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Clinical Burden and Inpatient Outcomes of Metastatic Versus Non-Metastatic Prostate Cancer: Analysis of the National Inpatient Sample

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Research Article

Keywords: prostate cancer, metastatic disease, National Inpatient Sample, in-hospital mortality, health disparities

Posted Date: September 9th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10232153/v1

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Additional Declarations: No competing interests reported.

Abstract

Background:

Metastatic prostate cancer (mPC) carries substantial clinical and economic burden, but its comparative inpatient outcomes relative to non-metastatic disease (nmPC) remain incompletely characterized using contemporary, nationally representative data.

Methods:

We performed a retrospective, cross-sectional analysis of the 2021–2022 National Inpatient Sample, identifying non-elective prostate cancer hospitalizations in adults ≥ 18 years and classifying them based on metastatic status using ICD-10-CM coding. Multivariable logistic and linear regression models evaluated independent associations of metastatic status with in-hospital mortality, length of stay, and total hospital cost.

Results:

Among 285,495 prostate cancer hospitalizations, 44.5% had metastatic prostate cancer. In-hospital mortality was higher among mPC hospitalizations (7.14% vs. 4.61%; adjusted OR 1.57, 95% CI 1.45–1.69), strengthening after adjustment for in-hospital complications (aOR 1.94, 95% CI 1.77–2.11). mPC was associated with longer length of stay (+ 0.48 days) and higher total cost (+$495.91), greater palliative care use (19.43% vs. 7.10%), and less frequent routine home discharge (38.05% vs. 49.72%).

Conclusion:

Metastatic prostate cancer is independently associated with greater in-hospital mortality, resource utilization, and post-acute care needs compared with non-metastatic disease, even after accounting for in-hospital complications, underscoring the need for early palliative integration and equitable access to subspecialty care.

Introduction

Prostate cancer is the second most common cancer in men in the United States, with approximately one in eight men expected to receive a diagnosis over time [1]. It is also the most common cancer among men across 112 countries globally, with the incidence of advanced disease increasing alarmingly [2]. In 2024 alone, an estimated 299,010 new cases were diagnosed in the United States, accounting for nearly 15% of all new cancer diagnoses, and more than 35,000 men died from the disease [1]. Despite decades of progress in screening and treatments, prostate cancer continues to impose an enormous and

unequally distributed burden on the healthcare system; the burden increases manifold once the disease spreads beyond the prostate.

Population-based tumor registry analyses have demonstrated a statistically significant increase in the incidence of metastatic prostate cancer starting around 2009, with steep rises observed particularly in men aged 45 to 74 years [3]. This shift in disease stage at presentation has serious clinical consequences - the five-year survival rate for patients with early, localized prostate cancer drops from over 99% to around 30% once distant metastases are present [4]. An analysis of SEER data through 2018 recognises that these rising incidence rates of metastatic presentation coincide temporally with the 2012 United States Preventive Services Task Force recommendations against routine PSA-based screening, a pattern observed across both racial and age groups [5].

This trajectory has direct implications for rates of cancer-related inpatient admissions. Nationally representative analyses have established that prostate cancer is among the three most common malignancies driving cancer-related hospitalizations in the United States [6]. Prior work has shown that despite a decline in the absolute volume of hospitalizations for metastatic prostate cancer over time, the per-episode economic burden has remained persistently elevated due to increased complexity when malignancy coincides with acute illnesses [7]. The factors associated with this include longer lengths of stay, higher in-hospital mortality, and greater rates of non-routine discharge in these patients compared to those admitted for non-oncologic conditions [6].

Prior studies have established that the mean total cost per inpatient admission is meaningfully higher for metastatic disease compared to non-metastatic presentations, and that among metastatic admissions, the majority of patients are aged 65 years or older with significant comorbid burden [8]. However, the comparative burden across complications, mortality, resource utilization, and discharge disposition of metastatic versus non-metastatic prostate cancer hospitalizations has been less systematically characterized. The existing literature has also not fully accounted for the granular differences in in-hospital complications like sepsis, acute kidney injury, venous thromboembolism, and urinary obstruction. The contemporary multivariable designs to establish the independent contribution of disease stage to mortality risk are yet to be employed.

From the perspective of racial equity, prostate cancer carries the widest disparities of any cancer, and these disparities manifest across every stage of the disease: from prevention and screening to treatment administered and clinical outcomes[9]. African-American men bear the highest prostate cancer incidence in the United States and have more than twice the risk of dying from the disease compared to White men because of factors like earlier age of onset, more aggressive tumor biology, and systemic inequities in access to care [10]. Within the inpatient setting, African-American patients are admitted more frequently with metastatic disease and experience higher in-hospital mortality, even after adjusting for demographic and clinical presentation differences [11] .

To address these gaps, we conducted a nationally representative, survey-weighted analysis of the Healthcare Cost and Utilization Project National Inpatient Sample (HCUP-NIS), the largest publicly

available all-payer inpatient database in the United States. Our analysis characterizes the clinical and demographic landscape of prostate cancer hospitalizations stratified by metastatic status, quantifies differences in in-hospital complications, mortality, length of stay, and total hospital cost, and employs multivariable logistic regression to identify independent predictors of in-hospital death. Our findings provide a recent, nationally representative foundation for understanding where the inpatient burden of prostate cancer is greatest and for whom the stakes are highest.

