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A claims-based analysis of prostate biopsy episodes when there is no evidence of a cancer diagnosis

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According to the Centers for Disease Control and Prevention (CDC), prostate cancer is the second most common cancer among males in the United States.[1] About one in eight males will be diagnosed with prostate cancer during their lifetime.[2] Clinical guidelines recommend that when screening for early detection of prostate cancer, clinicians should use prostate specific antigen (PSA) as the first screening test.[3] For patients with a newly elevated PSA result, follow up diagnostic tests include biomarkers, imaging, and/or prostate biopsy.[3,4] This study presents the cost of prostate biopsy episodes with and without potential prostate biopsy-related complications.

Key findings

Analysis of claims data for the following health insurance markets—commercial group, individual, and Medicare Advantage (MA)—suggests that:

- For patients not diagnosed with cancer before or after a prostate biopsy, in the four months preceding the prostate biopsy, more than 65% had a prostate specific antigen (PSA) test performed. At least 20% of the patients with a PSA test also had magnetic resonance imaging (MRI) prior to the biopsy. Transrectal ultrasounds and prostate cancer risk lab tests were utilized at lower rates prior to prostate biopsy. These results were consistent across all lines of business.
- We estimated the cancer positivity rate of prostate biopsies in patients without a history of prostate cancer to be approximately 50% for the commercial group and individual patients and about 60% for the MA population based on the new occurrence of claims with a prostate cancer or metastatic cancer diagnosis in the six months following the biopsy. These patients were excluded from this study to avoid capturing costs associated with cancer treatment so that the focus is on the cost of prostate biopsy episodes.
- About 15% of patients included in the analysis developed a new condition shortly after the biopsy that may have been a complication of the biopsy. For the purpose of this analysis, we defined a prostate cancer episode as all services incurred by the patient in the following time period: four months prior to two months following the day of the prostate biopsy. We attributed about 25% of the total costs for all prostate biopsy episodes included in our analysis to the patients who developed a potential complication (15% of the population included in the analysis). For this cohort of patients, about 44% of the total costs for the prostate biopsy episode were incurred in the two months following the procedure.
- In the two months following the biopsy, the most common newly identified conditions that were potential biopsy-related complications included urinary retention, lower urinary tract infection, and prostate inflammation.
- Conditions that were potential complications of the biopsy were associated with higher inpatient costs that were not accounted for by differences in the underlying risk mix of patients, with and without new conditions following prostate biopsy. Inpatient costs accounted for up to 23% of the total episode costs where potential complications were identified, compared to only 7% of the costs for patients without potential complications. Patients with evidence of sepsis, lower

urinary tract infection, and hematuria following the procedure had the highest inpatient costs in the population with potential complications.

The total cost of care for prostate biopsy episodes varied substantially based on whether or not the patient developed new conditions that were potential complications of the biopsy procedure. The number and the types of services received by the patient were major drivers of the cost differences, with inpatient admissions for infections being the main driver of costs for patients who developed potential biopsy-related complications. In general, the findings of the analysis were consistent across the different lines of business. For purposes of illustrating the association of potential complication conditions with biopsy episode cost differences, we segmented episodes into those with and without potential biopsy-related complications. However, our analysis of claims data did not allow us to draw conclusions about a cause and effect relationship between prostate biopsies and the development of new conditions that could be biopsy-related complications.

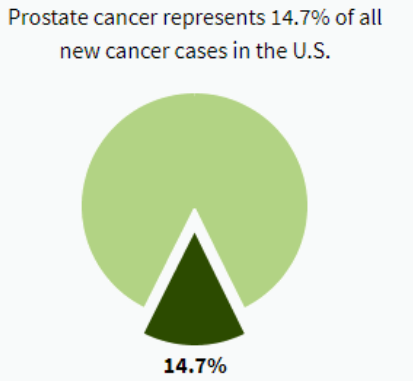
Background

INCIDENCE OF PROSTATE CANCER

Per 2016-2020 data, the rate of new U.S. cases of prostate cancer in the was 113.4 per 100,000 males per year.[5] In the United States, the National Cancer Institute estimates that there will be 288,300 new cases of prostate cancer and an estimated 34,700 people will die from this disease in 2023.[2] Prostate cancer accounts for 15% of all new cancer cases (See Figure 1).[5]

FIGURE 1. ESTIMATED NEW CANCER CASES 2023

	Common Types of Cancer	Estimated New Cases 2023	Estimated Deaths 2023
1.	Breast Cancer (Female)	297,790	43,170
2.	**Prostate Cancer**	**288,300**	**34,700**
3.	Lung and Bronchus Cancer	238,340	127,070
4.	Colorectal Cancer	153,020	52,550
5.	Melanoma of the Skin	97,610	7,990
6.	Bladder Cancer	82,290	16,710
7.	Kidney and Renal Pelvis Cancer	81,800	14,890
8.	Non-Hodgkin Lymphoma	80,550	20,180
9.	Uterine Cancer	66,200	13,030
10.	Pancreatic Cancer	64,050	50,550



Adopted from the National Institute of Health; National Cancer Institute Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Prostate Cancer Survival Statistics. https://seer.cancer.gov/statfacts/html/prost.html.

PROSTATE CANCER SCREENING

The American Cancer Society (ACS) recommends that patients have the opportunity to make an informed decision with their healthcare provider about whether or not to be screened for prostate cancer. The ACS suggests that this decision should be made following the receipt of information about the uncertainties, risks, and potential benefits of prostate cancer screening. The recommended age for beginning screening varies depending on the relative risk of the patient that takes into consideration race and family history.[6,7]

The following screening tests are used to look for possible signs of prostate cancer in asymptomatic patients:

- Prostate-specific antigen blood test (PSA): PSA is a protein made by cells in the prostate gland. The probability of having cancer increases as the PSA level in the blood increases.[8]
- Digital rectal exam (DRE): During a DRE, the doctor inserts a gloved, lubricated finger into the rectum to feel for any bumps or hard areas on the prostate that might be cancer.[8]

In 2021, about 37% of all males in the United States aged 55-69 years reported a PSA test in the past year.[9] An estimated 1,000,000 prostate biopsies are performed in the United States annually.[10] The cost of prostate biopsies is estimated to be about $2.5 billion annually,[11].

