The Impact of Underinsurance on Bladder Cancer Diagnosis, Survival, and Care Delivery

The Impact of Underinsurance on Bladder Cancer
Diagnosis, Survival, and Care Delivery

by

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I have reviewed this thesis. It represents work done by the author under my supervision and guidance.

Abstract

Purpose: Health inequity in the United States are closely linked to patients' ability to afford their care. We sought to determine the association between underinsurance and outcomes in bladder cancer, a disease that confers a substantial financial burden upon diagnosed individuals.

Methods: We used the Surveillance, Epidemiology, and End Results (SEER) registry and National Cancer Database (NCDB) to identify individuals aged <65 years who were diagnosed with bladder cancer from 2007 to 2014. We evaluated the association between insurance status and outcomes related to prognosis (diagnosis with advanced disease, cancer-specific survival) and care delivery (delay in care, treatment in a high-volume hospital, and receipt of neoadjuvant chemotherapy).

Results: Compared to those with private insurance, uninsured and Medicaid-insured individuals were nearly twice as likely to receive a diagnosis of muscle-invasive bladder cancer (Uninsured OR: 1.90; 95% CI: 1.70 – 2.12. Medicaid OR: 2.03; 95% CI: 1.87 – 2.20). These groups were also more likely to die of bladder cancer (Uninsured adjusted hazard ratio [AHR]: 1.49; 95% CI: 1.31 – 1.71. Medicaid AHR: 1.61; 95% CI: 1.46 – 1.79). Delays in treatment > 90 days were more likely for the uninsured (OR: 1.36; 95% CI: 1.12 – 1.65) and Medicaid-insured (OR: 1.22; 95% CI: 1.03 – 1.44) compared to the private-insured. Uninsured patients had lower odds of treatment in a high-volume facility (OR: 0.66; 95% CI: 0.52 – 0.83), and Medicaid-insured patients had lower odds of receiving neoadjuvant chemotherapy (OR: 0.74; 95%CI: 0.60 – 0.91).

Conclusions: Uninsured and Medicaid-insured individuals are more likely than those with private insurance to be diagnosed with advanced bladder cancer as well as die from the disease; they are also subject to poorer care quality. Expanding high-quality insurance coverage to marginalized populations may help to reduce the burden of this disease.

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Glossary of Abbreviations

ACA: Affordable Care Act

AHR: Adjusted hazard ratio

AJCC: American Joint Committee on Cancer

CI: Confidence interval

CoC: Commission on Cancer

CT: Computed tomography

cTNM: Clinical Tumor-Node-Metastasis staging

DSH: Disproportionate-share hospital

MRI: Magnetic resonance imaging

NAC: Neoadjuvant chemotherapy

NCDB: National Cancer Database

OR: Odds ratio

SEER: Surveillance, Epidemiology, and End Results

Introduction

Health inequity in cancer care is a pervasive and complex issue in medicine. This is especially true in the United States, where there is a significantly higher percentage of underinsured individuals compared to countries of comparable economic development.[1] For that reason, one of the major focuses of US health reform has been expansion of health insurance coverage – a contentious issue that impacts millions across the country.[2] Despite spending approximately twice as much as other high-income countries on health care, the US still has dismal ratings on metrics of equitable care provision among its citizens.[1,3] Coverage expansion is both a contentious issue and a complex undertaking that relies on a thorough understanding of the potential value added by insuring more individuals. While politicians debate this issue, those who lack insurance or have insufficient coverage policies continue to struggle accessing healthcare. The importance of adequate health insurance has become especially paramount in recent times, propelled by the ongoing development of advanced – and often costly – treatments for diseases such as cancer.

Bladder cancer may be especially sensitive to insurance status because its diagnostic workup and subsequent treatment regimen impart the highest lifetime cost per patient among all cancers from diagnosis to death.[4] Diagnosis generally involves a physician's evaluation, urinalysis with cytology, cystoscopy, and urinary tract imaging with computed tomography (CT) or magnetic resonance imaging (MRI); treatment may encompass chemotherapy, repeated endoscopic procedures, major surgery, and radiation.[5] For many with bladder cancer, these routine surveillance and treatment regimens are often protracted, arduous, and expensive. This costly pathway may therefore pose significant barriers for men and women who have poorer access to healthcare due to inadequate insurance. However, it is not well known how insurance status may affect important outcomes for patients with bladder cancer. Understanding the impact of insurance coverage on outcomes for such a costly disease can help to guide health policy initiatives that seek to provide high-quality cancer care to those with less financial means.

To our knowledge, there are scarce data that comprehensively assess differences (other than overall survival alone) in bladder cancer outcomes by insurance status. Niu et al, using data from New Jersey, previously showed that uninsured patients with bladder cancer face higher mortality risks compared to the insured.[6] However, it is unknown whether this finding remains true on the national scale. In addition, while mortality serves as a highly relevant endpoint, it is equally important to understand 1) how diagnosis patterns may differ by insurance status and thereby influence downstream effects on long-term outcomes such as survival, and 2) how particular aspects of care delivery may mediate differences in survival outcomes based on insurance status. Understanding these specific contributors to differences in long-term outcomes is the first step to targeting and mitigating them.

In this context, we designed a study with the objective of analyzing the impact of underinsurance on outcomes for bladder cancer. We used two comprehensive national cancer registries to determine the association between insurance status and patient outcomes in bladder cancer related to diagnosis with advanced disease, bladder cancer-specific survival, and care delivery. We focused on aspects of care delivery that have been shown to impart substantial influence on survival from bladder cancer: delays in care, treatment at high-volume facilities, and – for those who underwent major surgery – receipt of neoadjuvant chemotherapy prior to surgery. We hypothesized that, compared to individuals with private insurance, those who were uninsured or Medicaid-insured at diagnosis would be more likely to present with advanced bladder cancer, die from their disease, and fare poorer on care quality metrics for bladder cancer treatment.

