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### The cost burden of metastatic prostate cancer in the US populations covered by employer-sponsored health insurance

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#### Abstract

**Background:** Recent advancements in the clinical management of metastatic prostate cancer include several costly therapies and diagnostic tests. The objective of this study was to provide updated information on the cost to payers attributable to metastatic prostate cancer among men aged 18 to 64 years with employer-sponsored health plans and men aged 18 years or older covered by employer-sponsored Medicare supplement insurance.

**Methods:** By using Merative MarketScan commercial and Medicare supplemental data for 2009–2019, the authors calculated differences in spending between men with metastatic prostate

SUPPORTING INFORMATION

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Michal Horný: Conceptualization, data curation, formal analysis, and funding acquisition. K. Robin Yabroff: Conceptualization, funding acquisition, investigation, methodology, supervision, validation, and writing-review and editing. Christopher P. Filson: Supervision, validation, and writing-review and editing. Thomas B. Richards: Validation, and writing-review and editing. Donatus U. Ekwueme: Validation. Thomas B. Richards: Validation, and writing-review and editing. David H. Howard: Conceptualization, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, and writing-review and editing.

CONFLICT OF INTEREST STATEMENT

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Additional supporting information can be found online in the Supporting Information section at the end of this article.

cancer and their matched, prostate cancer-free controls, adjusting for age, enrollment length, comorbidities, and inflation to 2019 US dollars.

**Results:** The authors compared 9011 patients who had metastatic prostate cancer and were covered by commercial insurance plans with a group of 44,934 matched controls and also compared 17,899 patients who had metastatic prostate cancer and were covered by employer-sponsored Medicare supplement plans with a group of 87,884 matched controls. The mean age of patients with metastatic prostate cancer was 58.5 years in the commercial samples and 77.8 years in the Medicare supplement samples. Annual spending attributable to metastatic prostate cancer was \$55,949 per person-year (95% confidence interval [CI], \$54,074–\$57,825 per person-year) in the commercial population and \$43,682 per person-year (95% CI, \$42,022–\$45,342 per person-year) in the population covered by Medicare supplement plans, both in 2019 US dollars.

**Conclusions:** The cost burden attributable to metastatic prostate cancer exceeds \$55,000 per person-year among men with employer-sponsored health insurance and \$43,000 among those covered by employer-sponsored Medicare supplement plans. These estimates can improve the precision of value assessments of clinical and policy approaches to the prevention, screening, and treatment of prostate cancer in the United States.

#### **Keywords**

cost of illness; health care costs; insurance; Medigap; neoplasm metastasis; prostatic neoplasms

#### INTRODUCTION

Prostate cancer is the most commonly diagnosed invasive cancer and the second leading cause of cancer-related deaths among men in the United States.<sup>1</sup> Although most prostate cancers diagnosed in the United States are slow-growing and not typically lethal, the incidence of metastatic prostate cancer has been increasing since approximately 2010.<sup>2</sup> The National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) age-adjusted observed incidence rates for metastatic prostate cancer increased from 7.0 per 100,000 in 2010 (95% confidence interval [CI], 6.8–7.2 per 100,000) to 10.0 per 100,000 in 2019 (95% CI, 9.8–10.3 per 100,000), representing an average annual percent increase of 4.1% (95% CI, 3.1%–5.2%).<sup>2</sup>

During that period, the US Food and Drug Administration has approved several new therapies (e.g., abiraterone, apalutamide, cabazitaxel, enzalutamide, and sipuleucel-T) and diagnostic imaging tests (e.g., 18F-fluciclovine positron emission tomography) for both castration-resistant and treatment-naive metastatic prostate cancers.<sup>3</sup> The newly approved medications—with a monthly retail price exceeding \$12,000—are costly and thus have significant economic implications for patients and payers.<sup>4–7</sup>

Given the increased incidence of metastatic prostate cancer in the United States in recent years and the simultaneous introduction of costly therapies, it is essential to understand the cost burden of metastatic prostate cancer in light of these changes. Cost burden estimates are commonly used as inputs in model-based cost-effectiveness analyses assessing the value

