Healthcare Costs of Post-Prostate Biopsy Sepsis

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Sepsis following transrectal prostate biopsy occurs in 2%-5% of cases and the risk is increasing. We performed a comprehensive literature search for the cost of post-prostate biopsy sepsis to define the potential cost savings of reducing infectious complications. Reporting of cost is varied and presents a challenge to interpretation. Length of hospitalization ranged from 1.1 to 14 days and the percent admitted to an ICU ranged from 1.1% to 25%. The estimated cost of sepsis post-prostate biopsy, adjusted for inflation, ranged from $8,672 to $19,100. Healthcare costs of treating post-biopsy infection are substantial. Our findings should guide payers and policymakers, especially in value-based care models. UROLOGY 133: 11–15, 2019. © 2019 Elsevier Inc.

There will be an estimated 175,000 new cases and 32,000 deaths from prostate cancer in 2019.[1] Infectious complications of transrectal prostate biopsy are of particular concern due to increasing fluoroquinolone resistance, with up to 25% of men harboring resistant rectal flora at biopsy.[2,3] Fluoroquinolone-resistant Escherichia *Coli*, which cause more than half of all post-biopsy episodes of urosepsis, have risen from less than 1% of urinary tract infection isolates in the late 1990s to 10%-30% in many regions of the United States to over 50% in other parts of the world.[4,5] In parallel, many studies demonstrate a concomitant increase in the rate of sepsis following transrectal biopsy, which comprises the approach for 95% of all prostate biopsies in the US.[6-11]

Due to concern over rising infectious complications, antimicrobial resistance, and the associated healthcare costs, various strategies have been proposed to overcome these challenges. Targeted prophylaxis employs an antibiotic directed by prebiopsy rectal swab culture. Augmented antimicrobial prophylaxis employs more than one prophylactic antibiotic. Both augmented and targeted prophylaxis have been studied and incorporated into AUA guidelines.[12,13] However, outcomes of these strategies are mixed, and there is concern that augmented prophylaxis runs countercurrent to appropriate antibiotic stewardship.[14,15]

Transperineal biopsy is a promising alternative, with reported urosepsis rates of 0%-0.076%.[16,17] This approach avoids inoculating rectal flora into the sterile urinary tract. Some studies suggest that antibiotic prophylaxis may not even be necessary with this approach. This is reinforced by the Society of Interventional Radiology's Standards of Practice Guidelines, which deem antibiotic prophylaxis unnecessary for clean, percutaneous procedures.[18] Its widespread adoption, however, has likely been hindered by the perceived need for general anesthesia due to procedural discomfort.[19] The aim of our stuy is to evaluate the costs of a hospital admission for sepsis following transrectal prostate biopsy, and to explore the potential for cost savings of utilizing these alternative approaches.

METHODS

The review was conducted following the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[20] We searched Ovid MEDLINE, CINAHL (EBSCO), and Science Direct for studies published from 1970 through June 2018 and reviewed bibliographies of included studies. Search terms included all subject headings and combinations of associated keywords for "prostate biopsy" and "cost." There were no restrictions on the search in regard to language, study type, or biopsy protocol (transrectal or transperineal). We reviewed all papers at the abstract level. Abstracts believed to have post-biopsy sepsis healthcare costs were then reviewed in full with a structured format to determine whether they met our inclusion/exclusion criteria. Studies were included if data for individual or system-wide cost or healthcare burden related to post-biopsy infection hospital admission were referenced. Two reviewers (MG and MA) independently assessed articles for eligibility and extracted data. The reviewers independently assessed for risk of bias in included studies using the Newcastle-Ottawa scale, adapted for noncomparative studies.[21] This scale assesses bias in selection of study group, ascertainment of exposure, and assessment of outcome on a 5-point scale, with scores of 0-2, 3, and 4-5 indicating high, moderate, and low risk of bias, respectively.