DIAGNOSTIC TESTING FOR ABNORMAL PROSTATE CANCER SCREENING RESULTS

Traditionally, prostate biopsy has been performed for three general indications: abnormal DRE, increased PSA, and clinical suspicion of prostate cancer. PSA is an important biomarker that correlates with the risk of prostate cancer. In the United States, a PSA level of 4.0 nanograms per milliliter is the generally accepted threshold at which providers recommended prostate biopsy, although there is no PSA level below which prostate cancer can be definitively ruled out.[12] In case of an elevated PSA result that signals the patient might have prostate cancer, additional testing is usually recommended in order to assess the likelihood or determine that the patient actually has prostate cancer. Additional testing may include a repeat PSA test, prostate imaging, additional blood or urine lab tests, and/or prostate biopsy. Whether performed as the immediate next step following an elevated PSA result or after subsequent non-invasive diagnostic tests that continue to suggest the patient may have prostate cancer, prostate biopsy is the only test that can result in a diagnosis of prostate cancer[8] by obtaining multiple samples of the prostate that subsequently undergo examination by a pathologist.[13] Prostate biopsy is usually performed by a urologist using needles inserted into the prostate either transrectally or by a transperineal approach, with transrectal ultrasound scan (TRUS) guided prostate biopsy being the most commonly used technique in which 12 prostate tissue samples are generally taken.[14]

COMPLICATIONS OF PROSTATE BIOPSY

Among the harms associated with PSA screening is the performance of unnecessary prostate biopsies and the risks associated with those procedures. The cumulative percentage of false positive PSA results is estimated to be between 10% and 15% over several rounds of screening, with about a 5% risk of a false positive screen with a subsequent negative biopsy.[15] The United States Preventive Services Task Force (USPSTF) Grade C recommendation for PSA screening in males ages 55 to 69 (and Grade D recommendation in males 70 years and older) considers pain and adverse events associated with prostate biopsy to be among the harms of PSA-based screening.[16] The USPSTF's systematic evidence review specifically cites biopsy-related harms including moderate to severe pain, infectious complications, and hospitalizations.[17] The update of the American Urological Association's (AUA) white paper on the incidence, prevention, and treatment of complications related to prostate biopsy reports that the most common complications include infection and bleeding, with urinary obstruction/retention less frequently observed. Infection-related complications include urinary tract infection, prostatitis, epididymitis, orchitis, bacteremia, and sepsis.[18] Researchers have also identified other infectious complications of prostate biopsy such as vertebral osteomyelitis.[19,20] Bleeding complications are common but generally self-limited and mild, with the rate of rectal bleeding impacted by the number of core biopsies and anticoagulation.[18]

The timing of prostate biopsy complications varies by medical condition, but most initially occur shortly after the biopsy. A recent study of prostate biopsy approaches and complications analyzed hematuria, rectal bleeding, hematospermia, sepsis, and acute urinary retention between day 0 and day 2 (early) and between day 3 and day 15 (late), finding that 49% to 73% and 22% to 33% of patients had early and late side effects, respectively, associated with different biopsy approaches.[21] The complications also resolve on different timelines. For example, urinary retention, dysuria, and rectal bleeding typically resolve within seven days,[18,22] while erectile dysfunction typically resolves within three months after the biopsy[23] and hematospermia generally within four weeks.[24]

While some of the complications of prostate biopsy are typically mild and self-limited, the major risk associated with prostate biopsy is infection, which occurs in 5% to 7% of patients and results in hospitalization in 1% to 3%.[18] While researchers report that between 2001 and 2015 the overall rate of post-prostate biopsy infections stabilized since 2007, rates of emergency room encounters, acute inpatient hospitalizations, and intensive care unit (ICU) admissions continued to rise throughout this time period. This trend in higher acuity hospital utilization suggests that infections have increased in severity over time. Older age was associated with a higher risk of any infection as well as hospitalization, but the average age at the time of biopsy decreased over time, so age did not account for the increasing rate of severe infections.[19] Furthermore, comorbid conditions

were identified as independent risk factors for biopsy-related infections. In a systematic literature review describing risk factors for prostate biopsy-related infection, preventive strategies, and evidence-based management of infectious complications, researchers identified significant infectious risk factors that include urogenital infection, antibiotic use, international travel, hospital exposure, bacteriuria, previous transrectal biopsy, and resistance of fecal flora to antibiotic prophylaxis.[25] Some experts have suggested adjusting biopsy protocols or biopsy approaches for patients at high risk of infectious and other complications, while others recommend shared decision-making about the risks,[16] given that screening offers a small potential benefit of reducing the chance of death from prostate cancer in some patients while many patients will experience potential harms. Following an elevated PSA, prebiopsy imaging has been suggested as a triage tool for prostate biopsy,[26] while other experts point out that further assessments with urine- or blood-based molecular tests may reduce unnecessary biopsies. Note that none of these assessments can definitively rule out cancer.[12]

RATIONALE FOR STUDYING PROSTATE BIOPSY COMPLICATIONS AND COSTS

In the context of relatively widespread prostate cancer screening and calls for improvements in approaches to shared decision-making with patients when making screening decisions, there remain differences of professional opinion on the quality of the evidence that are reflected in the clinical guidelines for prostate cancer screening released by the different professional associations.[12] However, there is general consensus about the importance of decision aids that can assist in risk stratifying patients with respect to their likelihood of clinically significant prostate cancer. While prostate biopsy is a key procedure in the diagnosis and risk stratification of prostate cancer, minimizing the risk to patients of prostate biopsy complications and the associated healthcare costs that result from potentially avoidable prostate biopsies and complications continue to be important goals of physicians treating patients with an elevated PSA.[27] Therefore, we designed an analysis that would estimate the cost of contemporary prostate biopsies across multiple payer lines of business (commercial group, commercial individual, and MA) and estimate the incidence and incremental additional cost of potential biopsy-related complications over the cost of the prostate biopsy and total costs during the period of time immediately preceding and following the biopsy.