Although prostate cancer incidence increases with age—and thus is more common in older men—about two in five prostate cancers are diagnosed in men younger than 65 years.<sup>1</sup> The steepest growth of metastatic prostate cancer incidence has been projected in men aged 45–55 years.<sup>8,9</sup> This demographic is most commonly covered by employer-sponsored insurance.<sup>10</sup> Employer-sponsored health plans typically pay health care prices that are approximately twice as high as Medicare fees.<sup>11–13</sup> The objective of the current study was to provide updated information on the cost attributable to metastatic prostate cancer among (1) men aged 18–64 years with employer-sponsored health plans and (2) men aged 18 years or older covered by employer-sponsored Medicare supplement insurance.

#### MATERIALS AND METHODS

This retrospective, observational study was approved by the Emory University Institutional Review Board (No. STUDY00001791). We constructed the analytic sample using administrative records from the Merative MarketScan commercial database and the Medicare supplemental database for the years 2009–2019.<sup>14</sup> The two databases contain comprehensive records on health insurance enrollment, the use of and spending for inpatient and outpatient health care services, and outpatient prescription drugs. The Commercial database includes information on individuals aged birth to 64 years covered by employer-sponsored health insurance plans; the Medicare supplemental database includes information on people enrolled in traditional Medicare who are also enrolled in employer-sponsored Medigap plans.<sup>14</sup> For the latter group—although Medicare is the primary payer—the MarketScan data include health care payments by both Medicare and employer-sponsored Medicare supplement plans. Because the two databases draw from considerably different populations, we conducted a separate analysis for each population.

We constructed the sample of cases—patients diagnosed with metastatic prostate cancer—as follows: First, we identified patients aged 18 years or older with prostate cancer using the diagnosis-based condition algorithm from the Centers for Medicare & Medicaid Services Chronic Conditions Data Warehouse, revised 02/2021 (see Table S1).<sup>15</sup> MarketScan does not include cancer stage data from cancer registries. Among patients with prostate cancer, we classified metastatic prostate cancer in patients with at least one inpatient, one skilled nursing facility, or two hospital outpatient claims associated with the International Classification of Diseases, 9th edition, diagnosis codes 196.0–199.1 or the International Classification of Diseases, 10th edition, diagnosis codes C77.0-C80.1, billed on or after the first indication of prostate cancer diagnosis (see Table S2).<sup>16</sup> We excluded patients with fewer than 365 days of continuous enrollment before the first indication of metastatic disease to ensure that the analytic sample contained only newly diagnosed cases. We defined the index year as the year the patient was diagnosed with metastatic prostate cancer. Finally, we identified two subcategories of metastatic disease: (1) men with a diagnosis code for metastatic disease within 7 days of the first claim with a diagnosis code for prostate cancer; and (2) men with a diagnosis code for metastatic disease greater than 7 days after the first claim with a diagnosis code for prostate cancer. Table S3 shows a flowchart of the study

sample construction. We imputed missing values for state and Metropolitan Statistical Area (MSA) of enrollees' residence with hot-deck imputation (see Table S4).

From a pool of prostate cancer-free men with an overlapping health plan enrollment, we matched up to five controls to each case on age (capped at 90 years), the geographic area based on the MSA or the statewide non-MSA where the enrollee resided, and enrollment in prescription drug coverage. Controls were assigned the same index year as their corresponding case. We excluded cases with no matched controls (n = 9 [0.10%] of the commercial sample; n = 165 [0.91%] of the Medicare supplement sample; see Table S5).

