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Patterns of Care for Medicare Beneficiaries With Metastatic Prostate Cancer

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Abstract

Introduction: Therapeutic options for men with metastatic prostate cancer have increased in the past decade. We studied recent treatment patterns for men with metastatic prostate cancer and how treatment patterns have changed over time.

Methods: Using the Surveillance, Epidemiology, and End Results–Medicare database, we identified fee-for-service Medicare beneficiaries who either were diagnosed with metastatic prostate cancer or developed metastases following diagnosis, as indicated by the presence of claims with diagnoses codes for metastatic disease, between 2007 and 2017. We evaluated treatment patterns using claims.

Results: We identified 29,800 men with metastatic disease, of whom 4721 (18.8%) had metastatic disease at their initial diagnosis. The mean age was 77 years, and 77.9% of patients were non-Hispanic White. The proportion receiving antineoplastic agents within 3 years of the index date increased over time (from 9.7% in 2007 to 25.9% in 2017; $P < .001$). Opioid use within 3 years of prostate cancer diagnosis was stable during 2007 to 2013 (around 73%) but decreased through 2017 to 65.5% ($P < .001$). Patients diagnosed during 2015 to 2017 had longer median survival (32.6 months) compared to those diagnosed during 2007 to 2010 (26.6 months; $P < .001$).

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Drafting the manuscript: Howard, Richards.

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Statistical analysis: Howard.

Supervision: Filson, Ekwueme, Richards.

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Ethics Statement: This study was deemed exempt from Institutional Review Board review.

Conclusions: Most metastatic prostate cancer patients do not receive life-prolonging antineoplastic therapies. Improved adoption of effective cancer therapies when appropriate may increase length and quality of survival among metastatic prostate cancer patients.

Keywords

prostate cancer; metastasis; physicians' practice patterns; antineoplastic therapy; SEER-Medicare

Before 2010, androgen deprivation therapy (ADT) monotherapy was the standard of care for men with metastatic prostate cancer.[1] Many men with metastatic prostate cancer eventually stopped responding to ADT, and docetaxel was the only treatment option for men with castrate-resistant disease.[2] Since 2010, the Food and Drug Administration has approved several new treatments for metastatic prostate cancer, including radium-223, sipuleucel-T, abiraterone, and enzalutamide. Although these drugs are effective, they are more expensive than ADT or docetaxel.[3]

Understanding the real-world treatment of patients with metastatic prostate cancer can inform opportunities to optimize care delivery and survivorship. In this analysis, we examine treatment patterns for metastatic prostate cancer, use of opioid medications, and shifts to hospice care among Medicare beneficiaries with Medicare Part D fee-for-service prescription drug insurance coverage.

Methods

Dataset

We measured patterns of care using the Surveillance, Epidemiology, and End Results (SEER)–Medicare database for 2007 to 2017. The SEER-Medicare dataset linked tumor registry records with Medicare claims through December 31, 2019, for fee-for-service beneficiaries diagnosed in 17 SEER catchment areas, representing about one-third of the US population.

Sample Identification

We identified men diagnosed with metastatic prostate cancer using the M component of the American Joint Committee on Cancer (AJCC) staging system (the sixth edition for men diagnosed in 2007–2009, the seventh edition for men diagnosed in 2010–2015, and the SEER combined version for men diagnosed in 2016–2017). We identified 2 mutually exclusive groups of metastatic disease. The first group contained beneficiaries who had prostate cancer with metastases at initial diagnosis (AJCC M1) based on SEER registry data. We defined the index date for patients with registry-diagnosed metastasis as the SEER registry date of initial diagnosis of prostate cancer.

The second group included beneficiaries who had a SEER registry initial diagnosis of prostate cancer without metastasis (AJCC M0) but who subsequently had Medicare claims for metastatic disease (Supplemental Table 1, https://www.urologypracticejournal.com). We hereafter refer to this second group as claims-diagnosed metastasis. We defined the index date for patients with claims-diagnosed metastasis as the date of the first Medicare claim

listing metastatic disease. To exclude claims for "rule-out" diagnoses, we required this group of patients to have 1 inpatient claim for metastatic disease or 2 outpatient claims more than 30 days apart.

Supplemental Table 2 (https://www.urologypracticejournal.com) lists our exclusion criteria. We excluded men whose inclusion in SEER was based on a death certificate or autopsy record, who did not have a valid diagnosis date or date of birth, did not have adenocarcinoma histology, were age 65 or younger, were not continuously enrolled in Medicare Parts A and B in the 12 months before the index date and the earliest of 24 months after the index or the date of death, and were not continuously enrolled in Medicare Part D during this same period.

