episode is additionally assigned a procedural code which is coded in the Office of Population Censuses and Surveys.

We used HES recorded procedure specific codes (Classification of Intervention and Procedure Codes or OPCS-4) to identify patients for our study population [14]. Patients were included in our study if they had been coded as M702 (Transperineal needle biopsy of prostate) or M703 (Transrectal needle biopsy of prostate). All patients who were either readmitted or attended A and E in the first 28 days following their respective indexed procedure were identified and assigned an ICD-10 diagnosis for their presentation in order to classify patients for subgroup analyses [13]. The full list of applied ICD-10 codes is presented in the supplementary appendix 1. We focused on a period of 28 days following the indexed procedure, as this reflects common practice when assessing care quality. Financial costs were

based on NHS “payment by results” Healthcare Resource Group (HRG) tariffs for 2013 [15]. The cost of each HRG was calculated giving us a financial cost for each procedure specific complication. This helped us identify which complication was the main cost driver. We included patients who had undergone either a TR or TP prostate biopsy between April 2008 and March 2019, which was a retrospective evaluation of this prospectively maintained pseudonymised dataset. The HES data between April 2017 and March 2019 was separately evaluated in addition to the entire decade to see if recent patients were experiencing different sepsis and complication rates. For the sake of evaluation of trends of different study parameters, similar statistics between April 2012 and March 2016 were used for analysis to calculate p trend values. For the estimation of upstream costs of the biopsy procedures (TR and TP either under general or local anaesthetic), the UK national tariff system for 2019-2020 [16] and NHS implementation toolkit for the Precision Point^{TM} Transperineal Access System guidance [17] were used.

Statistical analysis

Data was descriptively analysed to summarise patient characteristics. Continuous variables were described using means and standard deviations and categorical variables were described using frequencies and percentages. Comparison between TP and TR biopsies for infection, sepsis and non-elective admission (NEL), within 28 days where tested using the proportion test in Rstudio (version 1.0.136) using prop.test function [18]. The average NEL admission cost for TP and TR biopsies were compared using the non-parametric Mann-Whitney test. To see if there was any difference in the distribution of the top ICD-10 diagnoses for NEL admission and infections, we used a chi-square test with Yate’s continuity correction. We compared TR and TP biopsies in different volume centres in order to determine complication rates based on the volume of biopsies conducted. We then tested whether the number of biopsies conducted affects the complication rates. Statistical significance was considered at $p< 0.05$.

Results

A total of 486,467 prostate needle biopsies were evaluated of which 387,879 were transrectal biopsies and 98,588 were transperineal biopsies (Table 1). Similar figures for the last two years were 76,106 and 37,077 respectively (Table 1). Within

the ten year period, patients coded with sepsis rates amounted to 0.53% and 0.31% for TR and TP cohorts respectively. For overall infection related parameters, the percentage of patients with general infections and urinary tract infections as per the coding were 1.16% vs 0.77% and 1.17% vs 0.96% respectively for TR and TP groups (Table 1). The rates of infection and sepsis were statistically significant for the TR compared to the TP group considering the confidence intervals (CI) of 99% ($p < 0.001$) (level of significance- high***). Over the last two years these differences remained highly significant with similar CI of 99% with sepsis rates of 1.12% and 0.42% for the two cohorts respectively (Table 1). The percentage distributions of the most common reasons for infections varied between the two cohorts (Table 2). Death rates within 28 days of biopsy were 0.07% and 0.05% for TR and TP cohorts. For the entire decade the non elective admission (NEL) rates were higher for TP group (4.14% vs 3.89%) (p 0.00032) (Table 1). Similar comparison in the last two years was not significant on analysis (p 0.1067) due to the reduction in NEL admissions in the TP cohort. There was a significant difference in the top ten reasons for NEL admissions between these two cohorts in the aforementioned time periods ($p < 0.001$) (Figure 1). Infective complications were the main reason for NEL admission in the TR cohort with respect to both time periods, whereas urinary retention was the predominant cause for NEL admission in the TP cohort throughout the study interval. The estimated expenses for NEL admissions for the entire decade were £33,589,527 and £7,179,926 respectively for the TR and TP cohorts (Table 3). In the last two years these figures were £6,510,692 and £2,276,039 respectively (Table 3). Both the timelines showed a highly significant difference in cost considerations ($p < 0.001$) between the two groups. The average cost per patient admission varied from £2,225 to £2,288 in the TR group whereas in the TP group it varied from £1,758 to £1,732 (Figure 2). Excess burden of cost per patient for managing NEL admission for the TR group in comparison to the TP group in last two years was £ 467.16. The p trend values for both infection and sepsis rates were < 0.001 with a consistent increase in infection rates for the TR group. The rates of sepsis have nearly tripled for the TR route in 2017-2019 compared to 2012-2016 (1.12% Vs 0.4%) ($p< 0.001$) (Table 4). TP biopsies have significantly picked up from 17.5% in 2012-2016 to 32.8% in 2017-2019 with the percentage for the entire decade standing at 20.3% ($p < 0.001$) (Figure 3). Complication rates and NEL admissions significantly reduced in centres which were performing more than 1500