We measured health care spending at the person-year level, starting with the index year until loss to follow-up measured by plan enrollment dates. Patients with metastatic prostate cancer and controls were censored at the date of disenrollment. The spending measure aggregated payments for all adjudicated health care claims paid by health plans or patients through cost-sharing mechanisms (i.e., deductible, coinsurance, copayment). To gain insight into drivers of spending, we stratified the analysis by spending type (physician services, inpatient facility services, outpatient facility services, and prescription drugs). We also calculated spending specifically for antineoplastic drugs and opioids. We identified antineoplastic drugs in the claims data using the Healthcare Common Procedure Coding System codes for docetaxel (J9170 or J9171), sipuleucel-T (Q2043), cabazitaxel (J9043), or radium RA 223 (A9606) and the National Drug Code numbers for abiraterone, apalutamide, and enzalutamide (see Table S6). We identified opioids in the claims data as any prescription drugs in the agonists or partial agonists therapeutic classes that are not buprenorphine using National Drug Code numbers (see Table S6). All spending measures were adjusted for inflation using the annual Consumer Price Index and were expressed in 2019 US dollars.<sup>17</sup>

We estimated the annual spending attributable to metastatic prostate cancer as the adjusted difference in total spending between cases and controls obtained from a two-part, multivariable model that controlled for patient's age, length of enrollment in the given calendar year, and comorbidities (acute myocardial infarction, Alzheimer disease, anemia, atrial fibrillation and flutter, chronic kidney disease, colorectal cancer, chronic obstructive pulmonary disease, congestive heart failure, depression, diabetes, ischemic heart disease, lung cancer, rheumatoid arthritis, and stroke).<sup>18–20</sup> The first part was a logistic regression model that estimated the likelihood of having positive spending as a function of the independent variables. The second part was a generalized linear model with a gamma distribution function and a log-link function that estimated the association between health care spending and the independent variables in the subsample of observations in which spending was positive. We clustered standard errors at the individual level. We used the delta method to calculate the standard error of the adjusted difference in expenditures between cases and controls.<sup>21</sup>

In sensitivity analyses, we stratified the analytic sample based on: (1) whether men had a diagnosis code for metastatic disease within 7 days of the first claim listing a diagnosis code for prostate cancer (suggesting the patient was initially diagnosed with metastatic disease) versus men with a diagnosis code for metastatic disease greater than 7 days after the first claim listing a diagnosis code for prostate cancer (suggesting the man was first diagnosed with metastatic disease)

with a localized or regional disease which later progressed into metastatic disease); (2) enrollment in prescription drug coverage; (3) calendar year; and (4) enrollment in fee-for-service versus fully or partially capitated plans.

Finally, we estimated the percentage of metastatic prostate cancer patients receiving antineoplastic drugs approved after 2010 using multivariable logistic regression models controlling for the calendar year, age, length of enrollment in the given calendar year, and comorbidities. We also estimated the conditional spending on these drugs using multivariable generalized linear models with the log-link and gamma distribution functions controlling for the same predictors.

We conducted the analyses in SAS, version 9.4, and Stata, version 17.0, with statistical significance at  $\alpha = 0.05$ .

#### RESULTS

We analyzed data from 9,011 metastatic prostate cancer patients with 44,934 matched controls covered by commercial insurance plans, and from 17,899 metastatic prostate cancer patients with 87,884 matched controls covered by employer-sponsored Medicare supplement plans. The commercial analytic sample included 20,433 person-years for metastatic prostate cancer patients and 101,795 person-years for controls; the Medicare supplement analytic sample included 37,098 person-years for metastatic prostate cancer patients and 181,398 person-years for controls. Table 1 shows the characteristics of the study subjects. Controls were similar to cases on the matching variables (age, geographic location, and enrollment in prescription drug coverage). The mean age for metastatic prostate cancer patients was 58.5 years in the commercial and 77.8 years in the Medicare supplement samples. The prevalence of comorbidities was generally higher among cases than control subjects in commercial and Medicare supplement samples.