Results

The analysis was performed on commercial group, individual, and MA claims from Milliman's Consolidated Health Cost Guidelines™ Sources Database (CHSD). We identified 97,434 male patients in our combined datasets between 2019 and 2021 with at least one outpatient prostate biopsy who had a minimum of twelve months of continuous insurance coverage pre-biopsy, a minimum of one month of coverage post-biopsy, and no evidence of prostate cancer in the twelve months preceding the biopsy. We then excluded all patients with evidence of a prostate or metastatic cancer diagnosis in the six months following the biopsy procedure, resulting in 46,036 patients, or 47% of the patients with an outpatient prostate biopsy, included in the analysis. Of the remaining 46,036 patients, there was a very small instance of patients with multiple biopsies over the period of data evaluated. For these patients, we reported on episodes based on the first instance of a prostate biopsy. We constructed prostate biopsy episodes running from four months pre- to two months post-prostate biopsy as described in detail in the Methodology section of this paper.

We observed that total healthcare costs in the two months following prostate biopsy varied substantially, in part dependent on the presence of potential biopsy-related complications following the procedure, and the cost differences were greater than would be expected by differences in the risk scores for patients with and without potential biopsy complications. We found that approximately 15% of the episodes showed new conditions that were potential biopsy complications in the two months post-biopsy, and these episodes accounted for approximately 25% of the total allowed costs across all episodes in the study. We expect that services provided for these new conditions that were potential complications were a major driver of the cost differences between the groups of patients with and without potential biopsy-related complications.

To better understand the healthcare costs associated with new conditions that were potential biopsy-related complications, we compared the costs of biopsy episodes with and without potential complications in each of the three lines of business: commercial group, individual, and MA. As illustrated in Figure 2, 15% of the patients included in our analysis had a potential biopsy-related complication newly identified in the two months following the prostate biopsy. These episodes incurred, on average, 82% more in claims costs in the two-month period following the biopsy compared to the episodes with no new conditions that were potential complications.

While new conditions identified post-biopsy that were potential biopsy complications played a role in the cost differential between the two cohorts, the risk scores of each market's patients with potential post-biopsy complications were higher, which could contribute to the cost differences observed between the groups with and without potential biopsy-related complications. The reported commercial and individual population risk scores are Health and Human Services Hierarchical Condition Categories (HHS-HCC) risk scores, and the reported MA population risk scores are the Centers for Medicare and Medicaid Services Hierarchical Condition Categories (CMS-HCC) risk scores. Thus, the risk scores should only be compared between each market's with and without potential complications cohorts, rather than across markets.

FIGURE 2: HIGH-LEVEL EPISODE SUMMARY

	Commercial	Medicare Advantage	Individual	Total
Number of Episodes	34,006	7,489	4,541	46,036
Number of Episodes With a Potential Complication	4,931	1,335	711	6,977
Proportion of Episodes With a Potential Complication[1]	14.5%	17.8%	15.7%	15.2%
Episodes Without a Potential Complication				
Average Patient Risk Score[2]	1.542	0.679	1.641	-
Allowed Medical Cost per Episode[3]	$9,038	$6,559	$8,106	$8,556
Episodes With a Potential Complication				
Average Patient Risk Score[2]	1.837	0.745	1.659	-
Allowed Medical Cost per Episode[3]	$16,749	$13,064	$14,249	$15,790
Potential Complication Allowed Cost Ratio[4]	**1.85**	**1.99**	**1.76**	**1.85**

[1] Episodes with a potential complication were identified by a specified complication diagnosis code in any diagnosis code position within two months post-biopsy.
[2] Risk scores reflected HHS-HCC risk scores for commercial and individual and CMS-HCC risk scores for MA. The costs shown have not been normalized to a 1.0 risk score level.
[3] Allowed medical cost reflected the total amount paid by the payer plus patient cost-sharing from four months pre-biopsy through two months post-biopsy.
[4] Compares the average allowed medical cost for episodes with potential complications to episodes without potential complications.

The costs and utilization for each major service category were tracked over the duration of episodes. The costs and utilization "during" the episode were all claims incurred on the same day as the prostate biopsy. Because inpatient biopsies were excluded, we expected that outpatient facility and professional service categories would experience the highest volume of claims in this period. In the two months post-biopsy, we expected higher utilization in the inpatient service category for episodes with new conditions that were potential biopsy-related complications.

Figure 3A confirms that the allowed cost on the day of the prostate biopsy was relatively similar for episodes with and without potential complications, with the majority of the costs attributed to the outpatient and professional service categories. We observed substantially higher inpatient allowed costs in the two months post-biopsy for episodes with potential complications.

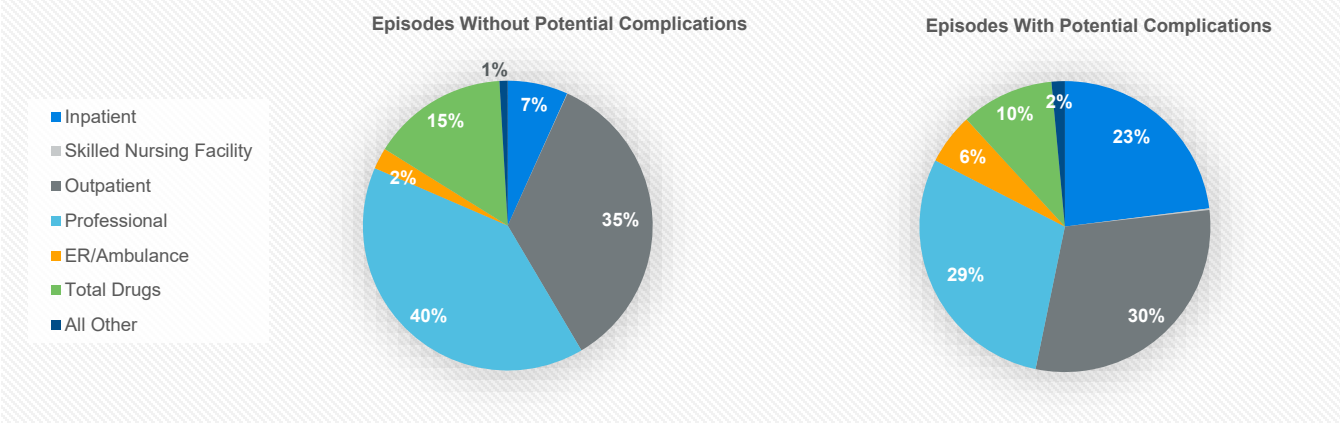
As shown in Figure 3A, for the episodes with potential complications, we also observed a significant allocation of inpatient costs on the day of the biopsy, which was unexpected as we only included in our analysis episodes where the biopsy took place in an outpatient setting. We confirmed that the prostate biopsy for these episodes occurred in an outpatient facility and that these episodes had an inpatient admission on the same day as the biopsy with an infection diagnosis code in the principal position on the inpatient claim.