Methods

Data Source

We used two national cancer registries: the Surveillance, Epidemiology, and End Results (SEER) database and the National Cancer Database (NCDB). SEER is a collection of 18 defined geographic areas (registries) sponsored by the US National Cancer Institute. It covers about 34% of the US population, and the registries chosen specifically such that the database demographics are nationally representative.[7] The NCDB, established by the Commission on Cancer (CoC) of the American Cancer Society, includes those seen at one of 1,500 CoC-accredited hospitals for any portion of their diagnosis or treatment and captures over 60% of US bladder cancer cases.[8] Both databases contain information on patient demographics and tumor characteristics. Data abstractors are trained to use a standard methodology for collecting sociodemographic and clinical information, and the data undergo regular audits to optimize internal validity. We used both of these databases in order to leverage the differing advantages of each one. For example, SEER has detailed survival statistics (e.g. cancer-specific survival) that NCDB does not collect. NCDB has more granular hospital level variables (e.g. hospital volume, time to treatment, provision of neoadjuvant chemotherapy) that are not available in SEER.

Cohort selection

For both database analyses, we identified individuals diagnosed with bladder cancer from January 1, 2007 to December 31, 2014. Analyses began in 2007 because this is the first year in which the SEER insurance variable became available; 2014 was the last available year of follow-up at the time of analysis. We restricted our analyses to those ages 18-64 to focus on a population with variability in insurance coverage, as people aged ≥ 65 are highly likely to be covered by Medicare. In addition, SEER considers insurance status designation for those aged ≥ 65 to be relatively unreliable (i.e. many classified as "uninsured" are Medicare-eligible).[7] We excluded individuals missing information on clinical TNM staging as well as those with unknown insurance status or survival follow-up time. We also excluded those who were diagnosed with a different cancer prior to their bladder cancer diagnosis (Figure 1). In SEER, all stages of disease were included. The NCDB analyses were restricted to those with localized (i.e. non-metastatic), muscle-invasive bladder cancer (cT2-4N0M0) in order to evaluate care delivery for those with aggressive disease, a population upon which much of the data on our specified care delivery outcomes are based. For the NCDB cohort, we excluded those with zero days elapsed between diagnosis and treatment because these individuals likely did not enter the database upon initial diagnosis. Staging systems were based on the American Joint Committee on Cancer (AJCC) guidelines, 6th edition.

Exposure variable

Our main exposure variable was insurance status at the time of diagnosis. Definitions of this variable for both SEER and NCDB are drawn from the North American Association of Central Cancer Registries (NAACCR) primary payer field. This included private insurance (including fee-for service, health maintenance organization, preferred provider organization, and TRICARE), Medicaid insurance (including Indian/Public Health Service), and uninsured.

Covariates

Sociodemographic covariates used in both databases included age at diagnosis, sex, race (white, black, other), ZIP code level median household income, ZIP code level education (based on percentage of adults without a high school degree), geographical region, and year of diagnosis. Clinical covariates included histologic type (urothelial vs. non-urothelial) and clinical tumor-node-metastasis (TNM) staging at diagnosis. Additional NCDB covariates (not available in SEER) included Charlson-Deyo comorbidity index, patient distance from hospital, and hospital case volume.[9] We defined case volume as the mean of the total volume of patients with clinically localized, muscle-invasive bladder cancer treated in the given facility in the year of the patient's diagnosis, accounting for caseload variation over the study timeframe.

Study Outcomes

Our study outcomes of interest using SEER were clinical diagnosis of muscle-invasive bladder cancer (defined as clinical stage $\geq$ T2) and bladder cancer-specific survival. Diagnosis of muscle-invasive bladder cancer is a relevant endpoint because it represents the lethal phenotype of the disease; the overwhelming majority of bladder cancer deaths are in individuals with muscle-invasive disease.[5] Outcomes of interest in the NCDB were receipt of neoadjuvant chemotherapy (NAC; $<$180 days before surgery among those who underwent radical cystectomy), delay $>$ 90 days in receipt of any treatment (surgery, chemotherapy, or radiation), and treatment at a high volume facility (top quartile in mean case volume). We chose these outcomes in particular because each has been shown to impact long-term survival in bladder cancer. Level I evidence demonstrating the improved efficacy of NAC prior to surgery versus surgery alone in prolonging life in individuals with advanced bladder cancer has made provision of NAC the current standard of care.[10-12] Delay in care greater than 3 months after receiving a diagnosis of muscle-invasive bladder cancer has been shown in several studies to be associated with poorer survival.[13,14] Lastly, there is a documented volume-outcome relationship in bladder cancer whereby improved survival outcomes are seen in patients who are treated in facilities that treat a large number of individuals with bladder cancer.[15,16]

Statistical analysis

Descriptive statistics were reported using frequencies and proportions for categorical variables; continuous variables were reported using medians and interquartile ranges (IQR). Baseline patient characteristics were compared using the chi-squared test for categorical variables. In the SEER analysis, we fit a multivariable logistic regression model to determine the association between insurance status and diagnosis of muscle-invasive bladder cancer. We then constructed a Fine and Gray competing risks regression model to assess the association between insurance status and bladder cancer-specific survival. Death from bladder cancer was the primary event of interest, and death from other causes was the competing event. In the NCDB analysis, multivariable logistic regression was used to assess outcomes of receipt of NAC, treatment delay > 90 days, and treatment at a high volume facility. We defined two-sided statistical significance as $p<0.05$. All analyses were performed using Stata v.14.0 (StataCorp, College Station, TX, USA). The Brigham and Women's Hospital institutional review board deemed this study exempt from formal review.

Results

Descriptive Characteristics: SEER Cohort

Overall, 29,525 patients were included in the SEER cohort. The median age was 58 (IQR: 52-61); the median survival time was 47 months (IQR: 23-72 months). The majority of patients had private insurance (83.6%), 10.6% had Medicaid insurance, and 5.7% were uninsured (Table 1). During the study period, 3,271 (11.1%) individuals died of bladder cancer; 1,498 (5.1%) died of other causes. Compared to those with private insurance, individuals with Medicaid or no insurance were more likely to be of black race, in the lowest income quartile, and diagnosed with higher cancer stages (T3/T4) as well as distant disease (N+/M+).

Diagnosis with Muscle-invasive Bladder Cancer: SEER Cohort

About one-fifth (20.9%) of patients were diagnosed with muscle-invasive bladder cancer (stage ≥ T2). On multivariable analysis, uninsured individuals were nearly twice as likely to receive a muscle-invasive bladder cancer diagnosis (OR: 1.90; 95% CI: 1.70 – 2.12; Table 2; Figure 2). Those with Medicaid insurance also had about twice the odds of being diagnosed with muscle-invasive bladder cancer (OR: 2.03; 95% CI: 1.87 – 2.20). Patient sociodemographic factors associated with higher odds of being diagnosed with muscle-invasive bladder cancer included black race (OR: 1.69; 95% CI: 1.53 – 1.86), female sex (OR: 1.16; 95% CI: 1.09 – 1.24), and being in the lowest income quartile (OR: 1.16; 95% CI: .04 – 1.29).