Outcomes of Interest

We measured receipt of treatment using inpatient, outpatient, physician office, hospice, and Part D claims within 1 and 3 years following the index date. We used SEER data, diagnostic and procedural codes linked to claims, and pharmaceutical claims to identify the following treatments or service types: physician-administered parenteral and oral prescription antineoplastic drugs (docetaxel, enzalutamide, abiraterone, sipuleucel-T, cabazitaxel), physician-administered and prescription ADT, orchiectomy, radiotherapy, oral opioids, and hospice care. Patients with metastatic disease may undergo radiotherapy for palliative reasons. We identified prescription opioids in Medicare Part D claims using drugs' names based on a list of opioid medications.[4]

Statistical Analysis

In our main set of analyses, we report the receipt of treatments at 1 and 3 years following the index date. To simplify the presentation of results, we assigned patients to the following treatment groups: antineoplastic drugs + ADT + hospice, antineoplastic drugs + ADT, antineoplastic drugs + hospice, ADT only, hospice only, other/none. We developed these groups based on commonly occurring treatment combinations.

We used χ^2 tests to compare proportions of patients receiving each type of treatment between groups. We estimated the significance of trends in the receipt of antineoplastic drugs and prescription opioids using multivariable logistic regression models where the outcome was whether the patient received treatment vs no treatment. The primary independent variable of interest was a variable indicating the year of patients' index date. Other covariates of interest included age, race/ethnicity, dual enrollment in Medicaid, stage at diagnosis, and indicators for comorbidities in the year before diagnosis, based on the Chronic Condition Flags file provided with the SEER-Medicare data (acute myocardial infarction, Alzheimer's, atrial fibrillation, chronic obstructive pulmonary disease, congestive heart failure, diabetes, ischemic heart disease, depression, arthritis, stroke, anemia, lung cancer, and colorectal cancer). We measured survival from the index date to the date of death or the last follow-up. We calculated Kaplan-Meier survival curves by the period of the index date and assessed differences between periods using log-rank tests. We performed analyses in Stata version 17. This study was deemed exempt from human subjects review by the Emory University Institutional Review Board (Study 00001791). The National Cancer

Institute prohibits recipients of SEER-Medicare data from sharing them with third parties, and so we cannot share the data. The programs we used to analyze the data are available upon request.

Results

We identified a total of 29,800 patients with metastatic prostate cancer from 2007 to 2017 (Supplemental Table 2, https://www.urologypracticejournal.com). Nineteen percent (n = 4721) had registry-diagnosed metastasis (Supplemental Table 3, https://www.urologypracticejournal.com). Patients with registry-diagnosed metastasis were more likely to be dual eligible for Medicaid (26.7%) than patients initially diagnosed with nonmetastatic disease but who went on to develop metastases (19.7%).

Compared to patients initially diagnosed with nonmetastatic disease, patients with registry-diagnosed metastasis were more likely to receive ADT (86.7% vs 52.5%), antineoplastic therapy (38.1% vs 25.8%), or radical prostatectomy (4.2% vs 1.5%) within 3 years of the index date (Table; all $P < .001$). Note that the outcome/treatment groups displayed in the Table are not mutually exclusive. Use of opioids and radiotherapy was similar between the patients with registry-diagnosed metastasis and those initially diagnosed with nonmetastatic disease. Patients ages 66 to 74 years were generally more likely to undergo treatment and receive prescription opioids compared to patients age ≥75 years ($P < .001$). Patients age ≥75 years were more likely to die within 3 years of the development of metastases or enter hospice ($P < .001$). Non-Hispanic Black patients were less likely to receive antineoplastic drugs compared to non-Hispanic White patients (28.4% vs 22.5%; $P < .001$). Differences between non-Hispanic White patients and Hispanic, and non-Hispanic patients with other race or race unknown were small. Non-Hispanic Black patients were also more likely to die within 3 years compared to non-Hispanic White patients (65.7% vs 61.5%; $P < .001$). Hospice use was lower among non-Hispanic Black (34.9%), Hispanic (32.8%), and non-Hispanic other race/unknown race patients (25.5%) compared to non-Hispanic White patients (37.8%; $P < 01$).

Trends in specific treatment/service combinations are displayed in Figure 1, including findings for all patients (Figure 1, A) and those with registry-diagnosed metastasis (Figure 1, B and Supplemental Table 4, https://www.urologypracticejournal.com). ADT only was less common in more recent periods (all patients: 46.1% during 2007–2010 vs 36.2% during 2015–2018; $P < .001$). The proportion receiving the combination of antineoplastic agents and ADT (drug/ADT) increased from 6.8% in 2007 to 2010 to 19.7% in 2015 to 2018 ($P < .001$). The proportion of patients who received hospice care only did not change significantly (7.7% during 2007–2010, 8.1% during 2015–2018; $P = .09$). Many more patients received hospice following receipt of other treatments, such as ADT, as shown in the Table.

The use of antineoplastic therapy among all metastatic prostate cancer patients increased over time, both at 1 year and 3 years of follow-up from the index date (Figure 2 and Supplemental Table 5, https://www.urologypracticejournal.com). In 2007, 15.5% of patients in the cohort received antineoplastic therapy at some point within 3 years of diagnosis. The

proportion increased to 33.4% by 2017 ($P < .001$). Receipt of prescription opioids at some point in the 3-year period following the index date (Figure 3) remained relatively stable from 2007 through 2013. After 2013, opioid use decreased from 73.4% in 2013 to 63.5% in 2017 ($P < .001$).