FIGURE 3A: TOTAL ALLOWED COSTS PMPM BY SERVICE CATEGORY

	Episodes Without Potential Complications				Episodes With Potential Complications[2]			
Service Category	**Four Months Pre-Biopsy**	**Biopsy Day**	**Two Months Post-Biopsy**	**Total[1]**	**Four Months Pre-Biopsy**	**Biopsy Day**	**Two Months Post-Biopsy**	**Total[1]**
Facility Inpatient	$389	$0	$186	**$575**	$929	$48.31	$2,655	**$3,632**
Skilled Nursing Facility	$2	$0	$1	**$3**	$14	$0	$13	**$28**
Facility Outpatient	$1,237	$1,187	$549	**$2,973**	$1,599	$1,412	$1,736	**$4,747**
Professional	$1,352	$1,494	$575	**$3,421**	$1,726	$1,481	$1,416	**$4,622**
Emergency & Ambulance	$143	$8	$52	**$203**	$376	$34	$486	**$895**
Total Drugs[3]	$863	$10	$429	**$1,302**	$1,054	$11	$567	**$1,632**
All Other[4]	$51	$2	$25	**$79**	$120	$3	$111	**$234**
All Services Total	**$4,037**	**$2,702**	**$1,817**	**$8,556**	**$5,817**	**$2,989**	**$6,983**	**$15,790**

Figure 3B illustrates the difference in service category distribution of the total episode spend on an allowed basis between the episodes with and without new conditions that were potential biopsy-related complications. The largest difference was inpatient spending, which was 23% of episode spending for episodes with potential complications compared to 7% for episodes without potential complications. For episodes without potential complications, post-biopsy costs were mainly driven by professional and outpatient facility services.

FIGURE 3B: DISTRIBUTION OF TOTAL ALLOWED COSTS



[1] Allowed medical cost reflected the total amount paid by the payer plus patient cost-sharing from four months pre-biopsy through two months post-biopsy.
[2] Episodes with a potential complication were identified by a specified complication diagnosis code in any diagnosis code position on any claim in the two months post-biopsy.
[3] Included all drugs received under the medical and prescription drug benefits.
[4] Included services not captured elsewhere, primarily home health and DME services.

Figure 4 details the prevalence of specific conditions that are potential biopsy-related complications for all episodes over the two months post biopsy. Many episodes with potential complications showed multiple conditions and were, therefore, included in multiple categories in Figure 4. Thus, adding the prevalence rates across potential complications is not appropriate.

In order to best capture potential complications following biopsies, the potential complication prevalence represented the first instance of a specified diagnosis code for the condition during the two-month post-biopsy period. For some conditions that may be chronic but that could also be potential biopsy-related complications (bacteriuria, dysuria, erectile dysfunction,

hematuria, sacral/perineal pain, and urinary retention), we did not count these conditions as potential complications in the post-biopsy period if the patient experienced these same conditions within the six-month period prior to the biopsy. It would not be possible in those circumstances to distinguish an ongoing chronic medical condition from a potential biopsy-related complication, and we did not want to overestimate potential complications of the biopsy.

The most common new conditions that were potential complications occurring within the two months following the prostate biopsy were urinary retention, prostate inflammation/infection, and lower urinary tract infection.

FIGURE 4: POTENTIAL COMPLICATION PREVALENCE RATE

Potential Complication	Prevalence[1] In the First Month Post-Biopsy	Prevalence[1] In the Second Month Post-Biopsy
Bacteriuria	0.0%	0.0%
Dysuria	0.6%	0.2%
Epididymitis	0.2%	0.1%
Erectile dysfunction	1.3%	0.4%
Fever	1.1%	0.2%
Hematoma/hemorrhage of prostate	0.1%	0.0%
Hematospermia	0.3%	0.1%
Hematuria	1.7%	0.3%
Laceration of prostate	0.0%	0.0%
Lower urinary tract infection	2.6%	0.6%
Other complication of prostate biopsy	0.1%	0.0%
Prostate inflammation/infection	3.4%	0.4%
Pyelonephritis	0.0%	0.0%
Rectal hemorrhage	0.3%	0.2%
Sacral/perineal pain	1.1%	0.8%
Sepsis	0.9%	0.1%
Urinary retention	3.6%	0.6%
Vertebral osteomyelitis	0.0%	0.0%

[1] Episodes with a potential complication were identified by a specified complication diagnosis code in any diagnosis code position on any claim within two months post-biopsy.

To verify the reasonability of the results, the demographics of the patients in each episode were compared against expectations and clinical guidelines. The American Cancer Society recommends that average-risk males should begin prostate cancer screenings at age 50, high-risk males at age 45, and very high-risk males at age 40 (American Cancer Society Recommendations for Prostate Cancer Early Detection, 2023).[28]

- **Commercial market:** Of the 69,405 commercial market prostate biopsy episodes analyzed, 51% led to an eventual cancer diagnosis, leaving 34,006 patients without diagnosed prostate cancer who were included in the episode analysis. The remaining commercial market cohort's demographics aligned with the American Cancer Society's recommendations, as 78% of prostate biopsy episodes were in males ages 45 to 65 as displayed in Figure 5.
- **Medicare Advantage market:** Of the 19,005 MA market prostate biopsy episodes, 61% led to an eventual cancer diagnosis, leaving 7,489 patients without diagnosed prostate cancer who were included in the episode analysis. The MA population's demographics in relation to the prostate cancer screening recommendations were not easily interpretable as

the majority of MA patients are ages 65 and older. However, 67% of the MA prostate biopsy episodes were for 65- to 75-year-old males.