Study quality metrics were assessed via modified STROBE criterion.[22] The primary outcome was defined as healthcare costs of hospitalization for infection following prostate biopsy. The cost,

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cost-basis, number of patients, and the year in which the healthcare costs were assessed were extracted. The May 2018 urban and inpatient hospital service consumer price indices[23] were used to adjust for inflation, as described by the Agency for Healthcare Research and Quality.[24] When authors did not specify what dollar year their estimates were based on, the year of publication was used to adjust for inflation. For international cohorts, the historical exchange rate from the federal reserve of the currency of the study sample compared to the US dollar was used, before adjusting for inflation as above.[25]

RESULTS

The search yielded 1094 citations of which 874 were screened after removing duplicate references, with 103 articles reviewed in full and 18 studies meeting the inclusion criteria (Fig. 1).[5-10,26-37] Ten of the 18 studies were characterized as low risk for bias, with 6 and 2 studies judged to have moderate or high risk, respectively. Many studies failed to properly define and assess the outcome of hospitalization for infection, while almost all clearly captured a consecutive set of biopsies. Individual sources of bias for each study are recorded in Supplementary Table 1. The cost of post-biopsy sepsis in the United States within the last 10 years, adjusted for inflation, ranged from $8,672 to $19,100 (Table 1). Among all included studies, hospital length of stay ranged from 1.1 to 14 days and ICU admissions ranged from 1.1% to 25% (Table 2).

There was a significant variation in both the study design and costing methodology across studies. The largest study by Evans et al utilized the Marketscan database, which reports gross payments to hospitals by insurance providers.[26] The absence of Medicare and other self-pay patients in this dataset may have increased healthcare cost results, although this study was strengthened by its broad patient population. Halpern et al were able to circumvent bias generated by selective insurance providers by utilizing the Statewide Planning and Research Cooperative System, a database which includes all payers. However, the hospital charges reported