TP biopsies in a decade or 500 TP biopsies in two years ($p < 0.001$). For the TR group complications were significantly less if the number of biopsies reached 5000 per decade or 500 in two years ($p < 0.001$).

Discussion

Transrectal biopsy uses a transfaecal route to allow the procedure to be performed under a simple local anaesthetic. The transperineal route avoids this contaminated approach but traditionally used more resources as it required sedation or a general anaesthetic. To the best of our knowledge, this data evaluating 486,467 needle biopsies of the prostate over one entire decade is the highest volume data presenting a comprehensive analysis on hospital readmissions within 28 days of biopsy and cost analysis (upstream and downstream) in a Healthcare system. There is a clear difference in downstream costs as well as sepsis / infection rates between these two procedures. This highlights a need for a sustainable change in practice pattern for the future. Essentially we need the benefits of the transperineal approach without the costly theatre utilisation and general anaesthetic. Local anaesthetic TP biopsy addresses both these issues for the best suitable outcomes. Our analysis has highlighted multiple points worthy of note.

Firstly, the most insightful evidence is that, there is a distinct difference between TP vs TR biopsy in terms of infective complication rates. By and large considering the rates of infections, which may vary from UTI to sepsis, the TR biopsy complications are significantly higher than the TP route of biopsy considering confidence intervals (CI) of 99% ($p < 0.001$). Moreover, this difference has stayed constant over the entire decade including the last two years. Considering the sepsis rates, the realistic picture is quite frightening as TR biopsy sepsis rates have more than doubled in the last two years in comparison to the entire decade (1.12% Vs 0.53%) ($p< 0.001$), whereas the rates of sepsis have not increased so alarmingly for the TP cohort (0.42% vs 0.31%) (p 0.0427). Nonetheless mortality rates are reasonably low and comparable in both the groups. Additionally TP sepsis rates represent true figures and not sepsis associated with urinary retention. The percentage of patients with retention as well as sepsis amounted to only 0.13% in a decade and 0.15% in the last two years out of all the TP biopsies performed. These findings corroborate with the global literature and similar figures have been quoted across different datasets from different parts of the world including the United

Kingdom [5], New York [6], the Surveillance Epidemiology and End Results (SEER) database [4], the Victorian Admitted Episodes Database (VAED)[8], the Prostate Cancer data Base (PCBaSe)Sweden [9] and Canada [10]. The UK dataset from 2000 to 2008 for TR biopsy distinctly highlights the increase in the rates of UTI and or sepsis by an Odds ratio of 1.72 (CI 95%) [5]. Our cohort adds to this study but the level of significance is distinct with a CI of 99% ($p < 0.001$).

The European Association of Urology (EAU) recently released a 'caution statement' for Fluoroquinolone (FQ) resistance with reference to urinary tract infections [19]. It is likely that antibiotic resistance, especially to Fluoroquinolone's (FQ), stands as the main culprit for this increase in infections especially for TR biopsies which has been confirmed in multiple retrospective studies [10, 20], prospective studies [21] and systematic reviews [22]. At least until 2012, 84 participating centres from the Global Prevalence study of Infections in Urology (GPIU) were using FQ as the antibiotic group of choice for prophylaxis before prostate biopsy [21]. Though the most trusted antibiotic group for the prophylaxis of TR prostate biopsies where being used from 1998 until as recent as 2011[23 - 26], the real world data at this stage potentially questions this policy. The EAU committee also suggested targeted prophylaxis based on rectal swab cultures [27] or if not available then to use the alternative approach of TP biopsy of prostate [19].