Methods

Data Source

We conducted a retrospective, cross-sectional analysis of hospital discharge records from the 2021–2022 National Inpatient Sample (NIS). This study utilized data from the National Inpatient Sample (NIS), the largest publicly available all-payer inpatient database in the United States, maintained by the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality (AHRQ). The NIS encompasses an approximately 20% stratified sample of all domestic inpatient hospitalizations and, when weighted, provides nationally representative estimates of over 35 million hospitalizations annually. Data from calendar years 2021 and 2022 were analyzed. Because the NIS consists of de-identified, publicly available administrative data, this study was exempt from Institutional Review Board review. This study used de-identified, publicly available discharge-level data from the National Inpatient Sample (NIS), maintained by the Agency for Healthcare Research and Quality (AHRQ) through the Healthcare Cost and Utilization Project (HCUP). Per established guidance, the HCUP NIS is explicitly listed among datasets whose research use does not require IRB review or an exempt determination, as it does not involve human subjects as defined by federal regulations (45 CFR 46) [12].

Study Population

Hospitalizations were identified using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes. Prostate cancer hospitalizations were identified using ICD-10-CM code C61 (malignant neoplasm of the prostate) in any diagnostic position. Carcinoma in situ (D07.5) and benign neoplasm (D29.1) of the prostate were excluded as they do not represent malignant disease. Metastatic prostate cancer (mPC) was defined by the co-occurrence of a prostate cancer code with a diagnosis of secondary malignancy in regional lymph nodes (C77.x), other digestive organs or respiratory and intrathoracic organs (C78.x), or other sites (C79.x). Hospitalizations meeting the prostate cancer criteria without any of these secondary malignancy codes were classified as non-metastatic prostate cancer (nmPC).

The study cohort was restricted to non-elective admissions among adult patients aged 18 years and older, consistent with prior NIS-based oncologic studies. Elective admissions were excluded to focus the analysis on acute inpatient care and minimize heterogeneity introduced by planned procedures. As this

study used the full universe of eligible NIS discharge records meeting inclusion criteria during the study period rather than a drawn sample, no a priori sample size calculation was performed .

Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes included length of hospital stay (LOS, in days) and total inflation-adjusted hospital costs (in US dollars). Total hospital costs were derived from hospital charges using HCUP cost-to-charge ratios and subsequently adjusted for inflation to 2022 dollars using a hospital-specific Consumer Price Index (CPI) deflator of 1.04, based on the Hospital Producer Price Index published by the US Bureau of Labor Statistics.

Covariates and Comorbidities

Baseline patient-level covariates included age, race and ethnicity, median household income quartile based on patient ZIP code, and primary expected payer (Medicare, Medicaid, private insurance, or self-pay/other). Hospital-level covariates included bed size, geographic region, and teaching status (rural, urban non-teaching, or urban teaching).

Comorbidity burden was quantified using the Elixhauser comorbidity index as defined by HCUP methodology, which assigns individual comorbidity flags across clinical categories. The total number of comorbidities (elixsum) was subsequently categorized as 0, 1, 2, or ≥ 3 for analytical purposes. For multivariable analyses, this was further collapsed into 0–2 vs ≥ 3 comorbidities because of sparse lower-frequency categories.

In-hospital complications of interest were identified using ICD-10-CM diagnosis codes and included: sepsis (A40.x, A41.x, and additional organism-specific codes including A26.7, A22.7, A02.1, A42.7, A37.7, A32.07, A54.86, and severe sepsis codes R65.20–R65.21), acute kidney injury (N17.x), urinary obstruction or retention (N13.x, R33.8, R33.9), acute myocardial infarction (I21.x), deep vein thrombosis (I82.4x, I82.62, I82.60, I82.890, I82.90, I82.C1, I82.B1, I82.A1), pulmonary embolism (I26.x), and shock (R57.x, R65.21, T81.1x, T79.4x, T78.2x). Septic shock was separately identified using code R65.21. Mechanical ventilation was identified through ICD-10-PCS procedure codes (5A1935Z, 5A1945Z, 5A1955Z). ICU-level care was defined as a composite proxy variable encompassing the presence of either mechanical ventilation or shock. A palliative care consultation was identified by the presence of the ICD-10-CM code Z51.5x in any diagnosis field.

Discharge disposition was categorized into four groups: routine home discharge, transfer to a short-term hospital, discharge to a skilled nursing or other facility, and discharge with home health care, based on the DISPUNIFORM variable in the NIS.

To reduce misclassification bias, metastatic status was defined using a validated combination of ICD-10-CM secondary malignancy codes (C77–C79) rather than a single code, and in-hospital complications

were identified using multi-code definitions inclusive of organism- and site-specific variants. Comorbidity burden was quantified using the standardized HCUP Elixhauser algorithm to minimize inter-institutional coding variability

Statistical Analysis

All analyses were conducted using survey-weighted methods to account for the complex stratified sampling design of the NIS, using DISCWT as the discharge weight, NIS_STRATUM as the stratification variable, and HOSP_NIS as the primary sampling unit, as specified by HCUP analytic guidelines.

Baseline characteristics and in-hospital outcomes were compared between metastatic and non-metastatic prostate cancer hospitalizations using weighted Pearson chi-square tests for categorical variables and weighted linear contrasts for continuous variables. Survey-weighted proportions and means with 95% confidence intervals were reported for all outcomes.