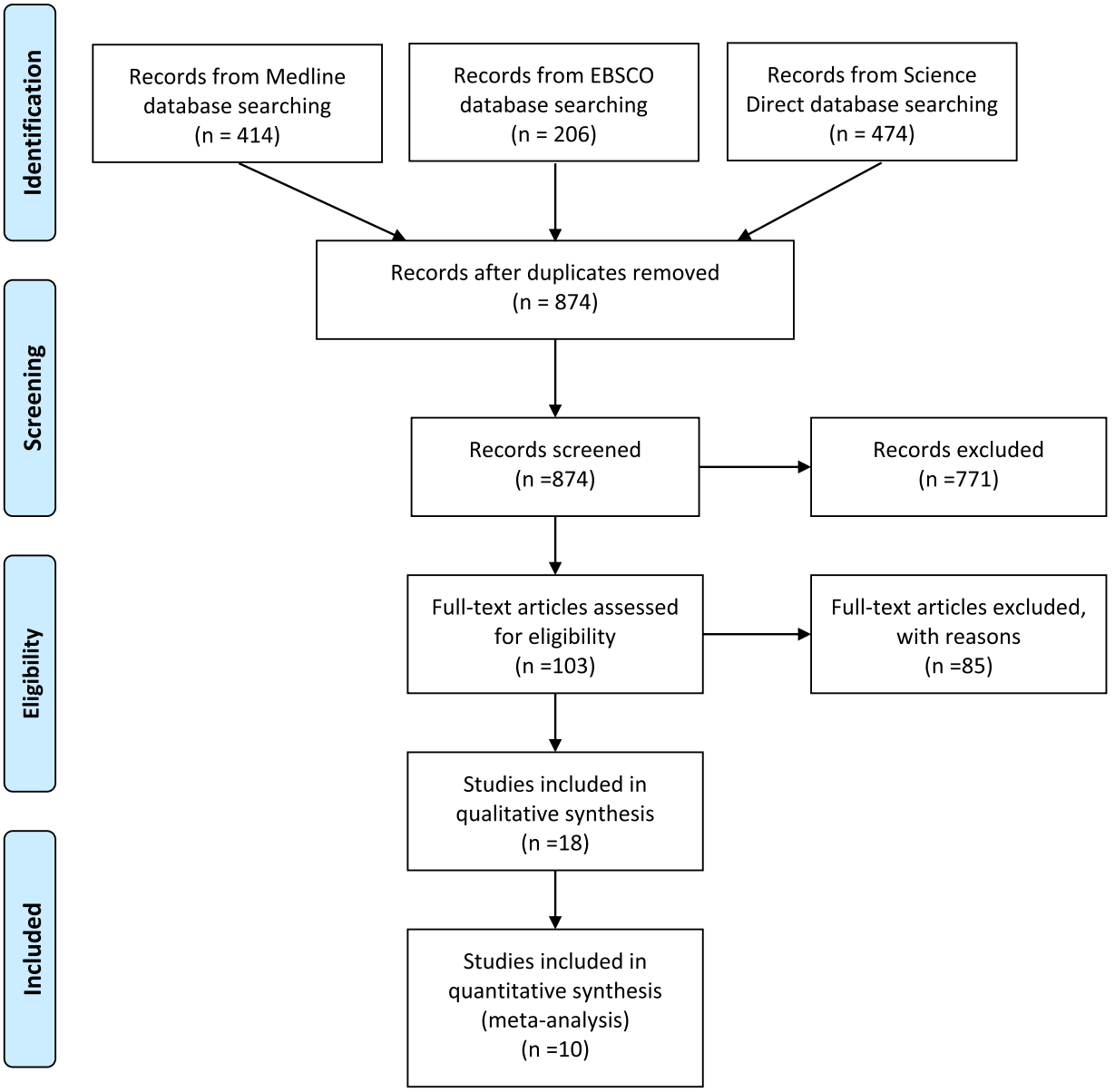

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram for study selection. (Color version available online.)

Table 1. Adjusted costs for included studies

Author	Country	Cases	Average Cost of Urosepsis ($)	CPI IP Adjusted Cost ($)
Evans et al. (2017)[25]	US	5385	14,499	19,121
Halpern et al. (2017)[10]	US	151	4219	5076
Adibi et al. (2013)[26]	US	11	5900	8959
Remynse et al. (2011)[30]	US	6	5410	8215
Duplessis et al. (2012)[31]	US	3	5711	8672
Larsson et al. (1999)[32]	Sweden	1	849	2720
Batura et al. (2013)[34]	UK	1813-2610*	6944*	8801*
Roth et al. (2015)[33]	Australia	218	6844	9026
Chiu et al. (2017)[36]	Netherlands	92	3102	3578
Thomsen et al. (2015)[35]	Denmark	37	3416	4329

CPI IP, inpatient consumer price index.
* = estimated.

were subject to inflation and reflect neither the true cost of services nor dollars exchanged.[10] The study by Adibi et al may most closely approximate a uniform cost basis, using a single institution's billing department to provide the actual cost to the hospital from a selected cohort of patients.[27] Unfortunately, this single-institution number is not readily generalizable, and the relatively small sample size (11 patients over 1 year) accentuates the inherent variation in the billable components of admission.

Similar limitations were found when examining international studies. For example, while a state-wide database in Victoria, Australia was able to capture all infectious admissions over 5 years, the cost data was estimated via a national cost standard guide based on services rendered.[34] Similarly, a study by Batura et al from the UK also used its National Health Service to estimate the cost of a daily hospital bed[35] while a Danish study generated cost from a random subset of just 10 patients in a single institution.[36] Chiu et al examined a prospective multi-institutional cohort linked to the Dutch Cancer Registry,[37] calculating the percentage of cost avoided relative to their own standard biopsy cost, which is likely a more generalizable figure when comparing costs to other healthcare systems. Altogether, the cost of urosepsis in international studies ranged from $3,578 to $9,026, in adjusted US dollars.

DISCUSSION

Healthcare costs and resource utilization to treat urosepsis after prostate biopsy are significant and increasing due to more infectious events resulting from greater antimicrobial resistance. Our review revealed several important findings. First, the cost of post-biopsy infection is high. Evans et al estimated the national burden of post-prostate biopsy infection in the Medicare population to be $623 million.[26] Similarly, the estimated cost in England and Wales was £7.7-11 million ($12.6-18 million) in 2013.[35] This provides significant opportunities for cost-reduction strategies. One study of rectal swabs for targeted prophylaxis by Taylor et al revealed a net cost savings of $4,499 per infectious complication avoided.[38] The number needed to treat (swab) to avoid infection was 38. Adibi et al demonstrated a similar figure for augmented prophylaxis, reducing total costs and complications by $43,500 over 300 patients with an average savings of $145 per individual biopsy.[27] With regard to transperineal biopsy, cost effectiveness studies are lacking. However, given the $19,100 cost per complication as the upper limit of our reported range, the margin for cost savings is large, especially as the adoption of in-office biopsy reduces procedural cost.[39]