The adjusted attributable spending for metastatic prostate cancer was \$55,949 (95% CI: \$54,074 to \$57,825) per person-year in the commercial population and \$43,682 (95% CI: \$42,022 to \$45,342) per person-year in the population covered by Medicare supplement plans (Table 2). Outpatient facility services were the largest category of attributable spending per person-year in commercial (\$24,725; 95% CI: \$23,748 to \$25,701) and Medicare supplement populations (\$14,112; 95% CI: \$13,179 to \$15,045). In the commercially insured population, physician services were the second largest type of attributable spending per person-year (\$13,966; 95% CI: \$13,407 to \$14,525), followed by spending on prescription drugs (\$8720; 95% CI: \$8136 to \$9305), while in the Medicare supplement population, spending on physician services (\$11,160; 95% CI: \$10,776 to \$11,544) was similar to spending on prescription drugs (\$11,150; 95% CI: \$10,662 to \$11,638). Spending on antineoplastic drugs was \$12,761 per person-year (95% CI: \$11,984 to \$13,539) in the commercially insured population and \$13,620 per person-year (95% CI: \$13,031 to \$14,208) in the Medicare supplement population.

In the commercially insured population, attributable spending per person-year in patients with a diagnosis code for metastatic disease within seven days of the first claim listing

a diagnosis code for prostate cancer (\$57,062; 95% CI: \$52,702 to \$61,423) was similar to spending for patients with a diagnosis code for metastatic disease greater than 7 days after the first claim listing a diagnosis code for prostate cancer (\$56,725; 95% CI, \$54,662–\$57,787) (Table 2). In the Medicare supplement population, the attributable spending per person-year was lower for patients with a diagnosis code for prostate cancer (\$36,840; 95% CI, \$33,517–\$40,163) than for those with a diagnosis code for metastatic disease greater than seven days after the first claim listing a diagnosis code for prostate cancer (\$44,933; 95% CI, \$43,083–\$46,782).

We observed no difference in attributable spending on medical services (excluding expenditures on prescription drugs) between patients with and without prescription drug coverage in each population (Table 2). We also observed no difference in attributable spending between patients enrolled in traditional (fee-for-service) health plans and those enrolled in fully or partially capitated health plans (Table 2).

Between 2010 and 2019, the attributable spending on metastatic prostate cancer in the commercially insured population grew from \$51,815 per person-year (95% CI, \$46,732–\$56,899 per person-year) to \$57,755 per person-year (95% CI, \$51,666–\$63,843 per person-year) (Figure 1). In the population covered by Medicare supplement plans, the attributable spending grew from \$31,100 per person-year (95% CI, \$28,057–\$34,144 per person-year) in 2010 to \$64,562 per person-year (95% CI, \$57,957–\$71,168 per person-year) in 2018, when it surpassed the attributable spending in the commercially insured population.

The use of antineoplastic drugs by patients with metastatic prostate cancer increased from 14.5% (95% CI, 12.0%–16.9%) in 2010 to 29.5% (95% CI, 27.3%–31.7%) in 2019 in the commercially insured population, and it increased by a similar percentage, from 10.9% (95% CI, 9.4%–12.4%) in 2010 to 27.2% (95% CI, 24.5%–29.8%) in 2019, in the Medicare supplement population (Figure 2). Spending on antineoplastic drugs per person-year among patients receiving these drugs rose in both commercially insured and Medicare supplement populations from \$21,492 (95% CI, \$18,096–\$24,887) and \$15,256 (95% CI, \$13,281–\$17,230) in 2010, respectively, to \$72,926 (95% CI, \$67,664–\$78,188) and \$70,764 (95% CI, \$66,878–\$74,650) in 2018, respectively (Figure 3). Spending on antineoplastic drugs per person-year among patients receiving these drugs dropped to \$63,519 (95% CI, \$58,006–\$69,032) in 2019 in the commercially insured population.

#### DISCUSSION

This study presents recent estimates of the economic burden of treating metastatic prostate cancer in men aged 18–64 years covered by commercial health insurance and men enrolled in employer-sponsored Medicare supplement plans in the United States. By using administrative claims data from 2009 to 2019, we estimated the mean annual attributable cost of metastatic disease at \$55,949 per person-year in the commercial population and \$43,682 per person-year in the Medicare supplement population, expressed in 2019 US dollars.