Two multivariable survey-weighted logistic regression models were constructed to evaluate the independent association of metastatic prostate cancer with in-hospital mortality. The first model (Table 3) adjusted for patient demographics (age, race/ethnicity, income quartile, primary payer), comorbidity burden, and hospital characteristics (region, teaching status, bed size). The second, extended model (Table 4) additionally incorporated in-hospital complications as covariates to assess the contribution of metastatic status to mortality beyond its effect on complication risk. To evaluate the independent association of metastatic prostate cancer with LOS and total hospital cost, two separate multivariable survey-weighted linear regression models were constructed using the same demographic, comorbidity, and hospital covariates as the base logistic model. Race/ethnicity, median household income quartile, and primary payer are supplied by HCUP with a designated 'missing/unknown' category rather than requiring imputation; these cases were retained in their respective category for descriptive comparisons and excluded from multivariable models when the category represented missingness rather than a substantive group. No other study variables had missing data, as covariates and outcomes were derived from mandatory ICD-10-CM/PCS diagnosis and procedure fields. No subgroup, interaction, or sensitivity analyses were performed for the present study. A two-sided p-value of less than 0.05 was considered statistically significant for all analyses. All statistical analyses were performed using Stata v17 MP (StataCorp, College Station, TX).

Results

Baseline Characteristics

As shown in Table 1, patients hospitalized with non-metastatic prostate cancer were slightly older on average than those with metastatic disease (76.29 vs. 74.51 years, $p<0.001$). White patients comprised the largest racial group in both cohorts (68.78% non-metastatic vs. 64.33% metastatic), while Black

patients represented a greater proportion of metastatic hospitalizations (21.84% vs. 18.51%). According to Table 1, the metastatic cohort carried a substantially higher comorbidity burden, with 97.58% of metastatic hospitalizations involving patients with three or more Elixhauser comorbidities, compared to 90.86% in the non-metastatic group (p<0.001). Medicare was the predominant payer in both cohorts; however, metastatic hospitalizations had a notably higher proportion of Medicaid-covered patients (7.01% vs. 3.75%, p<0.001). As further detailed in Table 1, metastatic hospitalizations were more commonly concentrated at large hospitals (50.37% vs. 46.69%) and urban teaching centers (76.89% vs. 74.80%), with all hospital-level comparisons reaching statistical significance.

In-Hospital Complications, Palliative Care, and Discharge Disposition

Table 2 presents in-hospital complication rates, palliative care utilization, and discharge disposition across both cohorts. Urinary obstruction or retention was markedly more prevalent among metastatic hospitalizations (29.17% vs. 19.57%, p<0.001). Rates of deep vein thrombosis (4.29% vs. 3.12%), septic shock (4.98% vs. 3.73%), and shock (6.86% vs. 5.65%) were similarly elevated in the metastatic cohort (all p<0.001). Sepsis (19.04% vs. 18.06%, p=0.003) and ICU-level care (8.30% vs. 7.47%, p<0.001) were modestly more common among metastatic hospitalizations, whereas mechanical ventilation was slightly less frequent in the metastatic cohort (3.38% vs. 3.72%, p=0.029) In contrast, acute myocardial infarction occurred less frequently among metastatic hospitalizations (5.03% vs. 7.12%, p<0.001). No statistically significant differences were observed in rates of acute kidney injury (p=0.380) or pulmonary embolism (p=0.104). As shown in Table 2, palliative care was utilized nearly three times as often in the metastatic cohort (19.43% vs. 7.10%, p<0.001). With respect to discharge disposition, metastatic patients were less likely to be discharged routinely to home (38.05% vs. 49.72%) and more frequently required home health care (32.32% vs. 24.49%) or transfer to a skilled nursing or other facility (27.62% vs. 23.53%).

In-Hospital Mortality

As detailed in Table 5, crude in-hospital mortality was higher among metastatic hospitalizations (7.14%; 95% CI 6.81–7.48%) relative to non-metastatic hospitalizations (4.61%; 95% CI 4.38–4.86%), yielding an overall mortality rate of 5.74% (95% CI 5.54–5.94%). On multivariable survey-weighted logistic regression (Table 3), metastatic prostate cancer was independently associated with significantly greater odds of in-hospital death compared to non-metastatic disease (adjusted OR 1.57, 95% CI 1.45–1.69, p<0.001). Each additional year of age was associated with incrementally higher mortality odds (aOR 1.02 per year, p<0.001), while hospitalization in the highest household income quartile was associated with lower