For the last two years, the NEL admission rates for the TP group have reduced from 4.14% to 3.54% in comparison with the TR group, which showed relatively higher rates (3.74%vs 3.54%) (p 0.1067). Acute urinary retention stands as the most common reason for NEL admission following transperineal biopsy with respect to both the time periods. On the contrary, infection and sepsis have a major role to play in admissions for the TR group throughout the decade and especially in the last two years which showed 41% admissions as the consequence of infective aetiology (A419, N390, A415, N459 and T814). Considering the trend over the past decade and the comparison of figures from the 2012-2016 data, the slope for NEL admissions shows a negative value for both TR and TP cohorts ($p< 0.001$) (Table 4).

Though the recent figures for NEL admissions for both of these cohorts are reasonably low, the downstream cost consideration for these NEL admissions is the real eye opener. Significantly higher cost is incurred for managing NEL admission for the TR group than for the TP group for the entire decade as well as for the last two

years ($p < 0.001$). Overall downstream expenditure for the TR vs TP group has the considerable difference of £ 4,234,653 and £ 26,409,601 for years 2017-2019 and for the entire decade respectively. The NHS has to allocate nearly £3.2 million per year for managing readmissions following TR biopsies. It is to note that the majority of admissions for TP biopsies were for urinary retention rather than infections. This would explain the reduced hospital stay and expenditure on antibiotics and intensive care management in the TP group, which may be the reason for the higher cost in the TR cohort. Previously, based on the 2011 statistics for re-admission rates in the NHS, an estimated £ 7.7-11.1 million was required for managing post TR biopsy admissions. These figures were based on assumptions of average hospital bed costs of 14.2 days for managing gram negative sepsis with an individual day estimate of approximately £ 300 per patient [28]. Similar data from the VAED database in Australia evaluating 34,865 TR biopsies, estimated the burden for managing readmissions to be approximately £ 4137 [8]. Another comparison from a different health care system, mentioned that the median total charge for infectious complications following prostate biopsies to be $4,129 (IQR 711-19,185) which included data from 9472 TR biopsies and 421 TP biopsies [6]. To emphasize, tax payers could save a significant amount of money if higher proportions of biopsies are done rather than transrectally. Assuming that all TR biopsies within the decade were done transperineally, the downstream savings for managing NEL admissions would have been £ 7,501,655.28 considering a 4.14% admission rate (16058 admissions with £ 467.16 savings per admission). However these TP procedures would need to be performed as an outpatient under local anaesthetic (LA) to reduce the cost and resource of a general anaesthetic (GA). Considering estimations for the upstream cost of the procedures throughout the decade, approximate cost incurred by the NHS for all these biopsies would be nearly £ 243,335,084 as per the UK national tariff system for 2019-2020 (£ 332 for TR biopsy under LA and £ 1162 for TP biopsy under GA) [16]. Presuming that all the biopsies would have been done by a GA TP route for minimising the infective complications and saving on downstream cost, the NHS would have required £ 565,274,654as an upstream cost. Needless to say, it does not seem to be a viable option. However, if all the biopsies were done by a LA TP route, approximate upstream cost would have been £ 182,425,125 (£ 375 per procedure) [17]. This translates into a massive upstream saving of approximately £ 60,909,959 in comparison to the current estimated expenditure.

Lastly, the output which was gathered from this analysis for the corresponding number of biopsies performed in comparison to the complication rates as per the individual centres, suggested that a cut off of 1500 biopsies per decade or 500 biopsies within two years significantly changes the complication rates as well as NEL admission rates for TP biopsies ($p < 0.001$). Likewise, in the entire decade different ranges of biopsies of 0-1500, 1501-3000 and 3001-4500 distinguished the complication and readmission rates between different hospitals. The similar division for last two years gave the estimated ranges of 0-500, 501-1000 and 1001-1500 for the optimal results.

Interestingly, certain parameters need to be considered before hypothesizing the need to shift our practice pattern to all prostate biopsies being performed through a LA TP route. Since their inception, TP biopsies have been modified from the standard template biopsy [29, 30] to magnetic resonance imaging targeted biopsy [31 - 33] and from biopsies performed under general anaesthetic [31] to local anaesthetic with precision point and other needle guidance [34, 35]. With the advent of multiparametric MRI before biopsy in recent times, the practice patterns have changed [36]. In biopsy naïve men the MRI targeted biopsy has been shown to have superiority over standard TR biopsy in the PRECISION trial which included MRI fusion biopsies from the TR and TP route as per the expertise in the participating centre [37]. The oncological diagnostic equivalence of TP and TR biopsies has been proven in systematic reviews [38, 39]. Additionally, the typical area of the anterior transition zone which is usually missed in TR biopsy has a higher tendency of being picked up on TP biopsy [40].