Figure 4 displays the Kaplan-Meier curves for overall survival for all patients by the period of diagnosis. For 3 years of follow-up, median survival was 26.5 months for patients with an index date from 2007 to 2010, 27.5 months for patients with an index date from 2011 to 2014, and 32.6 months for patients with an index date from 2015 to 2017 ($P < .001$ based on a log-rank test).

Discussion

This analysis of patterns of care among Medicare beneficiaries with metastatic prostate cancer has several key findings. First, the use of antineoplastic therapy has increased rapidly over the last decade. In 2017, 33.4% of the cohort used these therapies within 3 years of diagnosis compared to only 15.5% in 2007. Second, overall survival has improved, coinciding with the adoption of antineoplastic therapy. Third, there has been a decrease in the use of prescription opioids, particularly after 2013. Finally, the proportion of patients using hospice has not changed markedly.

For prostate cancer patients diagnosed in the past decade, there has been a rapid expansion of options for systemic therapy. Developments include new antineoplastic agents for use in the second-line setting after the development of castration resistance and, more recently, as up-front therapy for treatment-naïve patients with advanced prostate cancer. As expected, we observed a consistent increase in the uptake of antineoplastic therapy among our sample of Medicare beneficiaries with metastatic prostate cancer. However, use within 3 years of the development of metastases has plateaued at around 30% starting in 2014. There may be additional opportunities to improve survival through increased adoption of antineoplastic therapies. An analysis of the Flatiron Health Database found that over 70% of patients with metastatic castration-resistant prostate cancer diagnosed between 2013 and 2017 received antineoplastic therapy.[5] Our data do not allow us to distinguish castration-sensitive vs castration-resistant disease. Aside from differences in disease progression, we believe that the difference between our results and theirs is due to either (1) mortality in our sample among patients prior to progression to castration-resistant disease or (2) the nonrepresentativeness of the Flatiron database, which samples from oncology practices.

There are many possible reasons why patients with metastatic cancer may forgo antineoplastic therapy. Lack of access to a medical oncologist may be a barrier to treatment.[6,7] Though a growing proportion of urologists prescribed antineoplastic therapy during 2013 to 2017, nearly 90% of providers who prescribed abiraterone and enzalutamide in 2013 were medical oncologists, and half of the prescriptions were limited to one-fifth of the prescribing medical oncologists.[6,7] Some patients may not be able to afford these drugs, which can cost thousands of dollars per month.[8] A recent study reports that 30% of Medicare beneficiaries with Part D coverage, especially those without additional coverage for out-of-pocket costs, did not initiate a prescription for anticancer drugs.[9] Efforts to

mitigate cost barriers could include financial assistance and dose reductions that maintain efficacy.[9,10] Black men were less likely to receive antineoplastic drugs, possibly because of the cost. Black men also experienced higher mortality rates. It is unclear if the greater use of antineoplastic drugs would have increased survival among Black men. Alternatively, men who die with castration-sensitive disease, possibly due to unrelated causes, will be less likely to receive therapy initially approved for men with castration-resistant disease.

During the 2012 to 2014 time period, results of studies were reported on abiraterone and enzalutamide for patients with castration-resistant prostate cancer.[11–13] The final survival analysis results from the phase 3 TITAN study were published in 2021 and showed that apalutamide plus ADT improved overall survival and delayed castration resistance in patients with metastatic castration-sensitive prostate cancer.[14] Other trials have also documented the benefits of antineoplastic drugs in patients with castration-sensitive disease.[15] The Food and Drug Administration approved abiraterone for men with metastatic, castration-sensitive disease in early 2018,[16] and so our results do not fully capture the use of abiraterone and other antineoplastic drugs among men with castration-sensitive disease.

In this analysis, the increased use of antineoplastic therapy among metastatic prostate cancer patients was associated with a decrease in the use of prescription opioid medications after 2013, with a steeper drop-off after 2016. One possible explanation for these trends would be the palliation of pain through the antineoplastic therapeutic effect, demonstrated in clinical trials examining the efficacy of medications like abiraterone.[17] However, opioid prescriptions among all Medicare beneficiaries were largely stable through 2012[18] but decreased from 2013 to 2018.[19] The trend after 2012 was likely related to greater recognition and publicity surrounding the addictive properties of long-acting opioid therapy.[19] However, this wariness may have had unintended consequences in limiting pain control for cancer patients who needed it. The most significant decreases in opioid prescribing were among patients who self-reported higher pain levels.[20]