mortality compared to the lowest quartile (aOR 0.88, 95% CI 0.78–0.99, p=0.027). A comorbidity burden of three or more Elixhauser conditions conferred markedly elevated mortality odds (aOR 3.18, 95% CI 2.38–4.25, p<0.001). Hospitalization at urban teaching or non-teaching facilities was associated with lower in-hospital mortality relative to rural hospitals (aOR 0.86 and 0.83, respectively, both p<0.05). No statistically significant racial or ethnic differences in mortality were identified in this model. Private insurance was independently associated with higher mortality odds compared with Medicare (aOR 1.22, 95% CI 1.08–1.38, p=0.001). In the extended multivariable model additionally adjusting for in-hospital complications (Table 4), metastatic disease remained a significant and independent predictor of in-hospital mortality, with a strengthened effect estimate (aOR 1.94, 95% CI 1.77–2.11, p<0.001). Among the complications examined, mechanical ventilation (aOR 5.77, 95% CI 4.84–6.87) and ICU-level care (aOR 4.18, 95% CI 3.31–5.28) were the strongest independent predictors of in-hospital death. Sepsis (aOR 2.03, 95% CI 1.82–2.27), acute kidney injury (aOR 1.78, 95% CI 1.63–1.95), and shock (aOR 1.72, 95% CI 1.36–2.19) were also independently associated with higher mortality odds. Private insurance remained independently associated with higher mortality odds in this model as well (aOR 1.38, 95% CI 1.20–1.59, p<0.001). Notably, as shown in Table 4, urinary obstruction or retention (aOR 0.61, 95% CI 0.55–0.68) and septic shock (aOR 0.55, 95% CI 0.45–0.68) demonstrated inverse associations with in-hospital mortality, findings that likely reflect survivor bias or differential patterns of clinical recognition and administrative coding.

Length of Stay and Hospital Costs

As summarized in Tables 5 and 6, metastatic prostate cancer hospitalizations were associated with longer mean length of stay (6.64 vs. 5.91 days) and higher mean total hospital costs ($19,908 vs. $18,368) compared to non-metastatic hospitalizations. After multivariable adjustment (Table 6), metastatic disease remained independently associated with a significantly prolonged length of stay (+0.48 days, 95% CI 0.35–0.61, p<0.001) and greater total hospital costs (+$495.91, 95% CI $72.14–$919.68, p=0.022).

Table 1. Baseline characteristics of non-metastatic versus metastatic prostate cancer hospitalizations in the National Inpatient Sample

Characteristic	Non-metastatic	Metastatic	P value
Age, mean (SE), years	76.29 (0.07)	74.51 (0.08)	<0.001
Race/ethnicity			<0.001
White	68.78%	64.33%	
Black	18.51%	21.84%	
Hispanic	7.85%	8.50%	
Asian or Pacific Islander	2.27%	2.45%	
Native American	0.28%	0.39%	
Other	2.30%	2.49%	
Elixhauser comorbidity burden			<0.001
0 comorbidities	0.01%	0.00%	
1 comorbidity	2.22%	0.00%	
2 comorbidities	6.91%	2.42%	
≥3 comorbidities	90.86%	97.58%	
Median household income quartile for patient ZIP Code			0.017
1st quartile (lowest income)	25.38%	26.66%	
2nd quartile	24.69%	24.07%	
3rd quartile	24.83%	24.52%	
4th quartile (highest income)	25.09%	24.75%	
Primary expected payer			<0.001
Medicare	81.99%	77.56%	
Medicaid	3.75%	7.01%	
Private insurance	13.38%	13.86%	
Self-pay / other	0.87%	1.57%	
Hospital region			0.004
Northeast	21.18%	21.43%	
Midwest	20.77%	22.11%	

South	36.76%	35.25%	
West	21.28%	21.21%	
Hospital bed size			<0.001
Small	23.54%	21.10%	
Medium	29.77%	28.53%	
Large	46.69%	50.37%	
Hospital location/teaching status			<0.001
Rural	8.23%	7.33%	
Urban non-teaching	16.97%	15.78%	
Urban teaching	74.80%	76.89%	

Table 2. In-hospital complications, palliative care use, and discharge disposition among non-metastatic versus metastatic prostate cancer hospitalizations

Variable	Non-metastatic	Metastatic	P value
Sepsis	18.06%	19.04%	0.003
Acute kidney injury	34.86%	35.22%	0.380
Urinary obstruction/retention	19.57%	29.17%	<0.001
Acute myocardial infarction	7.12%	5.03%	<0.001
Deep vein thrombosis	3.12%	4.29%	<0.001
Pulmonary embolism	2.75%	2.99%	0.104
Shock	5.65%	6.86%	<0.001
Mechanical ventilation	3.72%	3.38%	0.029
ICU admission / ICU-level care	7.47%	8.30%	<0.001
Septic shock	3.73%	4.98%	<0.001
Palliative care use	7.10%	19.43%	<0.001

Discharge disposition	Non-metastatic	Metastatic	P value
Routine home discharge	49.72%	38.05%	<0.001
Transfer to a short-term hospital	2.25%	2.01%	
Skilled nursing facility / other facility	23.53%	27.62%	
Home health care	24.49%	32.32%	

Table 3. Multivariable survey-weighted logistic regression for in-hospital mortality among prostate cancer hospitalizations