These updated estimates can improve the precision of value assessments of US clinical and policy approaches to the prevention, screening, and treatment of prostate cancer. For example, a commonly cited estimate of the mean annual cost burden of metastatic (stage IV) prostate cancer in the United States is \$8118 (in 2004 US dollars) per person per year.<sup>22</sup> If adjusted for inflation to 2019 US dollars, the estimate would be \$10,986. This estimate is from a study that relied on SEER–Medicare data in 1991–2002 when managing metastatic prostate cancer involved bone and computed tomography scans of the pelvis for staging and androgen-deprivation therapy given as 3-month or 6-month depot injections.<sup>22</sup> Since then, several new, effective, and costly therapies and diagnostic imaging tests have been approved by the US Food and Drug Administration and adopted into clinical practices.<sup>3–7</sup>

A more recent study of SEER–Medicare data during 2007–2017 estimated the mean annual attributable cost of metastatic prostate cancer at \$31,427 (adjusted to 2019 US dollars) per person per year.<sup>6</sup> Although this updated estimate accounts for the recent changes in the clinical management of the disease, it applies to older men who are covered by traditional fee-for-service Medicare and not to the many patients with prostate cancer covered by employer-sponsored health insurance. The difference between the estimates in this report and the more recent SEER–Medicare study<sup>6</sup> is likely because commercial plans pay higher prices than Medicare, and potentially more aggressive disease-management strategies used in younger men with generally longer life expectancy.<sup>11–13,23–25</sup>

Studies evaluating the cost of metastatic prostate cancer treatment in the privately insured population typically document a higher cost burden compared with that in the Medicare population. A recent study of the MarketScan data from 2014 to 2016—a subset of our study period—estimated the lifetime incremental cost of metastatic prostate cancer treatment in the commercial population at \$82,336 for those previously diagnosed with localized disease and \$161,714 for those diagnosed with de novo metastatic disease, both expressed in 2018 US dollars.<sup>26</sup> By using newer data from 2016 to 2019, another study compared the treatment cost of nonmetastatic versus metastatic, castration-resistant prostate cancer, concluding that the mean incremental cost to payers was \$113,725.<sup>27</sup> However, that analysis focused only on patients with prostate cancer undergoing androgen-deprivation therapy, and thus these results may not generalize to different disease-management approaches. Finally, a study of men who were younger than 65 years in the first year after prostate cancer diagnosis estimated total health care costs at \$55,497 (in 2020 US dollars) per person per year.<sup>28</sup> That study did not estimate attributable costs of prostate cancer and included men diagnosed with prostate cancer at all stages.

Our findings also documented increasing trends in the cost burden of metastatic prostate cancer in men covered by employer-sponsored health insurance plans. Although the annual, inflation-adjusted attributable cost increased by approximately 11.5% (from \$51,815 to \$57,755) between 2010 and 2019 in the commercially insured population, it increased by 107.6% (from \$31,100 to \$64,562) in the population covered by employer-sponsored Medicare supplement plans. In both populations, a driver of the growing cost burden was the increasing use of costly antineoplastic drugs. Consider that, in 2010, only 14% and 11% of commercially insured patients and patients covered by employer-sponsored Medicare supplement plans received antineoplastic drugs, respectively, yet the proportions in the

two populations rose to 29% and 27%, respectively, in 2019. These results suggest that physicians are more comfortable treating patients with newer drugs than docetaxel, which is associated with a higher risk of serious adverse events.<sup>29</sup> In addition, the conditional, adjusted annual spending on antineoplastic drugs grew substantially in both populations at 15% and 19% per year, respectively. Newer drugs are often substantially more costly than older drugs, reflecting the demand for effective cancer therapies and payers' reluctance to tightly manage oncology drugs as they do for other drug classes.<sup>30</sup>

At the same time, it is important to acknowledge the survival gains that have been observed with the dissemination of novel therapeutic options for prostate cancer. A recent cost-effectiveness analysis has demonstrated just over 1 year of improvement in population-level survival among Medicare beneficiaries with advanced prostate cancer in 2014–2016 compared with those diagnosed in 2007–2009.<sup>3</sup> The study estimated the incremental cost per life-year gained at \$83,000 in 2017 US dollars, demonstrating a *good value* of the novel prostate cancer therapies to Medicare beneficiaries. Although the spending attributable to metastatic prostate cancer treatment is considerably higher in the population of patients covered by employer-sponsored plans—as demonstrated by this study—the survival gains are also likely greater than among Medicare beneficiaries. More research is needed to fully assess the value of the novel therapeutic options for prostate cancer among younger patients covered by employer-sponsored insurance.