We did not observe any marked change in the use of hospice care among our cohort of advanced prostate cancer patients. The stability theoretically could be related to improved cancer-specific outcomes, delaying a need for hospice for some patients, and countered by increased uptake of hospice care over time among those who need it. Our measurements of care receipt in the first few years after onset may be insufficient to capture hospice use among a patient population with median survival approaching 3 years. When hospice care permits death at home, families perceive the quality of death as superior to death at a hospital.[21] We observed that compared to non-Hispanic White patients and non-Hispanic Black patients, patients from some racial and ethnic minority groups were less likely to use hospice care and antineoplastic drugsd—similar to what has been reported elsewhere.[22,23]

Our cohort included only Medicare beneficiaries with fee-for-service coverage. The study may not reflect patterns among men aged < 66 years at diagnosis, men in managed care plans, or privately insured or underinsured individuals in the US. Our claims-based definition for metastases may result in some patients inaccurately designated as having a metastatic disease (ie, a “rule out” diagnosis or accidental medical record carryover from

prior visits). Claims-based ascertainment of metastatic disease typically undercounts patients with metastatic disease.[24]

The claims-based definition of metastatic cancer among cases initially diagnosed as M0 does not permit an assessment of the burden of disease, which may be smaller than that typically seen among cases diagnosed as M1 metastatic cancer, or perhaps be associated with a slow PSA doubling time; both can impact decision-making related to the intensity of treatment received. These factors may partially explain the differences in treatment patterns and outcomes between men with metastatic disease at initial diagnosis vs those with a delayed development of metastatic disease. SEER-Medicare does not capture treatment provided by Veterans Administration facilities or self-pay care.

Conclusions

Our analysis highlights that recently approved antineoplastic medications are used more frequently among Medicare beneficiaries with metastatic prostate cancer. However, room remains to improve care delivery for patients with metastatic prostate cancer. Examples include improving uptake of medications like abiraterone and enzalutamide for those eligible, ensuring opioid therapy is offered and used for those in severe pain where appropriate, and minimizing disparities in receiving hospice care at the end of life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosure:

The findings and conclusions in this report are those of the authors. They do not necessarily represent the official position of the Centers for Disease Control and Prevention.

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

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Data Availability:

The datasets generated during and/or analyzed during the current study are available in from the National Cancer Institute, https://healthcaredelivery.cancer.gov/seermedicare/.

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Study Need and Importance:

Treatment options for men with metastatic prostate cancer have expanded with the introduction of new treatments, including radium-223, sipuleucel-T, abiraterone, and enzalutamide. Although these drugs are effective, they are more expensive than androgen deprivation therapy or docetaxel. Understanding the real-world treatment of patients with metastatic prostate cancer can inform opportunities to optimize care delivery and survivorship. We sought to describe the treatment of Medicare beneficiaries with metastatic prostate cancer using data from the Surveillance, Epidemiology, and End ResultseMedicare database for 2007 to 2017. The database links tumor registry records to Medicare claims for fee-for-service Medicare beneficiaries. We identified men with metastatic disease based on registry records and, separately, diagnosis codes for metastatic disease.

What We Found:

In our sample of 29,800 patients, we found that the share receiving androgen deprivation therapy only within 3 years of developing metastatic disease decreased (46.1% in 2007–2010 vs 36.2% in 2015–2018; Figure). The proportion receiving antineoplastic agents and ADT increased from 6.8% in 2007–2010 to 19.7% in 2015–2018 and was 33.4% among beneficiaries who developed metastatic prostate cancer in 2017. The proportion of patients who received hospice care only did not change significantly (7.7% during 2007–2010, 8.1% during 2015–2018). Opioid use within 3 years of prostate cancer diagnosis was stable during 2007 to 2013 (around 73%) but decreased through 2017 to 65.5% (not shown). Survival time increased: median survival was 26.5 months for patients with an index date from 2007 to 2010, 27.5 months for patients with an index date from 2011 to 2014, and 32.6 months for patients with an index date from 2015 to 2017.

Limitations:

Our sample may not reflect patterns of care among Medicare beneficiaries in managed care plans or those younger than age 65. Our claims-based definition for metastases may misclassify patients.