Variable	Adjusted OR	95% CI	P value
Metastatic vs non-metastatic prostate cancer	1.57	1.45–1.69	<0.001
Age, per 1-year increase	1.02	1.02–1.03	<0.001
Race/ethnicity			
Black vs White	1.07	0.96–1.19	0.229
Hispanic vs White	1.05	0.91–1.20	0.499
Asian/Pacific Islander vs White	1.22	0.98–1.50	0.069
Native American vs White	1.42	0.80–2.50	0.228
Other vs White	1.17	0.93–1.47	0.179
Median household income quartile			
2nd vs 1st quartile	0.98	0.88–1.09	0.656
3rd vs 1st quartile	0.94	0.84–1.05	0.303
4th vs 1st quartile	0.88	0.78–0.99	0.027
Elixhauser burden			
≥3 vs 0–2 comorbidities	3.18	2.38–4.25	<0.001
Hospital location/teaching status			
Urban non-teaching vs Rural	0.83	0.70–0.97	0.023
Urban teaching vs Rural	0.86	0.74–1.00	0.044
Hospital region			
Midwest vs Northeast	0.89	0.79–1.01	0.065
South vs Northeast	0.87	0.78–0.97	0.015
West vs Northeast	1.17	1.04–1.32	0.009
Hospital bed size			
Medium vs Small	1.03	0.93–1.15	0.531
Large vs Small	0.99	0.90–1.10	0.874
Primary expected payer			
Medicaid vs Medicare	1.07	0.88–1.30	0.477
Private insurance vs Medicare	1.22	1.08–1.38	0.001
Self-pay/other vs Medicare	0.99	0.67–1.46	0.973

Table 4. Extended multivariable survey-weighted logistic regression for in-hospital mortality among prostate cancer hospitalizations

Variable	Adjusted OR	95% CI	P value
Metastatic vs non-metastatic prostate cancer	1.94	1.77–2.11	<0.001
Age, per 1-year increase	1.04	1.03–1.04	<0.001
Black vs White	0.96	0.85–1.08	0.488
Hispanic vs White	0.93	0.79–1.09	0.368
Asian/Pacific Islander vs White	1.09	0.85–1.39	0.494
Native American vs White	1.41	0.82–2.43	0.218
Other vs White	1.07	0.82–1.39	0.633
2nd vs 1st income quartile	0.98	0.87–1.11	0.809
3rd vs 1st income quartile	0.97	0.86–1.10	0.645
4th vs 1st income quartile	0.89	0.78–1.01	0.077
≥3 vs 0–2 comorbidities	1.53	1.14–2.06	0.004
Urban non-teaching vs Rural	0.66	0.54–0.79	<0.001
Urban teaching vs Rural	0.66	0.56–0.77	<0.001
Midwest vs Northeast	0.84	0.73–0.96	0.013
South vs Northeast	0.80	0.70–0.90	<0.001
West vs Northeast	1.14	0.99–1.30	0.060
Medium vs Small bed size	0.96	0.85–1.08	0.474
Large vs Small bed size	0.91	0.81–1.02	0.102
Medicaid vs Medicare	1.11	0.89–1.38	0.368
Private insurance vs Medicare	1.38	1.20–1.59	<0.001
Self-pay/other vs Medicare	1.21	0.80–1.82	0.375
Sepsis	2.03	1.82–2.27	<0.001
Acute kidney injury	1.78	1.63–1.95	<0.001
Urinary obstruction/retention	0.61	0.55–0.68	<0.001
Acute myocardial infarction	1.32	1.15–1.53	<0.001
Deep vein thrombosis	1.14	0.92–1.41	0.242
Pulmonary embolism	1.37	1.09–1.71	0.006
Shock	1.72	1.36–2.19	<0.001

Mechanical ventilation	5.77	4.84–6.87	<0.001
ICU-level care	4.18	3.31–5.28	<0.001
Septic shock	0.55	0.45–0.68	<0.001

Table 5. Mortality, length of stay, and inflation-adjusted hospital cost among non-metastatic and metastatic prostate cancer hospitalizations

Outcome	Non-metastatic	Metastatic	Overall
In-hospital deaths, weighted n	7,305	9,070	16,375
In-hospital mortality rate, % (95% CI)	4.61 (4.38–4.86)	7.14 (6.81–7.48)	5.74 (5.54–5.94)
Length of stay, mean days (95% CI)	5.91 (5.82–5.99)	6.64 (6.54–6.74)	6.23 (6.16–6.30)
Total hospital cost, mean USD (95% CI)	$18,368 ($18,033–$18,704)	$19,908 ($19,492–$20,324)	$19,054 ($18,743–$19,365)

Footnote: Values are survey-weighted national estimates or survey-weighted means with 95% confidence intervals.

Table 6. Adjusted associations of metastatic prostate cancer with length of stay and total hospital cost

Outcome	Adjusted effect of metastatic vs non-metastatic prostate cancer	95% CI	P value
Length of stay, days	+0.48 days	0.35 to 0.61	<0.001
Total hospital cost, USD	+$495.91	$72.14 to $919.68	0.022

DISCUSSION

Our analysis demonstrates that metastatic prostate cancer is associated with a significantly greater clinical and economic burden compared to non-metastatic disease. Among an estimated 285,495 non-

elective prostate cancer hospitalizations meeting inclusion criteria, 44.5% involved mPC and 55.5% involved nmPC. The incidence of distant-stage prostate cancer has continued to increase following the 2012 U.S. Preventive Services Task Force (USPSTF) recommendation against routine PSA-based screening in all men. A large California-based cohort study of 387,636 cases demonstrated a 6.7% annual increase in distant-stage prostate cancer from 2011 to 2021 [16]. Over the same period, prostate cancer mortality, which had been declining at 2.6% per year between 2004 and 2012, plateaued and remained stable through 2021 [16]. Further characterizing the metastasis by site, national SEER data from 2010 to 2019 confirm that the incidence of prostate cancer with bone metastases increased significantly up to 2017, remaining stable thereafter, whereas visceral metastatic disease continued to increase at 12.3% per year during the entire study period [17]. An estimated 120,400 men were living with metastatic prostate cancer in the United States as of 2018, a number projected to exceed 192,500 by 2030 [18].