We do believe that every individual centre is facing the alarming issue of infectious complications of TR biopsy due to which the antibiotic policies have been changing in recent times to include targeted prophylaxis [27] or higher generation parenteral antibiotics such as Ertapenem (which acts against multi drug resistance E coli) [41]. In contrast, TP biopsies with first generation cephalosporin (Cefazolin) have been proven to have nearly zero infection rates [42]. In 1982, it was proven that the rate of bacteremia and symptomatic infections were significantly higher with higher rates of endotoxemia in TR compared to TP biopsies (100% vs 40%) [43]. Additionally, bacteraemia in patients undergoing TP biopsies was predominantly due to skin contaminants [43]. Albeit in a smaller pool of biopsies, the authors urged for the role of TP route [43]. The HES dataset also suggests the move towards the TP

route and LATP biopsies to be the best affordable approach. Though the most worrisome aspect of the TP biopsy at the moment stands to be the higher incidence of urinary retention, the statistics which we have are only for the standard template biopsies which involved nearly 20-24 cores or more and hence can be considered equivalent to a saturation biopsy. With higher volumes and precision with or without MRI targeting the rates of retention are bound to go down, which in fact is seen in a few series which involved procedures under local anaesthesia (< 5% rates of urinary retention) albeit in a small patient pool [34, 35]. As we can see the TP biopsies were under-utiliseduntil as recently as 2014 in a study from New York which stated that only 4.3% of biopsies were TP [6]. However, from our data it is quite reassuring to see that the TP biopsy numbers in the UK have significantly picked up from 17.5% in 2012-2016 to 32.8% in 2017-2019. Hence we urge the training of TP biopsy under local anaesthetic as a part of curriculum for trainees. With the reassuring statement from the EAU infectious committee published recently, we do believe that in years to come, the TP biopsy will replace the TR biopsy as a part of the guidelines [19].

For various reasons, there are certain limitations in this analysis. Lack of standardisation of technique especially for the TP cohort across hospitals, lack of standardised reporting of all post procedure events which may have been managed at the level of the general practitioner in certain situations, difficulties in assessment of functional outcomes of biopsies and lack of details of demographics for stratification of complication rates are the major drawbacks. This includes lack of information on patients that may have had biopsies transrectally that went on to have a TP biopsy within 12 months as this may have skewed rates for infection/sepsis. Along with this, certain errors which may have happened due to misreporting of ICD codes for the events, absence of information on exact days of hospitalisation for each group as per the type of event would be the minor drawbacks. Nonetheless, the large sample size would take care of the majority of these biases. We are currently interrogating the Imperial College Discovery Dataset which incorporates the HES data as well as details of events managed by the local health care provider including general practitioners in the UK. This will allow us to further identify any additional morbidity and costs that may be missed by HES and picked up by primary care.

To reiterate, the TP biopsy is superior than the TR biopsy in terms of reduced infectious complication rates including sepsis and equivalent to TR biopsy for the non-elective admission rates with a dramatic saving in terms of burden of cost for

management of complications and readmissions. We are reassured by the fact that TP biopsies have rapidly increased to 32.8% of prostate needle biopsies in the last two years in the NHS but this rapid rise will cost the tax payer if performed under GA in theatres.

Conclusions

Evaluation of nearly half a million prostate needle biopsies in the NHS over the entire decade gives sufficient evidence for the distinct advantages of transperineal biopsy over transrectal biopsy of the prostate in terms of reduced infections and burden of expenditure for the management of admissions. This valuable data seems quite promising to consider the decision of shifting the practise pattern by adapting the TP route over the TR route especially in the current antibiotic resistance era. There is asignificant increase in the utilization of TP biopsies especially in the last two years but this has a huge resource implication if performed under GA. Switching all prostate biopsies to LA TP route would have significant upstream and downstream savings.