Survival Outcomes: SEER Cohort

During the study period, 11.1% of individuals died of bladder cancer and 5.1% died of other causes. The multivariable competing risk regression demonstrated that, compared to patients with private insurance, uninsured individuals were more likely to die of bladder cancer (adjusted hazard ratio [AHR]: 1.49; 95% CI: 1.31 – 1.71; Table 3). Medicaid patients were also more likely to die of bladder cancer compared to those with private insurance (AHR: 1.61; 95% CI: 1.46 – 1.79). Other factors associated with poorer bladder cancer-specific mortality included black race (AHR: 1.27; 95% CI: 1.13 – 1.43), female sex (AHR: 1.09; 95% CI: 1.01 – 1.19), and non-urothelial histology (AHR: 1.45; 95% CI: 1.30 – 1.62).

Care Delivery Outcomes: NCDB Cohort

The NCDB cohort contained 6,428 individuals with clinically localized muscle-invasive bladder cancer. Overall, 587 (9.1%) of these patients were uninsured and 886 (13.8%) were on Medicaid. Compared to those with private insurance, uninsured and Medicaid-insured individuals had a higher percentage of individuals who were black, at the lowest income quartile, and at the lowest education level (Table 3).

On multivariable analysis, uninsured individuals had significantly lower odds of receiving treatment in a high volume hospital compared to those with private insurance (OR: 0.66; 95% CI: 0.52 – 0.83; Table 4). There was no significant association between Medicaid insurance and treatment at a high volume hospital (OR: 0.86; 95% CI: 0.71 – 1.04). Other factors associated with treatment at a high volume hospital were younger age and longer distance between patient residence and treating hospital (Table 5). Uninsured individuals also had significantly higher odds of experiencing delays in any treatment >90 days (OR: 1.36; 95% CI: 1.12 – 1.65; Table 5); similar outcomes were seen in the Medicaid-insured (OR: 1.22; 95% CI: 1.03 – 1.44). Black patients also experienced higher odds of treatment delays (OR: 1.89; 95% CI: 1.54 – 2.33).

Those treated in high volume hospitals were significantly less likely to experience treatment delays.

After restricting the cohort to those who underwent radical cystectomy, there were 4,347 individuals in the cohort; 37.6% had received NAC. Multivariable logistic regression showed that Medicaid-insured patients had lower odds of receiving NAC (OR: 0.74; 95%CI: 0.60 – 0.91; Table 6). Uninsured individuals also had lower odds of receiving NAC, although this association was not statistically significant (OR: 0.79; 95% CI: 0.61 – 1.02; p=0.065). Receiving treatment in a high-volume facility was significantly associated with receipt of NAC (OR: 1.49; 95% CI: 1.21 – 1.83). Higher comorbidity burden and non-urothelial histology were associated with lower odds of receiving NAC.

Discussion

Using two national cancer registries, we found that individuals aged younger than 65 who were uninsured or on Medicaid insurance had higher odds of being diagnosed with muscle-invasive bladder cancer and were more likely to die of the disease compared to their private insured counterparts. Underinsurance also associated with treatment delays, failure to receive guideline-directed therapies, and provision of care in lower volume facilities. To our knowledge, this is the first study using national data to comprehensively assess the impact of underinsurance status on these outcomes in bladder cancer. Our findings have broad implications for the ongoing policy debate in the US regarding the provision of health insurance.

Although our findings confirmed our hypothesis that uninsured individuals would have worse outcomes than those with private insurance, it may appear surprising that those with Medicaid coverage had nearly identical outcomes to the uninsured. One possible explanation is that many Medicaid coverage plans may fail to meet their beneficiaries' needs for complex cancer care. While there is evidence that Medicaid increases overall health care access for low-income individuals,[17] state measures such as increased out-of-pocket costs and restrictions on specialist care may subdue the benefits of Medicaid coverage for a financially burdensome disease such as bladder cancer.[18] It has in fact been shown in other cost-intensive cancers (e.g. colorectal, head and neck) that Medicaid coverage, compared to private insurance, is associated with poorer long-term outcomes that are similar to those of the uninsured.[19-22] In addition, many of the previously documented insurance-based health disparities have been demonstrated in screening-detectable cancers (e.g. breast, prostate, colorectal).[23-26] Our analysis uniquely shows that this gap in care also exists in a cancer that is not commonly detected by screening. It will be crucial to keep these barriers in mind as the nationwide debate on Medicaid expansion continues.

There are many points in the bladder cancer care spectrum at which one who is uninsured or underinsured may fail to receive life-prolonging care. For example, insurance barriers can prevent timely specialty referrals and thereby lead to increased incidences of advanced cancer diagnoses.[27] This is consistent with our finding that uninsured and Medicaid-insured individuals were twice as likely to be diagnosed with muscle-invasive bladder cancer compared to those with private insurance. These patients likely face increased cost-based barriers to urology referral after initial presentation in the primary care setting as well as substantial financial burdens in undergoing expensive diagnostic evaluation for bladder cancer (i.e. cystoscopy and CT imaging). Uninsured individuals may face even greater difficulty in getting an adequate workup for bladder cancer if they are not well connected to a primary care physician to begin with. Navigating the complex US healthcare system can prove insurmountable for those without a guide in primary care. As we demonstrate in our study, the consequences of this failure to access care can be dire and ultimately increase the risk of mortality. This underscores the imperative need to improve access to both primary care as well as specialty referrals in the underinsured. Not only can accessible care improve general health maintenance, but it may also stem the development of lethal disease.