In-hospital mortality was significantly higher among mPC hospitalizations when compared to nmPC hospitalizations (7.14% vs 4.61%). On multivariable survey-weighted logistic regression for mPC in-hospital mortality adjusted for age, race/ethnicity, median household income, comorbidity burden, and hospital characteristics (Table 3), metastatic disease was associated with a 57% increase in the odds of in-hospital mortality compared to nmPC (adjusted OR 1.57; 95% CI 1.45–1.69, $p < 0.001$). In a second multivariable model that additionally includes inpatient complications as covariates (Table 4), the odds ratio for metastatic disease increased substantially to 1.94 (95% CI, 1.77–2.11), suggesting that metastatic disease itself remains a significant independent predictor for in-hospital mortality even after accounting for inpatient complications. Prior studies have shown that among U.S. men diagnosed with metastatic prostate cancer between 2000 and 2016, 77.8% of deaths were attributable to prostate cancer itself, and deaths from three of the most common non-cancer causes, including cardiovascular diseases, chronic obstructive pulmonary disease, and cerebrovascular diseases, occurred at rates significantly higher than the age-matched general population (SMR 1.34, 1.19, and 1.31, respectively) [19]. This analysis not only reiterates our findings on the natural history of mPC but also highlights the multisystem organ burden these patients carry upon hospital admission. Patients with mPC were also younger on average than those with nmPC (74.51 vs. 76.29 years), yet nearly all (97.58%) had three or more comorbidities, compared with 90.86% of nmPC patients, reflecting a disproportionately high baseline comorbidity burden that likely predisposes them to adverse inpatient events.

Further analysis of these inpatient complications revealed several differences between mPC and nmPC hospitalizations. Urinary obstruction or retention was significantly more prevalent in mPC hospitalizations (29.17% vs. 19.57%; $p < 0.001$), which can be expected with local tumor extension, pelvic lymphadenopathy, and lower spinal bone metastases, each of which contributes to obstructive uropathy. Deep vein thrombosis (DVT) was also significantly more common among mPC patients (4.29% vs. 3.12%; $p < 0.001$). A study using the Nationwide Prostate Cancer database in Sweden involving 92,105 men with and 466,241 without prostate cancer demonstrated that men with prostate cancer carry a 50% increased risk of venous thromboembolism (VTE) during the 5 years following cancer diagnosis compared with matched controls without prostate cancer [20]. However, among all solid tumors,

prostate cancer carries one of the lowest absolute cumulative VTE incidences globally (1.58%) [21]. Sepsis and septic shock were also elevated in mPC (19.04% and 4.98%) compared with nmPC (18.06% and 3.73%), as were shock (6.86% vs. 5.65%) and ICU admission (8.30% vs. 7.47%). Mechanical ventilation was modestly less common among mPC hospitalizations (3.38% vs. 3.72%, p = 0.029. Acute myocardial infarction was conversely more prevalent among nmPC hospitalizations (7.12% vs. 5.03%), which could be explained by nmPC patients being older on average and carrying a higher baseline cardiovascular risk profile relative to their cancer burden.

This greater complication profile translated into longer hospitalizations and higher costs. mPC hospitalizations were associated with a longer length of stay (6.64 vs. 5.91 days; adjusted difference + 0.48 days, p < 0.001) and higher total hospital costs ($19,908 vs. $18,368; adjusted difference +$495.91, p = 0.022). These differences carry meaningful implications across hundreds of thousands of hospitalizations nationally and do not account for indirect costs or post-discharge resource utilization. Prostate cancer remains among the top three contributors to cancer-related hospitalizations in the United States, with total cancer hospitalization costs rising 37.7% from 2008 to 2019 [6], placing a substantial and growing burden on hospital systems nationwide.

Using NIS data from 2010 to 2019, Olafimihan et al. found an overall prevalence of palliative care utilization of 13.1% among mPC hospitalizations, with an increasing trend over the study timeline [22], while Mistry et al. analyzed 2012 to 2013 NIS data, reporting a consultation rate of 10.4% among mPC admissions [23]. In our study, we found that palliative care was used significantly more often in mPC than in nmPC hospitalizations (19.43% vs. 7.10%; p < 0.001). The higher rate, compared with prior studies, indicates an upward trend towards palliative care integration. A systematic review and meta-analysis of specialist palliative care in adults with advanced illness, including 10 randomized controlled trials with 2,454 patients (72% of whom had cancer), demonstrated a small but significant improvement in quality of life (SMD 0.16, 95% CI 0.01–0.31), with a larger effect for cancer patients, especially those receiving palliative care early in their illness course [24]. A meta-analysis of outpatient specialty palliative care in advanced cancer demonstrated a 4.56-month improvement in median survival in high-quality randomized controlled trials [25]. A large propensity-matched cohort study of Medicare patients with metastatic cancer found that receipt of specialist palliative care was associated with decreased use of chemotherapy in the last 14 days of life (adjusted HR 0.59) and decreased ICU utilization at end of life (adjusted HR 0.86), alongside a nearly twofold increase in hospice enrollment for ≥ 3 days [26]. These findings support increased utilization of palliative care in mPC to enhance quality of life, reduce unnecessary interventions, and improve end-of-life care.