Conflict of interest

Mr Jim Adshead – Clinical advisor to Lightpoint Medical and receives expenses from Intuitive for Robotic surgical mentoring in the NHS

Mr Rick Popert - Reports honoraria for teaching and training paid as personal fees from BXTAccelyon, grants from NHS Innovation Accelerator, personal fees from BK Ultrasound, personal fees from Health Care of America (HCA), personal fees from 3D Biopsy, personal fees from American Urological Association, outside the submitted work.

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Figure legends

Figure 1- Top ten diagnoses of non elective admissions (NEL) in 2008-2019 and 2017-2019 following prostate biopsies (TP – transperineal, TR – transrectal)

Figure 2 – Average non elective admissions (NEL) admission cost per patient (TP – transperineal, TR – transrectal)

Figure 3- Trends for transrectal and transperinealbiopsies in last one decade (TP – transperineal, TR – transrectal)

Table 1 – 28 days outcomes post biopsy in transrectal and transperineal routes

Table 2 – 28 days infective complications post biopsy transrectal (TR) and transperineal (TP) routes

Table 3- Total cost for non elective readmissions and per patient cost for readmissions for transrectal and transperineal biopsies of prostate

Table 4- Trends of biopsies and complications and costs over last decade

ICD10 Description	Total Patients	Patients with Sepsis	Percentage of Patients with Sepsis	Patients with Non Elective Admission	Percentage of Patients with Non Elective Admission	Patients with Infection	Percentage of Patients with Infection	Patients with UTI	Percentage of Patients with UTI
2008-2019									
Perineal needle biopsy of prostate	98,588	310	0.31%	4,083	4.14%	757	0.77%	950	0.96%
Rectal needle biopsy of prostate	387,879	2,040	0.53%	15,092	3.89%	4,487	1.16%	4,520	1.17%
P value		<0.001		0.00032		<0.001		<0.001	
2017-2019									
Perineal needle biopsy of prostate	37,077	155	0.42%	1,314	3.54%	248	0.67%	266	0.72%
Rectal needle biopsy of prostate	76,106	850	1.12%	2,845	3.74%	1,139	1.50%	848	1.11%
p value		<0.001		0.1067		<0.001		<0.001	

Table 1 – 28 days outcomes post biopsy in transrectal and transperineal route

	TP	TR	TP (%)	TR (%)
2008-2019				
Escherichia coli [E. coli] as the cause of diseases classified to other chapters	209	1,368	24.39	25.14
Sepsis, unspecified	197	1209	22.99	22.22
Infection following a procedure, not elsewhere classified	165	1,309	19.25	24.06
Sepsis due to other Gram-negative organisms	104	807	12.14	14.83
Other specified bacterial agents as the cause of diseases classified to other chapters	67	331	7.82	6.08
Pseudomonas (aeruginosa) as the cause of diseases classified to other chapters	35	73	4.08	1.34
Nosocomial condition	27	122	3.15	2.24
Staphylococcus aureus as the cause of diseases classified to other chapters	23	56	2.68	1.03
Other bacterial infections of unspecified site	18	107	2.1	1.97
Others	12	59	1.4	1.08
Total	857	5,441		
chi-square with yate's correction	62.585			
p value	<0.001			
2017-2019				
Sepsis, unspecified	108	575	37.2	37.5
Escherichia coli [E. coli] as the cause of diseases classified to other chapters	56	278	19.3	18.1
Infection following a procedure, not elsewhere classified	48	300	16.6	19.6
Sepsis due to other Gram-negative organisms	42	285	14.5	18.6
Other specified bacterial agents as the cause of diseases classified to other chapters	13	29	4.5	1.9
Nosocomial condition	9	33	3.1	2.2
Other bacterial infections of unspecified site	7	21	2.4	1.4
Pseudomonas (aeruginosa) as the cause of diseases classified to other chapters	7	12	2.4	0.8
	290	1533		
chi-square with yate's correction n	15.698			
p value	0.028023			