We demonstrated worse bladder cancer-specific survival for the underinsured even after controlling for stage at diagnosis. Even with prompt evaluation, the frequent cystoscopic surveillance, imaging with CT/MRI, and medical/surgical treatments required to manage a disease with such a high recurrence rate can be incredibly expensive for someone who is poorly insured.[28-30] Those who are less able to pay for the standard of care may be forced to delay their care, opt for less costly but unproven alternatives, or forego care altogether. This theory is supported by our finding that uninsured and Medicaid-insured individuals with muscle-invasive bladder cancer were more likely to experience a delay > 90 days between diagnosis and receipt of either surgery, chemotherapy, or radiation. The demonstration of this finding after controlling for disease at diagnosis is striking – uninsured and Medicaid-insured individuals who are able to receive timely diagnoses still face barriers to timely treatments. Such delays in treating this aggressive form of bladder cancer are strongly associated with a higher mortality risk.[13,14] While a likely contributor to this delay is the direct cost of treatment, there are many other indirect costs of undergoing treatment for bladder cancer that may preclude some of these individuals from receiving it. For example, restrictive networks that limit the number of available specialists (e.g. urologic oncologists, medical oncologists, and radiation oncologists) can lead to travel times that prove prohibitive for some patients. Indeed, the burden of excessive travel distance has been previously shown to impart worse outcomes such as lower likelihood of receiving necessary surgery for aggressive bladder cancer and increased mortality.[31-33] Inability to take time off from work is also a common barrier for patients with bladder cancer, who often have to make repeated visits to receive treatment or surveillance check-ups. The pressures of workplace absenteeism are known to impart a disproportionate burden upon the lower income individuals who constitute the majority of the underinsured. Our data suggest that improving insurance coverage can shorten this diagnosis-to-treatment interval and ultimately lead to improved survival outcomes for this population. This can be accomplished by targeting actionable factors such as providing travel assistance vouchers or enhancing multidisciplinary care coordination that limits the number of required repeated visits for surveillance, treatment, and follow-up clinic visits.

Receipt of high quality care for clinically localized muscle-invasive bladder cancer differed by insurance status in our study. The survival benefit conferred by treating this disease at a high-volume center has been extensively documented.[15,16] However, uninsured patients were much less likely to receive treatment at a high volume facility in our dataset. The poorer survival outcomes in this group may thus be partially explained by an inability to access centers of excellence for a high-risk surgery such as a radical cystectomy. Many of these centers, often large academic hospitals, have clientele that travel from across the world for treatment. However, those with limited financial assistance may face greater difficulty in reaching these facilities. Receipt of NAC prior to radical cystectomy is another quality metric supported by level I evidence and endorsed by national guidelines.[11,12] Although overall uptake of NAC at the national level has been suboptimal,[34] Medicaid-insured patients in our dataset had significantly lower odds of receiving NAC compared to those with private insurance. Ensuring that Medicare coverage plans are concordant with evidence-based best practices can help improve care quality for these individuals. This requires both raising awareness about the prevalence of substandard care with respect to provision of NAC as well as advocating for improved coverage for a therapy that, though expensive, has robust evidence for improving survival.

The poorer outcomes seen in the underinsured facing a costly cancer diagnosis may be attributable to the heavy concentration of care for this vulnerable population in safety net hospitals. These hospitals bear the majority of the responsibility for caring for the underinsured in the US, and they are challenged with high patient demand and decreasing funding.[35] Federal assistance for these hospitals through disproportionate-share hospital (DSH) payments was slated to decrease gradually, balanced by the projected rise in coverage expansion under the Affordable Care Act (ACA).[36,37] However, opposition to the ACA has prevented coverage expansion from meeting its projections – over one dozen states have declined to expand Medicaid, and the individual mandate to obtain health insurance has been effectively negated. Meanwhile, DSH payments are still facing billion-dollar budget cuts. This will translate to a surge in uncompensated care that will only put further strain on safety net hospitals, some of which may face closure and thereby transfer this burden to nearby hospital systems.[38] Not only will this exacerbate the poorer clinical outcomes for the underinsured seen in our study, but these patients will also encounter increasing financial toxicity – high out-of-pocket costs that prevent them from being able to afford food, housing, and bills.

We found evidence of care disparities extending beyond insurance status. Black patients were more likely than white patients to receive an advanced stage diagnosis and die of bladder cancer. The latter can be at least partially explained by our finding that Black individuals also faced greater delays in care after diagnosis. This is in line with a previous finding from our group of lower rates of definitive treatment among Black patients with aggressive bladder cancer.[39] Concentration of care for racial minorities among lower quality hospitals, patient preference, and implicit provider bias are all potential explanations for why black individuals are adversely affected by bladder cancer. Women also fared poorer than men with respect to diagnosis of muscle-invasive bladder cancer and bladder cancer-specific survival. Current evidence attributes this much of this disparity to higher rates of delayed diagnosis and misdiagnosis (i.e.

misattributing hematuria and/or irritative voiding symptoms to a urinary tract infection and delaying bladder cancer workup) as well as lower rates of definitive treatment.[40-43]

Our study has unique strengths compared to prior research. Nguyen et al and Niu et al found that being uninsured was associated with higher stage at diagnosis and poorer survival in bladder cancer, respectively.[6,44] However, these studies used single-state registries with limited generalizability to the entire US population; by contrast, SEER is nationally representative. Nevertheless, our study has limitations. Although SEER and NCDB provide information on primary insurance at diagnosis, individuals' insurance coverage may change over the course of their treatment. It is also possible that some individuals who were previously uninsured obtained insurance just prior to diagnosis. Additionally, these databases do not provide specific insurance policy details that influence the type of care available to a patient, such as copays or extent of coverage network. We were also unable to assess the impact of behavioral risk factors (e.g. smoking, exposure to industrial chemicals) that may be associated with insurance status, as these factors are not robustly collected in the databases. In a similar vein, we were not able to account for potential unmeasured confounders that may have impacted our outcomes. Lastly, we restricted our analyses to those aged 18-64 to optimize heterogeneity of insurance status; however, our results may not be generalizable to those aged 65 and older.

Conclusions and Future Directions

Compared to those with private insurance, underinsured individuals were more likely to be diagnosed with muscle-invasive bladder cancer and had higher risk of death from bladder cancer. These individuals also had lower odds of receiving high-quality care. Uninsured patients had higher odds of facing delays in care and lower odds of being treated at a high-volume facility. Medicaid-insured patients had higher odds of care delays and lower odds of receiving NAC prior to surgery. Expanding high-quality insurance coverage will be essential to mitigate the burden of bladder cancer on the US population.