Discharge patterns among mPC patients highlight the physical debility associated with metastatic disease. Routine home discharge was significantly less common in mPC compared to nmPC (38.05% vs. 49.72%), while discharge to skilled nursing facilities (27.62% vs. 23.53%) and home health services (32.32% vs. 24.49%) were both more frequent. From a health systems perspective, the higher rates of skilled nursing facility and home health utilization in mPC hospitalizations further represent the inpatient resource burden in the post-acute care setting. National surveillance data confirm that across all cancer

types, discharge to long-term facilities from cancer-related hospitalizations increased by over 20.6% from 2008 to 2019 [6].

Race and ethnicity data in this cohort reveal a notable difference in the distribution of Black patients between the two groups: Black men comprised 21.84% of mPC hospitalizations compared with 18.51% of nmPC hospitalizations ($p < 0.001$). This finding is consistent with the well-established racial disparities in prostate cancer epidemiology. Black men in the United States bear a disproportionate burden of prostate cancer, with earlier age at diagnosis, more aggressive tumor features at presentation, higher rates of metastatic disease, and higher prostate cancer-specific mortality [10]. The age-adjusted prevalence of metastatic prostate cancer in Black men is over double that of White men (137.1 vs. 62.2 per 100,000) [18]. A 2024 meta-analysis of metastatic castration-resistant prostate cancer treatment cohorts (n = 9,462) found a pooled overall survival hazard ratio of 0.75 favoring Black men across systemic therapy regimens [27]. However, this treatment survival advantage is overshadowed by a greater disparity: Black men develop metastatic prostate cancer at more than twice the rate of white men, although this gap has been gradually narrowing over time, the incidence rate ratio remained 2.1 as recently as 2021 [28]. Studies in equal-access settings such as the Veterans Affairs system show that while racial disparities in prostate cancer incidence and early progression persist, outcomes in advanced disease stages appear to favor Black men, suggesting that standardized care mitigates but does not fully eliminate these disparities [29]. A meta-analysis of over one million patients found that when social determinants of health are adequately accounted for, Black men had significantly lower prostate cancer-specific mortality than White men (HR 0.86; 95% CI 0.77–0.96) [30], collectively implicating systemic inequity rather than intrinsic biology as the primary driver of racial disparities in this disease. To further support this, race was not an independent predictor of in-hospital mortality in our model. This may be because race is closely tied to income, insurance status, and other social factors that are difficult to disentangle in administrative data, or it may suggest that, once disease severity and hospital-level factors are accounted for, race may no longer independently influence short-term survival.

Patients with mPC were more frequently hospitalized at large-bed hospitals (50.37% vs. 46.69%) and urban teaching hospitals (76.89% vs. 74.80%), both of which were associated with lower mortality in adjusted analyses. Urban teaching hospital status was associated with a 14% reduction in the odds of in-hospital mortality compared with rural hospitals (aOR 0.86; 95% CI 0.74–1.00), and urban non-teaching status was associated with a 17% reduction (aOR 0.83; 95% CI 0.70–0.97). Notably, this protective association strengthened substantially in the complication-adjusted model (Table 4), where both urban teaching and urban non-teaching status were associated with a 34% reduction in mortality odds relative to rural hospitals (aOR 0.66 for both; 95% CI 0.56–0.77 and 0.54–0.79, respectively). This shift suggests that a meaningful portion of the survival advantage observed at urban hospitals may be mediated through more effective recognition and management of in-hospital complications, rather than reflecting baseline differences in patient risk alone, consistent with the availability of multidisciplinary oncology and palliative care teams, advanced supportive care infrastructure, and subspecialty expertise at academic medical centers [31]. Additionally, patients in the highest income quartile (4th quartile) demonstrated a modest but statistically significant survival advantage (aOR 0.88; 95% CI 0.78–0.99),

suggesting that socioeconomic factors continue to influence inpatient survival even after adjusting for clinical and hospital-level variables. Notably, private insurance was independently associated with significantly higher odds of in-hospital mortality compared with Medicare in both the base model (aOR 1.22; 95% CI 1.08–1.38) and the complication-adjusted model (aOR 1.38; 95% CI 1.20–1.59). This finding runs counter to the typically protective association of private insurance with cancer outcomes [32], et al and may instead reflect selection: because Medicare eligibility begins at age 65, privately insured patients in this non-elective cohort are necessarily younger on average, and early-onset prostate cancer has been shown to disproportionately represent more biologically aggressive, rapidly growing tumors with worse stage-for-stage and grade-for-grade prognosis than disease diagnosed in older men [33]. It is therefore possible that younger, privately insured patients hospitalized non-electively for prostate cancer represent a subgroup enriched for aggressive early-onset disease, rather than reflecting a true causal effect of insurance type on survival.