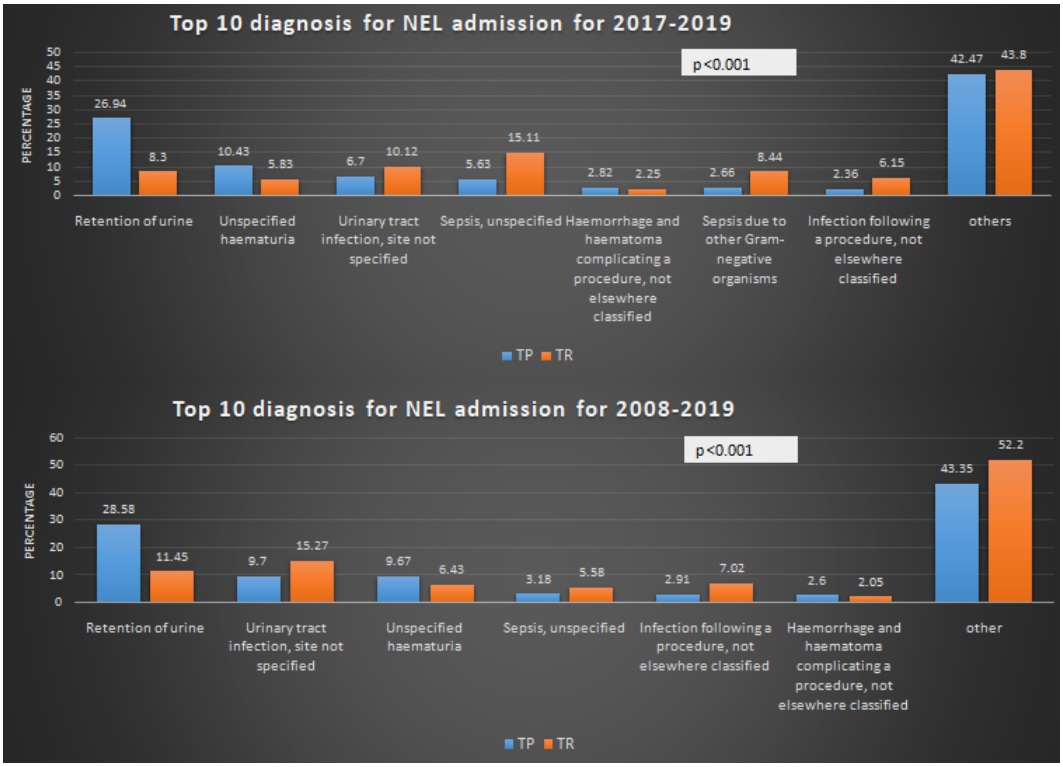
Table 2 – 28 days infective complications post biopsy transrectal (TR) and transperineal (TP) route

2008-2019					
ICD10 Code	**ICD10 Description**	**Number of Patients**	**Total Cost (of Readmissions) NEL within 28 days**	**Average Cost per Patient (of Readmissions) NEL within 28 days**	**p value**
M702	Perineal needle biopsy of prostate	4,083	£7,179,926.07	£1,758.49	<0.001
M703	Rectal needle biopsy of prostate	15,092	£33,589,527.56	£2,225.65	
2017-2019					
ICD10 Code	**ICD10 Description**	**Number of Patients**	**Total Cost (of Readmissions) NEL within 28 days**	**Average Cost per Patient (of Readmissions) NEL within 28 days**	**p value**
M702	Perineal needle biopsy of prostate	1,314	£2,276,039.67	£1,732.15	<0.001
M703	Rectal needle biopsy of prostate	2,845	£6,510,692.03	£2,288.47	

Table 3- Total cost for non elective readmissions and per patient cost for readmissions for transrectal and transperineal biopsies of prostate

		2008-2019	2012-2016	2017-2019	2008-2019(%)	2012-2016(%)	2017-2019(%)	slope	chi-square for trend	p value
	no. biopsies	486,467	195020	113,183						
	TP	98,588	34046	37,077	20.3	17.5	32.8	0.04291	4652.261	<0.001
	TRUS	387,879	160974	76,106	79.7	82.5	67.2			
NEL admission	TP	4,083	1,427	1,314	4.14%	4.19%	3.54%	-0.01181	28.13	<0.001
	TRUS	15,092	5,702	2,845	3.89%	3.54%	3.74%	-0.00147	18.379	<0.001
Infections	TP	757	225	248	0.77%	0.66%	0.67%	-0.00056	4.895	0.0269
	TRUS	4,487	1690	1,139	1.16%	1.05%	1.50%	0.00098	25.512	<0.001
Sepsis	TP	310	68	155	0.31%	0.20%	0.42%	0.00034	4.108	0.0427
	TRUS	2,040	644	850	0.53%	0.40%	1.12%	0.00186	189.312	<0.001
Average cost	TP	£1758.49	£1,630.17	£1,732.15					1.41	0.157
	TRUS	£2225.65	£2,233.45	£2,288.47					1.3	0.195