This study provides a foundation upon which further research is needed to understand how to best mitigate insurance-based disparities in care. Complementation of national cancer registry data with institutional data will allow for a more granular look at potential contributors to poorer outcomes among the underinsured. For example, it is important to better understand how differences in exposure to modifiable risk factors – such as smoking or occupational chemical hazards – may contribute to poorer outcomes among the underinsured. Mixed-methods approaches that pair these quantitative analyses with qualitative assessments of barriers to care provision for the underinsured will also reveal critical information about more specific barriers to accessing care faced by this vulnerable population. All told, a multifaceted investigation strategy will be required to tackle this complex problem and improve healthcare equity for individuals afflicted by bladder cancer.

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Tables

Table 1: Descriptive characteristics of patients with bladder cancer in the Surveillance, Epidemiology, and End Results (SEER) database, 2007 to 2014.

	Private Ins.	**Medicaid**	**Uninsured**	**Total**	
Patients, n(%)	24690 (83.62)	3139 (10.63)	1696 (5.74)	29525 (100.0)	
Age at Dx					p<0.001
<35	448 (1.81)	79 (2.52)	35 (2.06)	562 (1.9)	
35-44	1296 (5.25)	233 (7.42)	115 (6.78)	1644 (5.57)	
45-54	6102 (24.71)	939 (29.91)	581 (34.26)	7622 (25.82)	
55-64	16844 (68.22)	1888 (60.15)	965 (56.9)	19697 (66.71)	
Sex					
Male	19,159 (77.60)	2,273 (72.41)	1,364 (80.42)	22,796 (77.21)	p<0.001
Female	5,531 (22.40)	866 (27.59)	332 (19.58)	6,729 (22.79)	
Year of Dx					
2007-2010	12645 (51.22)	1329 (42.34)	853 (50.29)	14827 (50.22)	p<0.001
2011-2014	12045 (48.78)	1810 (57.66)	843 (49.71)	14698 (49.78)	
Race					p<0.001
White	21705 (87.91)	2506 (79.83)	1393 (82.13)	25604 (12.26)	
Black	1525 (6.18)	421 (13.41)	208 (12.26)	2154 (7.3)	
Other/Unknown	1460 (5.91)	212 (6.75)	95 (5.6)	1767 (5.98)	
Income					p<0.001
Q4 highest	6551 (26.53)	441 (14.05)	295 (17.39)	7287 (24.68)	
Q3	6102 (24.71)	717 (22.84)	352 (20.75)	7171 (24.29)	
Q2	6053 (24.52)	952 (30.33)	420 (24.76)	7425 (25.15)	
Q1 lowest	5984 (24.24)	1029 (32.78)	629 (37.09)	7642 (25.88)	
Education					p<0.001
Q1 lowest	6415 (25.98)	517 (16.47)	340 (20.05)	7272 (24.63)	
Q2	6552 (26.54)	808 (25.74)	289 (17.04)	7649 (25.91)	

Q3	6035 (24.44)	653 (20.8)	444 (26.18)	7132 (24.16)	
Q4 highest	5688 (23.04)	1161 (36.99)	623 (36.73)	7472 (25.31)	
Region					p<0.001
Northwest	4497 (18.21)	372 (11.85)	309 (18.22)	5178 (17.54)	
Midwest	2817 (11.41)	261 (8.31)	131 (7.72)	3209 (10.87)	
South	5602 (22.69)	741 (23.61)	670 (39.5)	7013 (23.75)	
West	11774 (47.69)	1765 (56.23)	586 (34.55)	14125 (47.84)	
Histology					p<0.001
Urothelial	23593 (95.56)	2885 (91.91)	1567 (92.39)	28045 (94.99)	
Non-urothelial	1097 (4.44)	254 (8.09)	129 (7.61)	1480 (5.01)	
Clin T stage					p<0.001
Ta/Tis	14925 (60.45)	1450 (46.19)	803 (47.35)	17178 (58.18)	
T1	5132 (20.79)	662 (21.09)	384 (22.64)	6178 (20.92)	
T2	2719 (11.01)	555 (17.68)	276 (16.27)	3550 (12.02)	
T3	1134 (4.59)	217 (6.91)	113 (6.66)	1464 (4.96)	
T4	780 (3.16)	255 (8.12)	120 (7.08)	1155 (3.91)	
Clin N stage					p<0.001
N0	23475 (95.08)	2836 (90.35)	1541 (90.86)	27852 (94.33)	
N+	1215 (4.92)	303 (9.65)	155 (9.14)	1673 (5.67)	
Clin M stage					p<0.001
M0	24029 (97.32)	2893 (92.16)	1607 (94.75)	28529 (96.63)	
M1	661 (2.68)	246 (7.84)	89 (5.25)	996 (3.37)	

Table 2: Multivariable logistic regression model demonstrating factors associated with diagnosis with muscle-invasive bladder cancer, Surveillance, Epidemiology and End Results (SEER) database, 2007 to 2014

Variable	Odds Ratio	Std. Err.	z	P-value	[95% Conf. Interval]	
Insurance Status						
Private Insurance (Ref)	-	-	-	-	-	-
Medicaid	2.028031	0.086254	16.62	<0.001	1.86583	2.204332
Uninsured	1.902152	0.1074624	11.38	<0.001	1.702771	2.124878
Age	1.019899	0.002154	9.33	<0.001	1.015686	1.024129
Sex						
Male (Ref)	-	-	-	-	-	-
Female	1.159651	0.0392835	4.37	<0.001	1.085157	1.239259
Year of Diagnosis	1.007144	0.006403	1.12	0.263	0.9946726	1.019773
Race						
White (Ref)	-	-	-	-	-	-
Black	1.688052	0.0855847	10.33	<0.001	1.528374	1.864412
Other/Unknown	0.8008462	0.0530616	-3.35	0.001	0.703317	0.9118999
Education						
Q1 lowest (Ref)	-	-	-	-	-	-
Q2	0.997239	0.0429348	-0.06	0.949	0.916541	1.085042
Q3	1.02596	0.0478133	0.55	0.582	0.9363997	1.124085
Q4 high	0.9801208	0.0525562	-0.37	0.708	0.8823409	1.088737
Income						
Q4 highest (Ref)	-	-	-	-	-	-
Q3	1.082518	0.0477082	1.8	0.072	0.992936	1.180181
Q2	1.0555	0.0536194	1.06	0.288	0.9554707	1.166002
Q1 lowest	1.15966	0.061786	2.78	0.005	1.04467	1.287307
Region						
Northeast (Ref)	-	-	-	-	-	-

Midwest	1.110165	0.0670689	1.73	0.084	0.9861961	1.249716
South	9.80E-01	5.45E-02	-0.36	0.717	8.79E-01	1.092886
West	1.203801	0.0529132	4.22	<0.001	1.104435	1.312108

Table 3: Descriptive Characteristics for individuals with localized muscle-invasive bladder cancer in NCDB Cohort, 2007-2014.