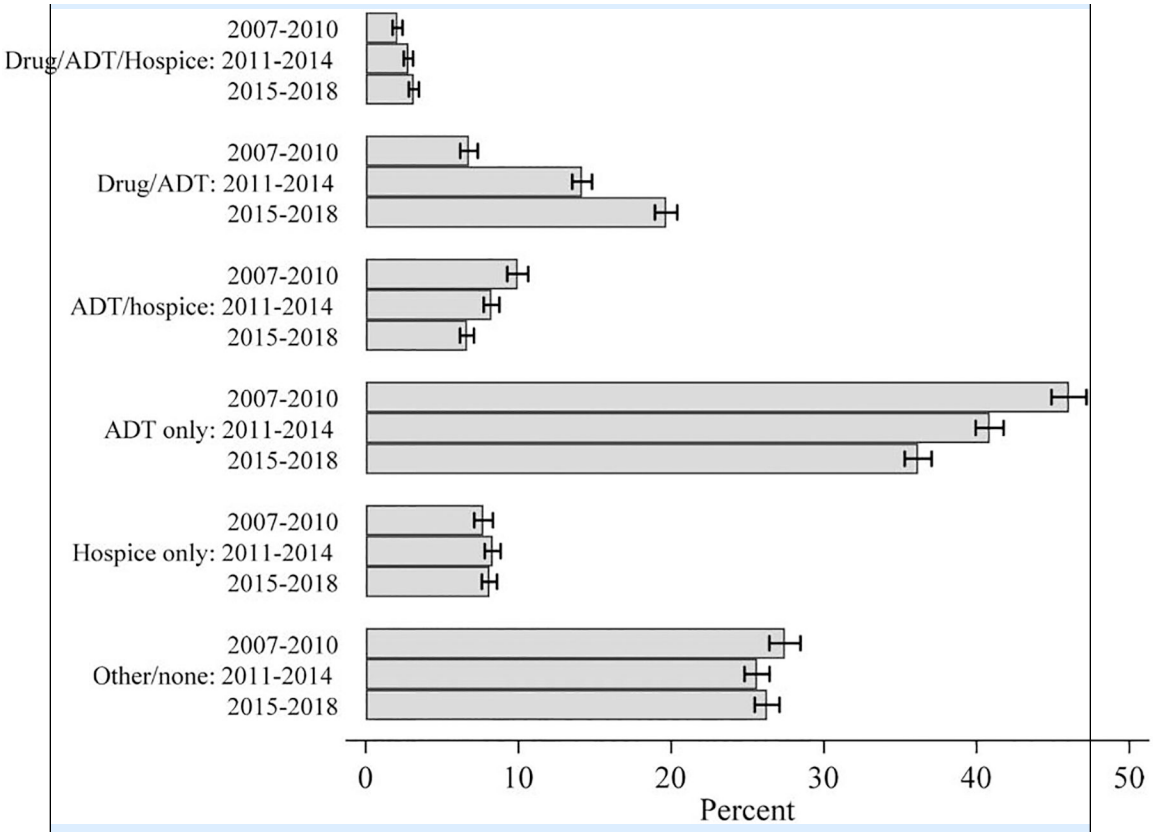

Figure.

Treatment and service combinations within 3 years of the index date for metastatic prostate cancer patients, initial cancer diagnosis 2007 to 2017, linked to Medicare claims through 2019. ADT/hospice indicates received ADT and transferred to hospice; ADT only, androgen deprivation therapy monotherapy; Drug/ADT, received ADT and antineoplastic agent; Drug/ADT/Hospice, transferred to hospice after receiving ADT and antineoplastic agent; Hospice only, transferred to hospice care without other therapy.

Interpretation for Patient Care:

While use of approved antineoplastic medications has increased, there is room to improve care delivery for patients with metastatic prostate cancer. Examples include improving uptake of medications like abiraterone and enzalutamide for those eligible, ensuring opioid therapy is offered and used for those in severe pain where appropriate, and minimizing disparities in receiving hospice care at the end of life.