- **Individual market:** Of the 9,024 identified individual market prostate biopsy episodes, 50% led to an eventual cancer diagnosis, leaving 4,541 patients without diagnosed prostate cancer who were included in the episode analysis. Ninety-two percent of individual market prostate biopsy episodes were for males ages 45 to 65, so this group's demographics aligned with expectations as displayed in Figure 5.

Appendix A presents the prostate biopsy episode results by market in greater detail.

FIGURE 5: DEMOGRAPHIC DISTRIBUTION[1]

Male	*Commercial Market*	*Medicare Advantage Market*	*Individual Market*
<45	1.0%	0.0%	0.7%
45-55	14.4%	0.4%	12.8%
55-65	63.9%	4.1%	78.8%
65-75	19.6%	67.1%	7.3%
75-85	1.1%	26.6%	0.3%
85+	0.0%	1.8%	0.0%
Total	**100.0%**	**100.0%**	**100.0%**

[1] Included prostate biopsy episodes with enrollment from four months pre-biopsy through two months post-biopsy.

Data, methodology, and limitations

DATA

We relied on Milliman's CHSD research database, which contains nationwide de-identified healthcare claims data for nearly 80 million unique individuals. The CHSD is a closed claims data set comprised of payer claim and membership data. We reviewed claims from 2019 through 2021 and limited our review to males with commercial, individual, or MA health insurance coverage.

Prostate biopsies were identified by HCPCS codes 55700 and 55705.

METHODOLOGY

The date of the first claim for a prostate biopsy was considered the index date for that patient. We excluded females, patients who did not have at least twelve months of continuous enrollment pre-index date, patients who did not have at least one month of continuous enrollment post-index date, patients whose prostate biopsy took place at an inpatient facility, and patients who had evidence of prostate or metastatic cancer during the twelve months pre-index date. We also excluded patients with coverage through Medicare Supplement. Lastly, patients with a prostate or metastatic cancer diagnosis during the six months post-index date were excluded as the focus for this analysis was on the costs incurred for prostate biopsies without findings of cancer.

Figure 6 shows the patient identification waterfall resulting from the episode selection criteria, starting from the total patients in the CHSD database for the selected period and ending with the final patient count used in the prostate biopsy episode analysis. The table also illustrates that nearly 53% of the patients identified with a prostate biopsy had a new prostate cancer diagnosis following the biopsy, excluding them from the remainder of the study.

FIGURE 6: PATIENT IDENTIFICATION WATERFALL

	Patients	Patients Dropped	Cumulative % Remaining
Total patients in starting data	78,731,865	n/a	
Total male patients in starting data	38,725,533	40,005,332	49.2%
Meets inclusion criteria: Has instance of prostate biopsy identified by HCPCS code	151,583	38,573,950	0.4%
Patient does not have first prostate biopsy code with inpatient place of service	151,183	400	99.7%
Patient has at least twelve months of pre-index enrollment and at least one month of post-index enrollment after the biopsy	107,198	44,385	70.7%
No prior evidence of prostate cancer[1]	97,434	54,149	64.3%
Passes all inclusion & exclusion criteria	**97,434**	**54,149**	**67.3%**
Remove episodes that result in cancer diagnosis[2]	46,036	51,398	47.2%
Final episodes	**46,036**	**51,398**	**47.2%**

[1] Evidence of prostate cancer defined as any of the following:
- Diagnosis code of prostate cancer in any diagnosis code position
- Diagnosis code of metastatic cancer in any diagnosis code position
- Procedure code for prostate cancer surgery
- Procedure code for prostate cancer treatment
- Procedure code for radiation therapy
- Administration or prescription fill for a prostate cancer-specific drug therapy.

[2] Episodes that result in cancer diagnosis defined as an episode with any the following within the six months post-biopsy:
- Diagnosis code of prostate cancer in any diagnosis code position
- Diagnosis code of metastatic cancer in any diagnosis code position

We defined a prostate biopsy episode as all claims for a patient incurred from four months prior through two months following the prostate biopsy, based on our evaluation of the time period that included the most relevant claim costs for prostate-related testing prior to the biopsy and conditions that were potential complications following the biopsy. In order to make this determination, we evaluated all claims incurred by the patient within a 12-month window prior to and following the procedure and found that most costs incurred outside of this window (four months pre- and two months post-biopsy) were unlikely to be related to prostate-related testing or conditions that were potential complications of the biopsy.

After identifying the final sample of prostate biopsy episodes, we identified potential complications arising in post-prostate biopsy using a list of complication-related diagnosis codes developed based on clinical judgment. Episodes were identified and flagged as having potential complications when a complication-related diagnosis was observed, listed in Figure 4 in the results section, in the two months post-biopsy as identified by a diagnosis code on any claim in any diagnosis code position. For a subset of the potential complications (bacteriuria, dysuria, erectile dysfunction, hematuria, sacral/perineal pain, and urinary retention) that could be chronic conditions, the condition was only counted as a potential complication if the patient did not have a history of the same condition in the six months prior to biopsy. There was a significant decline in the number of new conditions that were potential complications in the third month post-biopsy, when compared to the first two months post-biopsy. Additionally, based on a review of the medical literature and other studies of prostate biopsy complications, it would be clinically unreasonable to classify as potential biopsy-related complications those conditions that were first reported more than three months after the biopsy. Therefore, we defined each episode as the time period from four months pre-biopsy through two months post-biopsy in order to investigate the episode cost impact of potential biopsy-related complications.