Second, the overall number and quality of studies documenting cost is limited. There was a $10,000 difference in costs reported with studies using no consistent cost reporting methodology. In particular, some studies utilized

Table 2. Length of stay and ratio of intensive care admissions for included studies

Author	Country	Cases	Average Length of Hospitalization (Days)	ICU Admission Rate (%)
Evans et al. (2017)[25]	US	5385	3.00	
Nam et al. (2010)[9]	Canada	781	1.10	
Halpern et al. (2017)[10]	US	151	4.00	
Bruyere et al. (2015)[27]	France	76	2.10	2.60
Williamson et al. (2012)[28]	New Zealand	47	4.87	25
Sanders et al. (2013)[29]	New Zealand	40	3.40	10
Carignan et al. (2012)[6]	Canada	32	4.00	15
Feliciano et al. (2008)[8]	US	19	4.10	
Pinkhasov et al. (2012)[5]	US	12	5.00	17
Carmignani et al. (2012)[7]	Italy	9	9.00	
Batura et al. (2013)[34]	UK	1813-2610*	14.00*	
Roth et al. (2015)[33]	Australia	218	4.00	6.29
Chiu et al. (2017)[36]	Netherlands	92	5.00	1.08
Thomsen et al. (2015)[35]	Denmark	37	3.00	

* = estimated

hospital charges which have been shown to average more than twice the actual cost of delivering care.[40] Analyses using these cost figures were also lacking with few, if any, employing a component of time-driven activity-based costing to assess superiority in a given biopsy prophylaxis or approach.

Third, we found that the cost of urosepsis has increased over time, most notably with the cost presented by Evans et al.[26] This raises the concern that the oft-cited cost of $5900 may be obsolete.[27] While the study by Evans et al presents the largest national sample to date, confirmatory studies are needed.

Fourth, we observed the cost of urosepsis to be greater than an average hospital-acquired urinary tract infection, perhaps underscoring the severity of the complication. To provide perspective, the per admission cost to Medicare for a catheter-associated urinary tract infection, when adjusted for inflation, is $8,437.62.[41] This difference is likely tied to the increasing prevalence of fluoroquinolone-resistant *E. Coli* and appears particularly worrisome in the context of increased augmented prophylaxis adoption.[4]

Our findings must be interpreted within the context of study design. First, the variability in study size and design impaired our ability to perform meta-analysis. This underlines the need for more studies that explore the contemporary costs of urosepsis in order to better understand processes that may attenuate these costs beyond prevention. The relatively small sample size may contribute to the variation in healthcare costs between studies and effect length of stay and rate of ICU admissions, which varied widely. As mentioned previously, the calculation of cost varied between studies and continues to be performed without a clear standard for use in population or cost analyses. Our study was also limited by the retrospective nature of the included publications and their variation in date, leaving them subject to the ever-changing landscape of healthcare billing and costs.

Finally, we were only able to capture the direct healthcare-related costs of urosepsis after biopsy but could not account for the indirect costs including but not limited to increased convalescence, lost wages, time lost from work, and transportation. Our findings underscore the need for additional cost analyses and the need for additional population-based characterization that may lead to policy or targeted strategies to address this growing problem.

CONCLUSION

With a shift toward value-based care, it is imperative to prevent costly complications, such as biopsy related urosepsis. Avoiding these episodes can mitigate the annual cost of prostate cancer care, which is expected to exceed $19 billion by 2020.[42] The development of novel approaches for prostate biopsy, such as transperineal biopsy under local anesthesia or limiting the extent of biopsy to a targeted approach only may lower the risk of biopsy related urosepsis. These results should guide payers and policymakers, particularly as health systems move to value-based care models.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.06.011.

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