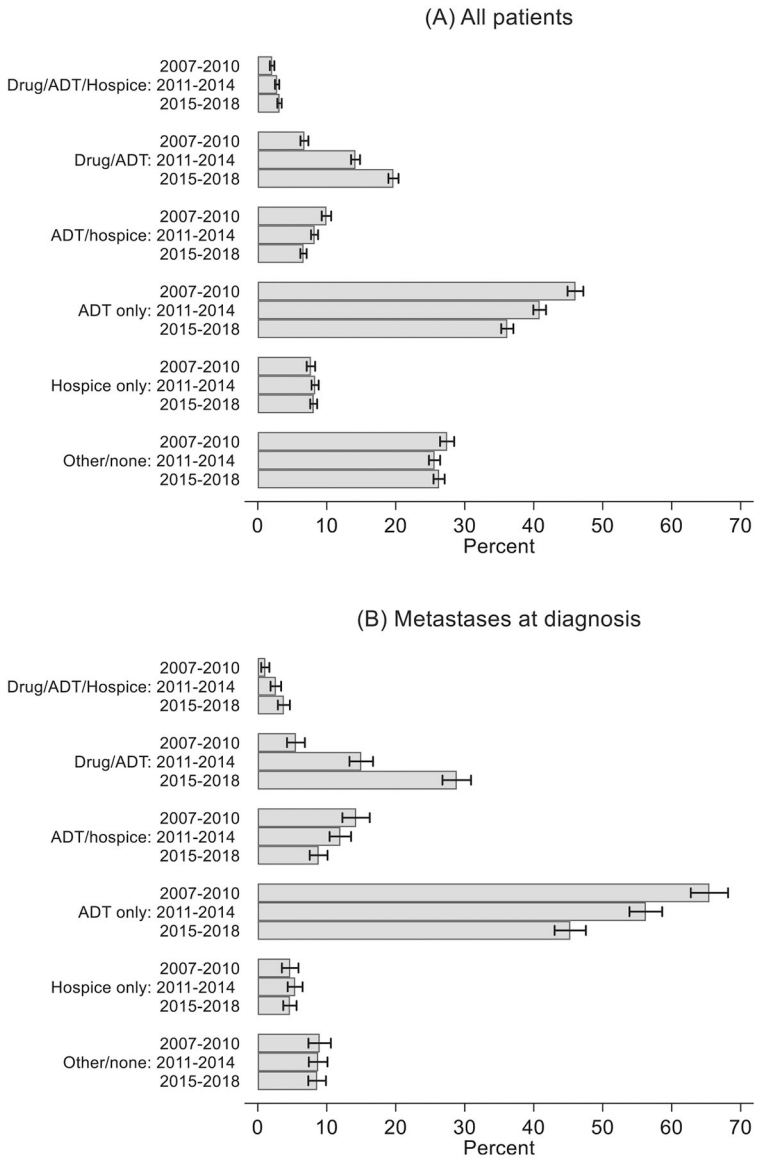

Figure 1.

Treatment and service combinations within 3 years of the index date for metastatic prostate cancer patients, initial cancer diagnosis 2007 to 2017, linked to Medicare claims through 2019. ADT/hospice indicates received ADT and transferred to hospice; ADT only, androgen deprivation therapy monotherapy; Drug/ADT, received ADT and antineoplastic agent; Drug/ADT/Hospice, transferred to hospice after receiving ADT and antineoplastic agent; Hospice only, transferred to hospice care without other therapy.

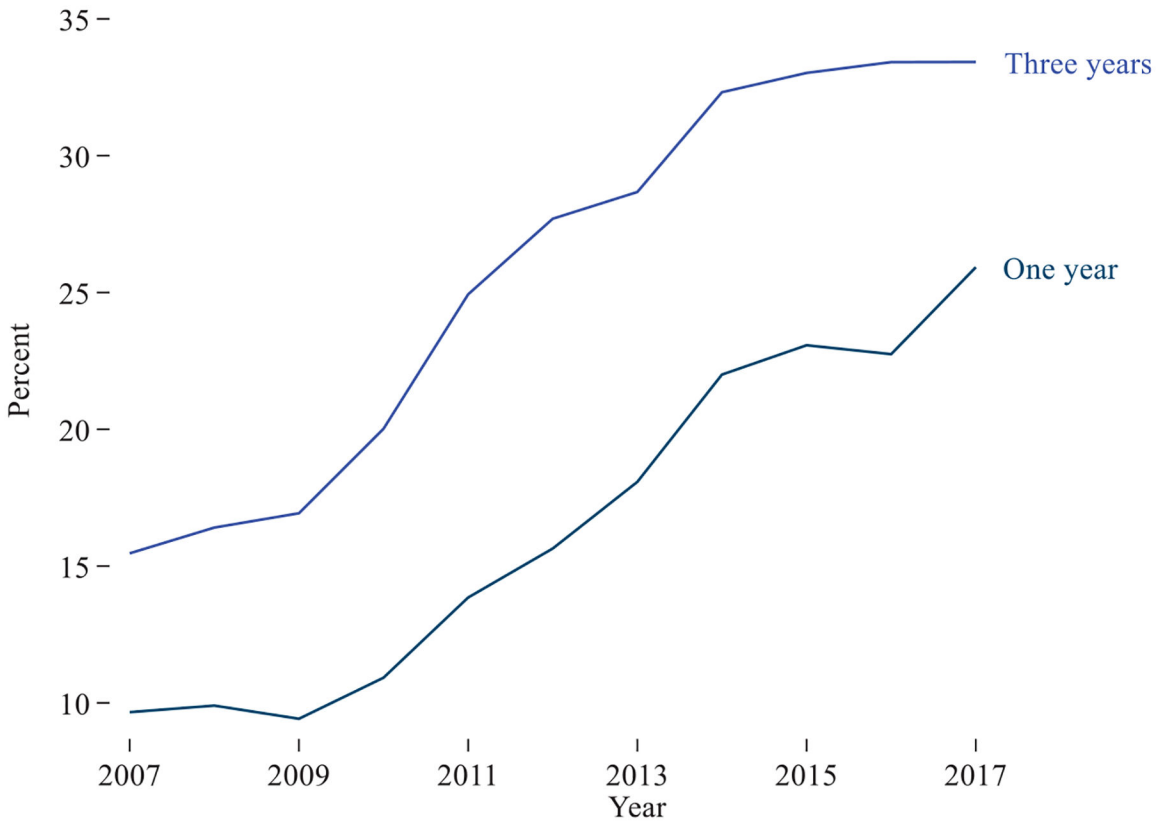

Figure 2.