For all prostate biopsy episodes, we grouped claims using Milliman's Health Cost Guidelines™ categories for inpatient, skilled nursing facility, outpatient facility, professional, emergency room/ambulance, prescription drugs, and other. Drug costs that were categorized into the professional and outpatient service categories were then reassigned to a total drugs category to place all drug-related costs in the same cost category for this study. All other services not captured elsewhere, primarily home health and durable medical equipment (DME) services, were captured in the category "All Other."

The episodes were analyzed in a longitudinal monthly manner by service category beginning with the first month of the episode to the day of the prostate biopsy to the end of the episode. The claims incurred prior to, on the day of, and following the prostate biopsy were isolated in the longitudinal analysis to differentiate the costs for the biopsy itself from the potential complication costs, as well as understand the diagnostic testing in the four months prior to the biopsy.

We categorized each patient using six age bands (<45, 45-54, 55-64, 65-74, 75-84, 85+) based on their age on the year of the biopsy and identified their risk score. The reported commercial and individual population risk scores are HHS-HCC risk scores, and the reported MA population is the CMS-HCC risk score. Thus, the risk scores should only be compared between each market's with and without potential complications cohorts, rather than across markets.

For purposes of normalizing medical cost over the time period of the analysis, we applied average cost trends to the midpoint of 2023. Trends used vary by line of business and service category. The annual trends applied can be found in Appendix B.

LIMITATIONS

This report was prepared for LynxDx, Inc., a life sciences company that manufactures a urine test that provides risk assessment information to guide clinical decisions for patients with an elevated PSA or abnormal DRE findings. Our findings are based on an analysis of insured individuals who had an outpatient prostate cancer biopsy procedure, the most common clinical scenario for prostate biopsy following an abnormal prostate cancer screening result. We did not include in the analysis those patients with prostate cancer identified prior to or shortly after the prostate biopsy, as these biopsies would be considered necessary and therefore not potentially avoidable based on the availability of other prostate cancer risk-related information. A prostate cancer biopsy is necessary for the diagnosis of prostate cancer. The potential biopsy-related complication rates and incremental costs may be different for patients diagnosed with prostate cancer compared to the population of patients without cancer that we analyzed.

Our claims data does not capture individuals who are uninsured or experience from plans that do not contribute to our proprietary databases. The results presented here are based on Milliman's analysis of the 2019–2021 commercial group, individual market, and MA data in Milliman CHSD.

The results presented herein are estimates based on the best information available at the date of the publication. Differences between our results and other analysis will arise due to variations in definitions, methodology, and data sources. We used ICD-10-CM diagnosis codes on claims to identify potential biopsy-related complications. Claims-based analyses reflect provider coding of healthcare encounters that may not capture all diagnoses relevant to an encounter and therefore may underestimate the rates of clinically meaningful new conditions that represent potential complications of prostate biopsy. Moreover, the true incidence of minor infectious and certain other complications (e.g., self-limited pain, prostatitis, cystitis, and epididymitis) may be underestimated, as these conditions may not have resulted in a diagnosis code reported on a claim. Finally, given patient healthcare use and provider practice patterns, we expect that most specific complication types represent a wide range of severity, from minor and self-limited for patients who sought care or were scheduled for routine follow up where the complication was identified to severe, requiring acute inpatient hospitalization. We did not attempt to distinguish between the severity of types of complications or severity within a given complication type but, rather, analyzed episodes without potential complications compared to episodes with at least one potential complication.

This report represents the opinion of the authors and is not representative of the views of Milliman. Milliman does not endorse public policy or advocacy positions on matters discussed in this report.

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Guidelines issued by the American Academy of Actuaries require actuaries to include their professional qualifications in all actuarial communications. Pamela Laboy, Keely Congdon, and Jack Tyson are members of the American Academy of Actuaries and meet the qualification standards for performing the analyses documented in this report.

Appendix A

PROSTATE BIOPSY EPISODE RESULTS BY MARKET

Commercial group

Figure 6 details the cost for prostate biopsy episodes by service category and potential complication type for the commercial population.

Approximately 15% of prostate biopsies had a potential biopsy-related complication in this population.

- **Four months pre-biopsy:** The patients with newly identified conditions that were potential complications in the two months post-biopsy had higher cost in the four months pre-biopsy period across inpatient, outpatient facility, professional, emergency, and drug categories. On average, pre-biopsy costs for the cohort of patients with potential complications were 43% higher than for those without evidence of potential complications following the procedure. The higher costs pre-biopsy can likely be partially attributed to the population's morbidity as represented by the risk score differential shown in Figure 2.
- **Day of biopsy:** With an 11% cost difference, the costs between the episodes with and without potential complications were more comparable between the two cohorts than the pre- and post-biopsy costs.
- **Two months post-biopsy**: The two-month post-biopsy costs for the cohort with potential complications were about four times higher than the costs for the cohort without potential complications in that time period. The inpatient service category had the largest differential between the episodes with and without potential complications. The cohort with potential complications had inpatient costs 16 times higher than episodes without potential complications. Inpatient costs for the cohort without potential complications accounted for approximately 10% of total spend during the two months post-biopsy, while inpatient costs for the cohort with potential complications accounted for approximately 38% of the spend during the two months post-biopsy. While the morbidity of the two patient cohorts was different (as shown by the risk score difference in Figure 2), we found that the costs incurred in the two months following the biopsy by patients with potential biopsy-related complications were four times higher than those incurred during the same period by the cohort of patients without potential complications; this compares to a cost differential between the two cohorts of 43% in the four months prior to the biopsy and 11% on the day of the procedure.