Variables	**Private Insur.**	**Uninsured**	**Medicaid**	**Total**	**p-value**
Patients, n(%)	4,955 (77.08%)	587 (9.13%)	886 (13.78%)	6428 (100%)	
Age					<0.001
<35	26	3	12	41	
	0.52	0.51	1.35	0.64	
35-44	176	31	71	278	
	3.55	5.28	8.01	4.32	
45-54	1,283	219	282	1,784	
	25.89	37.31	31.83	27.75	
55-64	3,470	334	521	4,325	
	70.03	56.9	58.8	67.28	
Sex					<0.001
Male	3,779	439	636	4,854	
	76.27	74.79	71.78	75.51	
Female	1,176	148	250	1,574	
	23.73	25.21	28.22	24.49	
Race					<0.001
White	4,503	500	712	5,715	
	90.88	85.18	80.36	88.91	
Black	291	69	123	483	
	5.87	11.75	13.88	7.51	
Other/Unknown	161	18	51	230	
	3.25	3.07	5.76	3.58	
Year of Dx					<0.001
2007-2010	2,579	328	405	3,312	
	52.05	55.88	45.71	51.52	
2011-2014	2,376	259	481	3,116	
	47.95	44.12	54.29	48.48	
Income					<0.001
>$63,000	1,709	111	147	1,967	
	34.49	18.91	16.59	30.6	
$48-62,999	1,412	151	233	1,796	
	28.5	25.72	26.3	27.94	
$38-47,999	1,145	179	260	1,584	
	23.11	30.49	29.35	24.64	
<$38,000	632	140	242	1,014	

	12.75	23.85	27.31	15.77	
Unknown	57	6	4	67	
	1.15	1.02	0.45	1.04	
Education					<0.001
>21%	619	141	217	977	
	12.49	24.02	24.49	15.2	
13-20.9%	1,234	169	268	1,671	
	24.9	28.79	30.25	26	
7-12.9%	1,717	177	276	2,170	
	34.65	30.15	31.15	33.76	
<7%	1,330	94	121	1,545	
	26.84	16.01	13.66	24.04	
Unknown	55	6	4	65	
	1.11	1.02	0.45	1.01	
CCI					<0.001
0	3,889	477	650	5,016	
	78.49	81.26	73.36	78.03	
1	850	82	171	1,103	
	17.15	13.97	19.3	17.16	
2+	165	18	42	225	
	3.33	3.07	4.74	3.5	
Unknown	51	10	23	84	
	1.03	1.7	2.6	1.31	
Location					<0.001
Northeast	1,117	59	186	1,362	
	22.54	10.05	20.99	21.19	
South	1,564	306	248	2,118	
	31.56	52.13	27.99	32.95	
Midwest	1,435	128	242	1,805	
	28.96	21.81	27.31	28.08	
West	762	84	175	1,021	
	15.38	14.31	19.75	15.88	
Unknown	77	10	35	122	
	1.55	1.7	3.95	1.9	
Great Cir. Distance*					<0.001
First	2,096	289	427	2,812	
	42.3	49.23	48.19	43.75	
Second	1,759	199	284	2,242	
	35.5	33.9	32.05	34.88	
Third	1,047	93	172	1,312	

	21.13	15.84	19.41	20.41	
Unknown	53	6	3	62	
	1.07	1.02	0.34	0.96	
Histology					<0.001
Urothelial	4,265	504	707	5,476	
	86.07	85.86	79.8	85.19	
Non-urothelial	620	77	162	859	
	12.51	13.12	18.28	13.36	
Unknown	70	6	17	93	
	1.41	1.02	1.92	1.45	
cT-stage					<0.001
cT2	3,932	423	618	4,973	
	79.35	72.06	69.75	77.36	
cT3	574	71	136	781	
	11.58	12.1	15.35	12.15	
cT4	449	93	132	674	
	9.06	15.84	14.9	10.49	
Hospital Volume					<0.001
1st Quartile	1,246	157	265	1,668	
	25.15	26.75	29.91	25.95	
2nd Quartile	1,162	189	205	1,556	
	23.45	32.2	23.14	24.21	
3rd Quartile	1,198	164	235	1,597	
	24.18	27.94	26.52	24.84	
4th Quartile	1,349	77	181	1,607	
	27.23	13.12	20.43	25	

*Great circle distance reported in tertiles, calculated as distance in miles between the patient's residence and the hospital that reported the case. First = 0-12.4 miles. Second = 12.5-49.9 miles. Third= 50+ miles.

Table 4: Multivariable logistic regression predicting treatment at a high volume facility, National Cancer Database (NCDB), 2007-2014

	Odds Ratio	Std. Err.	z	P>z	[95% Conf.	Interval]
Insurance						
Private insurance (ref)						
Uninsured	0.6627418	0.0793782	-3.43	0.001	0.5240754	0.8380981
Medicaid	0.8600162	0.0812826	-1.6	0.111	0.7145904	1.035038
Age	0.9839368	0.0055301	-2.88	0.004	0.9731574	0.9948356
Year of Dx	1.024104	0.0138132	1.77	0.077	0.997385	1.051538
Sex						
Male (ref)						
Female	0.9438614	0.0682382	-0.8	0.424	0.8191605	1.087546
Race						
White (ref)						
Black	1.175697	0.1523835	1.25	0.212	0.9119478	1.515726
Other/Unknown	0.8333373	0.1442542	-1.05	0.292	0.5935732	1.16995
Income						
>$63,000 (ref)						
$48-62,999	0.6171916	0.0559915	-5.32	0	0.5166532	0.7372944
$38-47,999	0.4715759	0.0497188	-7.13	0	0.383538	0.5798222
<$38,000	0.5207794	0.0676542	-5.02	0	0.4037147	0.6717892
Unknown	2.69E-07	0.0002034	-0.02	0.984	0	.
Education						
>21% (ref)						
13-20.9%	1.027287	0.1094161	0.25	0.8	0.8337394	1.265765
7-12.9%	0.9044848	0.1040288	-0.87	0.383	0.7219396	1.133187
<7%	0.9337627	0.1243489	-0.51	0.607	0.719254	1.212246
Unknown	526778.2	3.98E+08	0.02	0.986	0	.