Receipt of antineoplastic drugs following the index date for metastatic prostate cancer cases, initial cancer diagnosis 2007 to 2017, linked to Medicare claims through 2019. The index date is the date of diagnosis for patients with registry-diagnosed metastasis and the date of the first Medicare claim listing a diagnosis code for metastatic disease for patients initially diagnosed with nonmetastatic disease. “One year” and “three years” refer to the time period after index date.

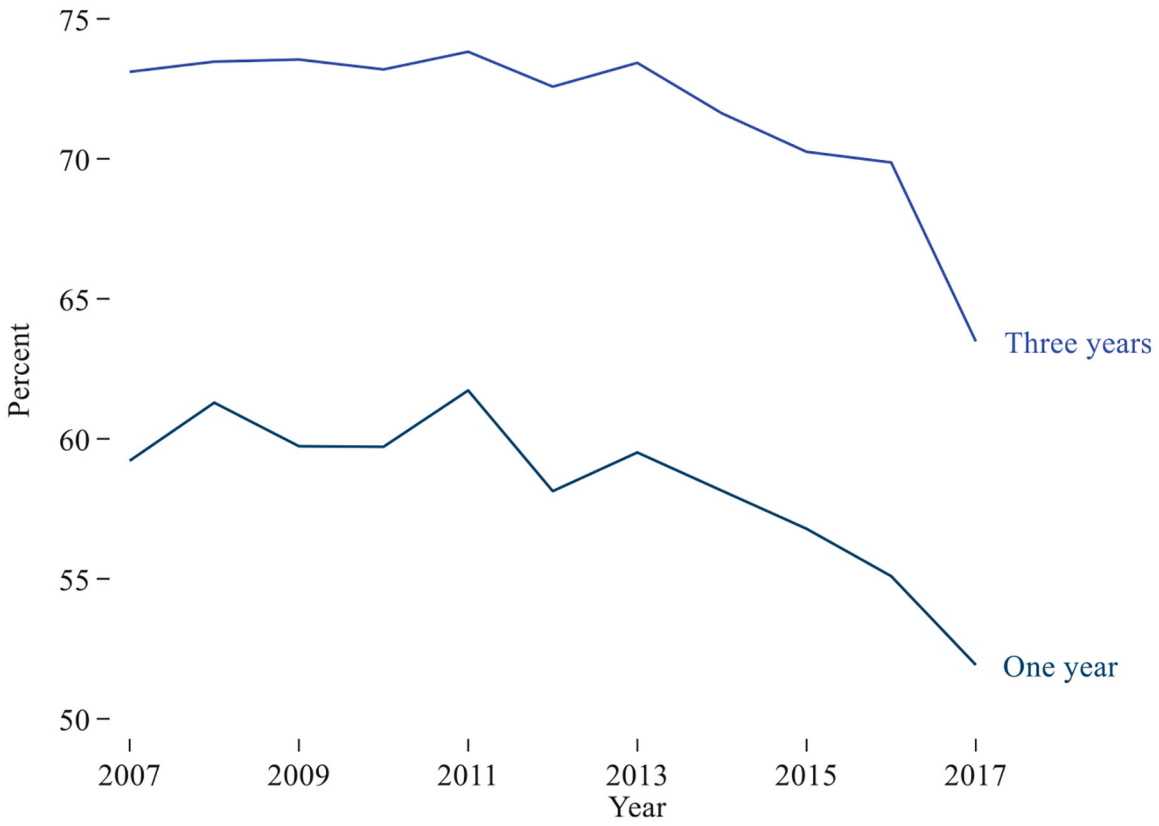

Figure 3.

Receipt of opioid prescriptions following the index date for metastatic prostate cancer cases, initial cancer diagnosis 2007 to 2017, linked to Medicare claims through 2019. The index date is the date of diagnosis for patients with registry-diagnosed metastasis and the date of the first Medicare claim listing a diagnosis code for metastatic disease following a Surveillance, Epidemiology, and End Results registry diagnosis of prostate cancer stage M0. “One year” and “three years” refer to the time period after index date.