FIGURE 6: AVERAGE SPEND PER EPISODE (COMMERCIAL)

	Episodes Without Potential Complications				Episodes With Potential Complications[2]			
Service Category	**Four Months Pre-Biopsy**	**Day of Biopsy**	**Two Months Post-Biopsy**	**Total[1]**	**Four Months Pre-Biopsy**	**Day of Biopsy**	**Two Months Post-Biopsy**	**Total[1]**
Facility Inpatient	$406	$1	$181	**$587**	$969	$49	$2,858	**$3,876**
Skilled Nursing Facility	$1	$0	$1	**$2**	$5	$0	$5	**$10**
Facility Outpatient	$1,336	$1,302	$575	**$3,213**	$1,731	$1,546	$1,888	**$5,164**
Professional	$1,431	$1,617	$596	**$3,644**	$1,850	$1,626	$1,507	**$4,982**
Emergency & Ambulance	$149	$9	$55	**$212**	$401	$35	$537	**$974**
Total Drugs[3]	$861	$11	$428	**$1,300**	$977	$12	$538	**$1,528**
All Other[4]	$50	$3	$25	**$78**	$110	$3	$103	**$215**
All Services Total	**$4,235**	**$2,942**	**$1,861**	**$9,038**	**$6,044**	**$3,270**	**$7,436**	**$16,749**

[1] Allowed medical cost reflected the total amount paid by the payer plus patient cost-sharing for four months pre-biopsy through two months post-biopsy.
[2] Episodes with a potential complication were identified by a specified complication diagnosis code in any diagnosis code position on any claim in the two months post-biopsy .
[3] Included all drugs received under the medical and prescription drug benefits.
[4] Included services not captured elsewhere, primarily home health and DME services.

In the four months pre-biopsy, as shown in Figure 7, 69% of the commercial prostate biopsy patients had a PSA test prior to the biopsy, incurring an average cost of $40 per test, while a small number of patients had DRE or computed tomography (CT) scans. Nearly a fifth of the patients received an MRI prior to their biopsy. Of the 69% of patients who received a PSA test during the four months pre-biopsy, almost 24% also received an MRI, as shown in Figure 8. This is consistent with clinical

guidelines recommending that the initial prostate cancer screening test be a PSA test, which may then be followed by other diagnostic tests such as MRIs.[4] Other tests, such as prostate cancer risk lab tests and transrectal ultrasound, were not widely used in the commercial group population included in our analysis.

FIGURE 7: FOUR MONTHS PRE-PROSTATE BIOPSY DISTRIBUTION OF PROSTATE-RELATED DIAGNOSTIC TESTS[1] (COMMERCIAL)

Test	*% of Patients*	*Average Cost per Test*
MRI	18.1%	$999
DRE	0.1%	$58
Transrectal ultrasound	2.2%	$189
Prostate cancer risk lab tests	1.2%	$777
PSA	68.7%	$40
CT	0.1%	$563

[1] Included commercial prostate biopsy episodes based on services incurred four months pre-biopsy.

FIGURE 8: FOUR MONTHS PRE-PROSTATE BIOPSY DISTRIBUTION OF PROSTATE-RLEATED DIAGNOSTIC TESTS FOR PATIENTS WHO HAD A PSA[1] (COMMERCIAL)

Test	*% of Patients*
MRI	23.5%
DRE	0.1%
Transrectal ultrasound	2.8%
Prostate cancer risk lab tests	1.5%
CT	0.1%

[1] Included commercial prostate biopsy episodes based on services incurred four months pre-biopsy.

Medicare Advantage

Figure 9 details the cost for prostate biopsy episodes by service category and potential complication type for the MA population. Approximately 18% of prostate biopsies had a potential biopsy-related complication in this population.

- **Four months pre-biopsy:** The spending in the four months pre-biopsy for patients with newly identified conditions that were potential complications was nearly 68% higher than that for patients without potential complications, which was largely due to difference in inpatient, outpatient facility, and drug spend. The cost differential between the two cohorts of patients prior to the biopsy procedure was partially explained by morbidity differences between the two populations. Refer to Figure 2 for an overview of cost and risk score differences for the two cohorts of MA patients.
- **Day of biopsy:** Considering that the services on the day of the biopsy would be expected to be similar across cohorts with and without potential complications post-biopsy, we expected the costs on the day of the biopsy to be fairly similar across the two groups. The costs of the episodes with and without potential complications were more comparable on the day of the biopsy than during the pre-biopsy and post-biopsy periods. However, on the day of the biopsy, the costs for the patients with potential complications were approximately 17% higher than the costs for patients without potential complications. As described previously, it is possible that care (e.g., inpatient hospitalization) for a new condition that was a potential complication of the outpatient prostate biopsy may have begun on the day of the biopsy, potentially contributing to this day of biopsy cost difference between the two cohorts.
- **Two months post-biopsy:** The two-month post-biopsy costs for episodes with potential complications were more than three times the cost of the episodes without potential complications, where this differential was driven by inpatient facility costs. This was a much higher cost differential between the two cohorts than that observed prior to and on the day of the procedure. While morbidity differences may partially explain the difference in costs between the two cohorts, we expect that the underlying costs for treating the potential complications were drivers of this cost differential. For example, cost differences due to inpatient admissions resulting from potential complications such as sepsis likely contributed to the observed differences.

FIGURE 9: AVERAGE SPEND PER EPISODE (MEDICARE ADVANTAGE)

	Episodes Without Potential Complications				Episodes With Potential Complications[2]			
Service Category	**Four Months Pre-Biopsy**	**Day of Biopsy**	**Twp Months Post-Biopsy**	**Total[1]**	**Four Months Pre-Biopsy**	**Day of Biopsy**	**Two Months Post-Biopsy**	**Total[1]**
Facility Inpatient	$299	$0	$182	**$482**	$857	$40	$2,260	**$3,157**
Skilled Nursing Facility	$9	$0	$4	**$12**	$56	$0	$52	**$108**
Facility Outpatient	$761	$704	$460	**$1,925**	$1,238	$911	$1,211	**$3,360**
Professional	$1,011	$941	$517	**$2,469**	$1,336	$947	$1,101	**$3,385**
Emergency & Ambulance	$109	$5	$39	**$153**	$289	$24	$296	**$609**
Total Drugs[3]	$948	$8	$467	**$1,423**	$1,421	$10	$695	**$2,126**
All Other[4]	$67	$1	$27	**$95**	$172	$3	$145	**$319**
All Services Total	**$3,203**	**$1,659**	**$1,697**	**$6,559**	**$5,369**	**$1,935**	**$5,760**	**$13,064**

[1] Allowed medical cost reflected the total amount paid by the payer plus patient cost-sharing for four months pre-biopsy through two months post-biopsy.
[2] Episodes with a potential complication were identified by a specified complication diagnosis code in any diagnosis code position on any claim in the two months post-biopsy.
[3] Included all drugs received under the medical and prescription drug benefits.
[4] Included services not captured elsewhere, primarily home health and DME services.