CCI						
0						
1	1.040011	0.085228	0.48	0.632	0.8856916	1.221218
2+	0.997285	0.1661155	-0.02	0.987	0.7195097	1.382299
Unknown	0.8823253	0.2524798	-0.44	0.662	0.5035645	1.545975
Location						
Northeast (ref)						
South	0.7258051	0.0647438	-3.59	0	0.6093832	0.8644693
Midwest	1.054476	0.0928137	0.6	0.547	0.8873905	1.253021
West	0.8126624	0.0824921	-2.04	0.041	0.6660487	0.9915494
Unknown	0.9225955	0.2342131	-0.32	0.751	0.560948	1.5174
Distance from hospital						
First (ref)						
Second	3.031564	0.2245159	14.98	0	2.621967	3.505147
Third	13.30862	1.140972	30.19	0	11.25014	15.74374
Unknown	11.66553	14.28654	2.01	0.045	1.057925	128.6335
Histology						
Urothelial (ref)						
Non-urothelial	1.017486	0.0923322	0.19	0.849	0.8516983	1.215545
Unknown	0.9991845	0.2642324	0	0.998	0.5950412	1.677816
cT stage						
cT2 (ref)						
cT3	0.974571	0.092046	-0.27	0.785	0.8098777	1.172756
cT4	0.8714163	0.0906824	-1.32	0.186	0.7106355	1.068574
_cons	1.07E-21	2.91E-20	-1.78	0.075	8.97E-45	128.2857

Table 5: Multivariable logistic regression predicting delay in care > 90 days, National Cancer Database (NCDB), 2007-2014.

	Odds Ratio	Std. Err.	z	P>z	[95% Conf.	Interval]
Insurance						
Private insurance (ref)						
Uninsured	1.364323	0.1344349	3.15	0.002	1.124717	1.654974
Medicaid	1.218642	0.1041083	2.31	0.021	1.030762	1.440769
Age	1.001989	0.0054244	0.37	0.714	0.9914141	1.012678
Year of Dx	0.9348057	0.0121976	-5.17	0	0.911202	0.9590208
Sex						
Male (ref)						
Female	0.8284908	0.0577493	-2.7	0.007	0.7226955	0.9497735
Race						
White (ref)						
Black	1.89345	0.2008805	6.02	0	1.537971	2.331095
Other/Unknown	1.104593	0.1676114	0.66	0.512	0.8204284	1.487181
Income						
>$63,000 (ref)						
$48-62,999	0.8021991	0.0706872	-2.5	0.012	0.6749585	0.9534266
$38-47,999	0.697474	0.0702664	-3.58	0	0.5724986	0.8497312
<$38,000	0.7809258	0.0944758	-2.04	0.041	0.6160728	0.9898913
Unknown	1.72E-06	0.001073	-0.02	0.983	0	.
Education						
>21% (ref)						
13-20.9%	0.8185713	0.0766936	-2.14	0.033	0.6812487	0.9835747
7-12.9%	0.6522981	0.0672197	-4.15	0	0.5330025	0.798294
<7%	0.5616987	0.0690169	-4.69	0	0.4414838	0.7146478
Unknown	126178.5	7.86E+07	0.02	0.985	0	.

CCI						
0 (ref)						
1	1.092695	0.0846409	1.14	0.252	0.9387815	1.271844
2+	1.233604	0.1897494	1.36	0.172	0.9125285	1.667651
Unknown	1.991736	0.4599238	2.98	0.003	1.266706	3.131756
Location						
Northeast (ref)						
South	0.8438645	0.0692266	-2.07	0.039	0.7185289	0.9910628
Midwest	0.5629306	0.0501871	-6.45	0	0.4726802	0.6704128
West	1.155832	0.1067699	1.57	0.117	0.9644174	1.385238
Unknown	0.8267542	0.2062179	-0.76	0.446	0.5070614	1.348007
Distance from hospital						
First (ref)						
Second	0.9525315	0.06487	-0.71	0.475	0.8335087	1.08855
Third	1.272885	0.1128396	2.72	0.006	1.06987	1.514422
Unknown	3.873821	4.664299	1.12	0.261	0.3658009	41.02365
Histology						
Urothelial (ref)						
Non-urothelial	1.183634	0.100842	1.98	0.048	1.001607	1.39874
Unknown	1.792953	0.3982008	2.63	0.009	1.160175	2.770856
cT stage						
cT2 (ref)						
cT3	0.745133	0.0703572	-3.12	0.002	0.6192434	0.8966154
cT4	0.9742924	0.0922185	-0.28	0.783	0.8093225	1.172889
Case volume						
1st quartile (ref)						
2nd quartile	0.8133718	0.0682142	-2.46	0.014	0.6900844	0.9586851
3rd quartile	0.6706375	0.0559286	-4.79	0	0.5695094	0.7897231
4th quartile	0.5108393	0.0461176	-7.44	0	0.4279956	0.6097182
_cons	5.79E+58	1.52E+60	5.16	0	2.75E+36	1.22E+81

Table 6: Multivariable logistic regression predicting receipt of neoadjuvant chemotherapy, National Cancer Database (NCDB), 2007-2014