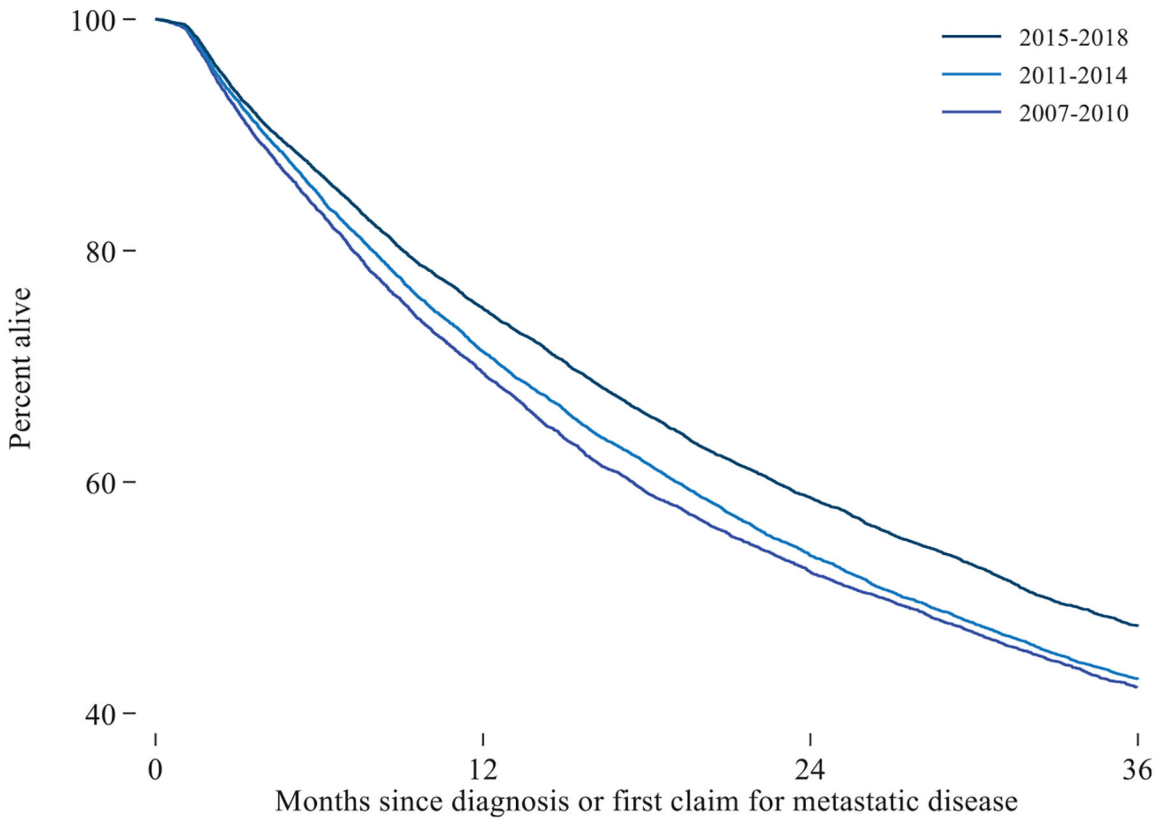

Figure 4.

Percent survival among metastatic prostate cancer patients by study period, initial cancer diagnosis 2007 to 2017, linked with Medicare claims through 2019. The graph shows Kaplan-Meier survival curves from the index date. The index date is the date of diagnosis for patients with registry-diagnosed metastasis (M1), and the date of the first Medicare claim listing a diagnosis code for metastatic disease following a Surveillance, Epidemiology, and End Results registry diagnosis of prostate cancer stage M0.

Table.

Outcome and Treatment Among Medicare Beneficiaries With Metastatic Prostate Cancer

	Metastases at diagnosis, No. (%)		By age (y), No. (%)		By race/ethnicity, No. (%)			
	No	Yes	66–74	75+	Non-Hispanic White	Non-Hispanic Black	Hispanic	Non-Hispanic, all other races, or unknown
Dead	15,152 (60.4)	3196 (67.7)	6565 (52.7)	11,783 (67.9)	14,268 (61.5)	1981 (65.7)	1156 (60.8)	943 (56.6)
ADT	13,159 (52.5)	4091 (86.7)	7046 (56.6)	10,204 (58.8)	13,271 (57.2)	1732 (57.5)	1201 (63.2)	1046 (62.7)
Antineoplastic drugs	6464 (25.8)	1800 (38.1)	3776 (30.3)	4488 (25.9)	6602 (28.4)	678 (22.5)	529 (27.8)	455 (27.3)
Prescription opioids	17,723 (70.7)	3444 (73.0)	9400 (75.5)	11,767 (67.8)	16,631 (71.6)	2073 (68.8)	1385 (72.9)	1078 (64.7)
Radiotherapy	10,416 (41.5)	1784 (37.8)	5812 (46.7)	6388 (36.8)	9826 (42.3)	994 (33.0)	712 (37.5)	668 (40.1)
Prostatectomy	1065 (4.2)	71 (1.5)	827 (6.6)	309 (1.8)	937 (4.0)	46 (1.5)	66 (3.5)	87 (5.2)
Hospice	8957 (35.7)	1934 (41.0)	3648 (29.3)	7243 (41.7)	8787 (37.8)	1052 (34.9)	623 (32.8)	429 (25.7)
Totals	25,079	4721	12,446	17,354	23,218	3014	1901	1667

Abbreviations: ADT, androgen deprivation therapy.

Outcome and treatment data for Medicare beneficiaries within 3 years of the index date for claims-diagnosed metastasis and registry-diagnosed metastasis, and totals for all categories of metastases by age at diagnosis and race/ethnicity, initial cancer diagnosis 2007 to 2017, linked to Medicare claims through 2019. Outcomes/treatments are not mutually exclusive. For example, a patient may have received ADT and antineoplastic drugs.

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