Limitations

Several limitations inherent to the administrative nature of the NIS data warrant consideration when interpreting these findings. First, the NIS relies on ICD-10-CM diagnostic and procedure codes for case identification and outcome ascertainment, which are subject to coding inaccuracies, variability in institutional coding practices, and potential misclassification bias. Clinical nuances such as disease burden, extent of metastatic spread, performance status, and treatment intent cannot be captured through administrative codes alone. Second, while metastatic disease was defined using secondary malignancy codes (C77–C79), the NIS does not permit differentiation by site of metastasis (e.g., bone-only versus visceral metastatic disease), which may carry distinct prognostic and clinical implications. Third, the cross-sectional, hospitalization-level design of the NIS precludes causal inference and does not allow for patient-level longitudinal follow-up. Readmissions, post-discharge mortality, outpatient resource utilization, and longer-term oncologic outcomes therefore fall outside the scope of this analysis. Fourth, as the NIS captures individual hospitalizations rather than unique patients, patients with multiple admissions during the study period may contribute more than one observation, potentially introducing a unit-of-analysis bias. Fifth, although comorbidity burden was quantified using the validated HCUP Elixhauser methodology, important clinical variables relevant to prostate cancer outcomes, including Gleason score, PSA level, prior systemic therapy, and lines of treatment received, are not available in the NIS. Sixth, the ICU-level care variable used in this study was a composite proxy derived from mechanical ventilation and shock diagnoses rather than a direct measure of ICU admission, which may underestimate true ICU utilization. Seventh, the study period of 2021–2022 represents two calendar years of data, which limits the ability to assess temporal trends in metastatic prostate cancer hospitalizations or to determine whether the observed patterns reflect stable long-term phenomena or time-specific artifacts related to healthcare delivery during the post-COVID-19 recovery period. Finally, while survey-weighted methods were applied to generate nationally representative estimates, the generalizability of these findings is contingent on the accuracy of the underlying NIS sampling and

weighting methodology, and results may not be fully applicable to healthcare systems outside the United States.

Conclusion

This nationally representative, survey-weighted analysis of the HCUP NIS demonstrates that metastatic prostate cancer is independently associated with significantly greater in-hospital mortality, longer length of stay, and higher total hospital costs compared to non-metastatic disease. A higher burden of in-hospital complications characterized metastatic hospitalizations; most notably urinary obstruction, venous thromboembolism, sepsis, and shock, greater palliative care utilization, and more frequent need for post-acute care services at discharge. Importantly, metastatic disease remained a significant and independent predictor of in-hospital mortality even after adjusting for the full spectrum of in-hospital complications, underscoring that the excess mortality risk in this population extends beyond what can be explained by acute clinical events alone.

These findings carry direct implications for hospital-based care delivery. The concentration of metastatic prostate cancer hospitalizations at large urban teaching centers and the associated survival advantage observed at these institutions are associated with better outcomes, potentially reflecting the role of multidisciplinary oncologic expertise and advanced supportive care infrastructure. The persistently low rates of palliative care utilization, even among metastatic hospitalizations, represent an actionable gap, given the well-established evidence that early palliative care integration improves quality of life, reduces unnecessary interventions, and may extend survival in advanced malignancy. The disproportionate representation of Black men among metastatic hospitalizations is consistent with well-established racial disparities in prostate cancer screening, early detection, and treatment access, and reinforces the importance of continued investigation into their upstream drivers rather than attributing differential outcomes to biological differences alone.

As the incidence of metastatic prostate cancer continues to rise nationally, these data provide a contemporary, population-level foundation for identifying where inpatient burden is concentrated. The associations observed here, have greater complication burden, mortality, and post-acute care need among metastatic hospitalizations which are consistent with, though not sufficient to establish, a role for earlier palliative care integration, more equitable access to subspecialty care, and expanded socioeconomic support as areas warranting further investigation.

Declarations

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

This study utilized de-identified, publicly available administrative data from the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS). In accordance with federal regulations governing human subjects research (45 CFR 46.101(b)), this study was exempt from Institutional Review Board review as it does not involve identifiable private information.

Consent to Participate

Not applicable. This study used de-identified publicly available administrative data; individual participant consent was not required.

Consent to Publish

Not applicable. This study used de-identified publicly available administrative data; no individual person's data, images, or identifiable information are presented in this manuscript.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Author Contribution

R.S conceptualized and designed the study, developed the analytical framework, performed all statistical analyses using the National Inpatient Sample database, and drafted the Methods and Results sections. A.K drafted the initial Discussion, Conclusion, and Limitation section. M.M drafted the Introduction section. M.M , A.C, B.G and M.V.K critically reviewed earlier drafts of the manuscript for important intellectual content. All authors critically reviewed and revised the manuscript, and approved the final version for submission.

Data Availability

Availability of Data and MaterialThe National Inpatient Sample (NIS) data used in this study are publicly available from the Healthcare Cost and Utilization Project (HCUP), maintained by the Agency for Healthcare Research and Quality (AHRQ). The NIS overview and access instructions are available at https://www.hcup-us.ahrq.gov/nisoverview.jsp.Code AvailabilityThe custom Stata code used to construct the analytic cohort and perform the statistical analyses in this study is available from the corresponding author upon reasonable request.Ethics Approval This study utilized de-identified, publicly available administrative data from the Healthcare Cost and Utilization Project (HCUP) National Inpatient

Sample (NIS). In accordance with federal regulations governing human subjects research (45 CFR 46.101(b)), this study was exempt from Institutional Review Board review as it does not involve identifiable private information.

Code Availability

The custom Stata code used to construct the analytic cohort and perform the statistical analyses in this study is available from the corresponding author upon reasonable request.

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