Compared to commercial episodes, MA episodes had a similar overall distribution of patients receiving different prostate-related tests prior to the prostate biopsy but the average cost per test was lower. With an average cost of $24, 65% of MA patients received a PSA test prior to their biopsy, as shown in Figure 10. Of the 65% of patients who received a PSA test in the four months pre-biopsy, approximately 20% also received an MRI, as shown in Figure 11.

FIGURE 10: FOUR MONTHS PRE-BIOPSY DISTRIBUTION OF PROSTATE-RELATED DIAGNOSTIC TESTS[1] (MEDICARE ADVANTAGE)

Test	**% of Patients**	**Average Cost per Test**
MRI	15.2%	$328
DRE	0.2%	$57
Transrectal ultrasound	2.8%	$116
Prostate cancer risk lab tests	2.5%	$713
PSA	65.2%	$24
CT	0.1%	$160

[1] Included MA prostate biopsy episodes based on services incurred four months pre-biopsy .

FIGURE 11: FOUR MONTHS PRE-BIOPSY DISTRIBUTION OF PROSTATE-RELATED DIAGNOSTICS FOR PATIENTS WHO HAD A PSA[1] (MEDICARE ADVANTAGE)

Test	**% of Patients**
MRI	19.5%
DRE	0.2%
Transrectal ultrasound	3.7%
Prostate cancer risk lab tests	3.2%
CT	0.2%

[1] Includes MA prostate biopsy based on services incurred four months pre-biopsy .

Individual Market

Figure 12 details the cost for prostate biopsy episodes by service category and potential complication type for the individual population. Approximately 16% of prostate biopsies had a potential biopsy-related complication in this population. The findings for this population were consistent with those for the commercial group and MA population, as summarized below for reference.

- **Four months pre-biopsy:** The four-month pre-biopsy spend for patients with potential complications was about 31% higher than episodes without potential complications, which was the lowest differential across the three markets.
- **Day of biopsy:** The episodes with potential complications had roughly 18% higher costs during the prostate biopsy, with 73% of the difference driven by outpatient facility costs.
- **Two months post-biopsy:** The two-month post-biopsy costs for episodes with potential complications were more than three times the cost of the episodes without potential complications. The costs incurred in the two months following the procedure for the cohort of patients with potential complications were mainly driven by inpatient services.

FIGURE 12: AVERAGE SPEND PER EPISODE (INDIVIDUAL)

	Episodes Without Potential Complications				Episodes With Potential Complications[2]			
Service Category	**Run-in**	**During**	**Run-out**	**Total[1]**	**Run-in**	**During**	**Run-out**	**Total[1]**
Facility Inpatient	$400	$0	$234	**$634**	$784	$61	$1,984	**$2,829**
Skilled Nursing Facility	$0	$0	$0	**$0**	$0	$0	$0	**$0**
Facility Outpatient	$1,247	$1,093	$489	**$2,829**	$1,360	$1,430	$1,668	**$4,459**
Professional	$1,298	$1,451	$508	**$3,257**	$1,596	$1,478	$1,376	**$4,450**
Emergency & Ambulance	$152	$2	$55	**$209**	$359	$44	$482	**$885**
Total Drugs[3]	$740	$11	$372	**$1,123**	$895	$7	$523	**$1,425**
All Other[4]	$37	$1	$17	**$55**	$94	$2	$106	**$202**
All Services Total	**$3,873**	**$2,558**	**$1,675**	**$8,106**	**$5,087**	**$3,022**	**$6,139**	**$14,249**

[1] Allowed medical cost reflected the total amount paid by the payer plus patient cost-sharing for four months pre-biopsy through two months post-biopsy.
[2] Episodes with a potential complication were identified by a specified complication diagnosis code in any diagnosis code position on any claim in the two months post-biopsy.
[3] Included all drugs received under the medical and prescription drug benefits.
[4] Included services not captured elsewhere, primarily home health and DME services.

The individual prostate biopsy episodes had similar diagnostic testing patterns in the four months pre-biopsy as the commercial and MA episodes. Figure 13 shows that 68% and 17% of the patients had at least one PSA test or MRI, respectively, within the four months prior to the biopsy. Of the 68% of patients who received a PSA test in the pre-biopsy period, approximately 23% also received an MRI, as shown in Figure 14.

FIGURE 13: FOUR MONTHS PRE-BIOPSY DISTRIBUTION OF PROSTATE-RELATED DIAGNOSTIC TESTS[1] (INDIVIDUAL)

Test	**% of Patients**	**Average Cost per Test**
MRI	17.5%	$910
DRE	0.2%	$68
Transrectal ultrasound	2.4%	$153
Prostate cancer risk lab tests	0.8%	$798
PSA	67.8%	$33
CT	0.1%	$747

[1] Included individual prostate biopsy episodes based on services incurred four months pre-biopsy.

FIGURE 14: FOUR MONTHS PRE-BIOPSY DISTRIBUTION OF PROSTATE-RELATED DIAGNOSTIC TESTS FOR PATIENTS WHO HAD A PSA[1] (INDIVIDUAL

Test	% of Patients
MRI	22.8%
DRE	0.2%
Transrectal ultrasound	3.1%
Prostate cancer risk lab tests	1.0%
CT	0.2%

[1] Included individual prostate biopsy episodes based on services incurred four months pre-biopsy .

Appendix B

ANNUAL COST TRENDS BY SERVICE CATEGORY

Service Category	Commercial	Medicare Advantage	Individual
Inpatient	4.0%	1.5%	4.0%
Outpatient	4.5%	5.5%	4.5%
Professional	3.5%	0.5%	3.5%
Office Administered Drugs	5.0%	7.5%	5.0%
Other	2.0%	2.0%	2.0%
Generic Drug	2.0%	0%	2.0%
Brand Drug	4.0%	4.0%	4.0%
Specialty Drug	1.5%	4.5%	1.5%

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