	Odds Ratio	**Std. Err.**	**z**	**P>z**	**[95% Conf.**	**Interval]**
Insurance						
Private insurance (ref)						
Uninsured	0.7871681	0.1022186	-1.84	0.065	0.6102865	1.015316
Medicaid	0.7438304	0.0783896	-2.81	0.005	0.6050189	0.91449
Age	0.9853318	0.0061054	-2.38	0.017	0.9734377	0.9973711
Year of Dx	1.279126	0.0196506	16.02	0	1.241186	1.318226
Sex						
Male (ref)						
Female	1.039201	0.0816109	0.49	0.624	0.890949	1.212123
Race						
White (ref)						
Black	1.223881	0.1774265	1.39	0.163	0.921171	1.626066
Other/Unknown	0.890569	0.1735742	-0.59	0.552	0.6078077	1.304875
Income						
>$63,000 (ref)						
$48-62,999	0.7904076	0.0787053	-2.36	0.018	0.6502679	0.9607491
$38-47,999	0.8759107	0.1005029	-1.15	0.248	0.699507	1.0968
<$38,000	0.7486272	0.1085597	-2	0.046	0.5634189	0.9947176
Unknown	4.006319	5.719198	0.97	0.331	0.244128	65.74663
Education						
>21% (ref)						
13-20.9%	1.110392	0.1331298	0.87	0.382	0.8778535	1.404529
7-12.9%	1.158081	0.1487799	1.14	0.253	0.9002937	1.489682
<7%	1.099025	0.1634487	0.63	0.525	0.8211371	1.470956
Unknown	0.1673813	0.3136313	-0.95	0.34	0.0042537	6.586409
CCI						
0 (ref)						
1	0.7727197	0.0689495	-2.89	0.004	0.6487384	0.9203952
2+	0.5926347	0.115059	-2.69	0.007	0.4050679	0.8670545

Unknown	0.6370691	0.2254703	-1.27	0.203	0.3183691	1.2748
Location						
Northeast (ref)						
South	0.7116942	0.0693118	-3.49	0	0.5880239	0.8613742
Midwest	0.7458243	0.0713252	-3.07	0.002	0.6183492	0.8995789
West	0.5440565	0.0633761	-5.23	0	0.4330012	0.6835951
Unknown	0.7702877	0.2145169	-0.94	0.349	0.4462749	1.329546
Distance from hospital						
First (ref)						
Second	1.090742	0.0858128	1.1	0.27	0.9348776	1.272592
Third	1.055964	0.1065607	0.54	0.589	0.8664664	1.286905
Unknown	2.188933	2.694262	0.64	0.524	0.1961218	24.43089
Histology						
Urothelial (ref)						
Non-urothelial	0.459568	0.0506927	-7.05	0	0.3702184	0.5704816
Unknown	1.541599	0.5106035	1.31	0.191	0.8054513	2.950555
cT stage						
cT2 (ref)						
cT3	1.48999	0.1498416	3.97	0	1.223437	1.814616
cT4	1.649601	0.1985174	4.16	0	1.302996	2.088406
Case volume						
1st quartile (ref)						
2nd quartile	0.8428617	0.0910151	-1.58	0.113	0.6820885	1.04153
3rd quartile	0.9310311	0.0960914	-0.69	0.489	0.7605223	1.139768
4th quartile	1.489837	0.1553612	3.82	0	1.214437	1.82769
_cons	2.00E-215	6.10E-214	-16.01	0	1.00E-241	3.80E-189

Figures

Figure 1: Consort diagram depicting selection criteria for the Surveillance, Epidemiology and End Results (SEER) Cohort, 2007-2014

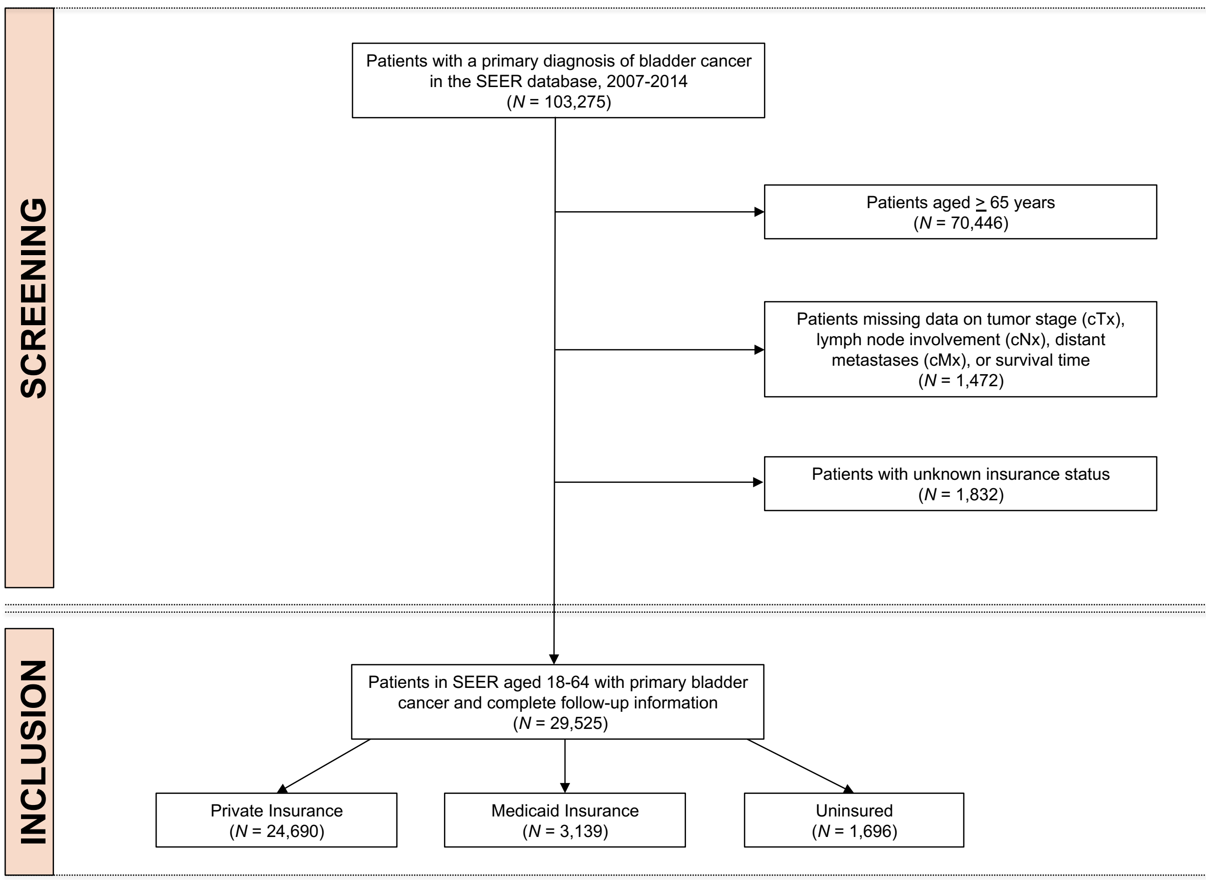

Figure 2: Forest plot depicting all study outcomes among individuals with private insurance, Medicaid insurance, and no insurance, 2007-2014.