Table 4- Trends of biopsies and complications and costs over last decade



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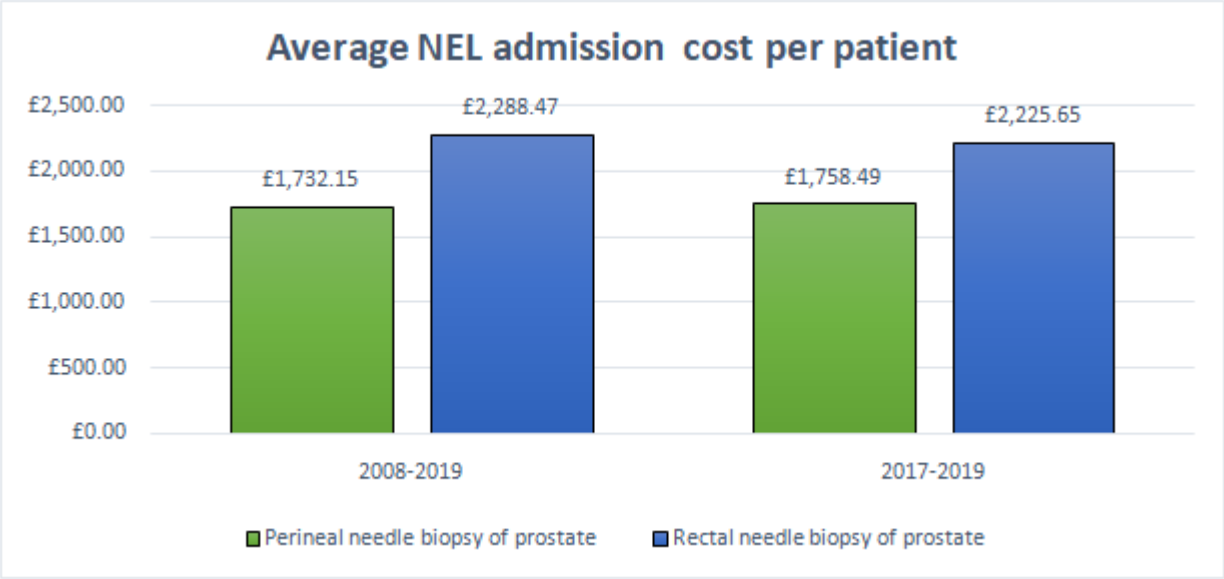

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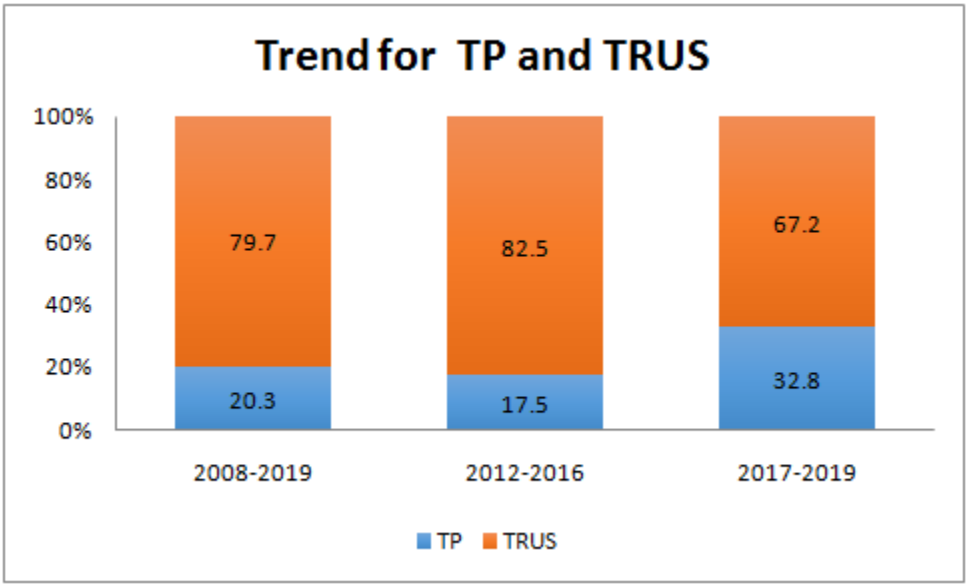

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