#### Limitations

The findings of this study should be interpreted within the context of its limitations. First, the MarketScan data did not include information from cancer registries about metastasis. We used diagnosis codes reported in claims and algorithms used in prior research to identify metastatic disease as an alternative. Although this approach is standard in analyses of administrative data, it is possible that it has misclassified some patients as having or not having the disease. Second, this study was retrospective and observational, and it is possible that some of the observed differences in health care spending between patients with metastatic prostate cancer and their controls were caused by unobserved factors. However, we followed the standard methodology for research when randomization is not feasible. Third, the MarketScan data do not identify decedents because of privacy. Therefore, we could not determine whether the loss to follow-up was because of death, loss of coverage, or a switch to another health plan. As such, we could not correct our cost burden estimates for the commonly observed increase in health care spending—especially among patients with cancer-in the last year of life. Fourth, our estimates are based on records of consumed care. Because employer-sponsored health plans commonly feature high patient cost-sharing requirements, some patients delay or forgo needed care or prescription fills because of costs.<sup>4,31–35</sup> Consequently, our estimates may be lower than they would be if all patients could afford to adhere to their recommended treatment regimens.

#### Conclusions

The cost burden attributable to treating metastatic prostate cancer in 2019 US dollars exceeds \$55,000 per person-year among working-age men with employer-sponsored health

insurance. Among those with employer-sponsored Medicare supplement coverage, the cost burden exceeds \$43,000 per person-year. These estimates can improve the precision of value assessments in US clinical and policy approaches to the prevention, screening, and treatment of prostate cancer.

#### **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

#### ACKNOWLEDGMENT

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#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are owned by Merative (Ann Arbor, Michigan). Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of Merative.

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#### FIGURE 1.

Adjusted spending per person-year attributable to metastatic prostate cancer, by year and type of insurance: MarketScan commercial and Medicare supplemental databases, 2009–2019. Adjusted spending attributable to metastatic prostate cancer is the difference in total annual spending between cases and controls obtained from a two-part, multivariable model that controlled for patient's age, length of enrollment in the given calendar year, and comorbidities (acute myocardial infarction, Alzheimer disease, anemia, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disease, colorectal cancer, congestive heart failure, depression, diabetes, ischemic heart disease, lung cancer, rheumatoid arthritis or osteoarthritis, and stroke). All dollar amounts were adjusted for inflation and are expressed in 2019 US dollars. The error bars represent 95% confidence intervals. Spending in the Medicare supplement sample in 2019 was excluded because of a substantial drop in the average price per claim compared with the previous years. USD indicates US dollars.



#### FIGURE 2.

Proportion of patients with metastatic prostate cancer who received antineoplastic drugs, by year and type of insurance: MarketScan commercial and Medicare supplemental databases, 2009–2019. The error bars represent 95% confidence intervals.



#### FIGURE 3.

Spending on antineoplastic drugs per person among patients with metastatic prostate cancer who received these drugs, by year and type of insurance: MarketScan commercial and Medicare supplemental databases, 2009–2019. Spending on antineoplastic drugs was adjusted using multivariable generalized linear models with the log-link and gamma distribution functions controlling for patient's age, length of enrollment in the given calendar year, and comorbidities (acute myocardial infarction, Alzheimer disease, anemia, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disease, colorectal cancer, congestive heart failure, depression, diabetes, ischemic heart disease, lung cancer, rheumatoid arthritis or osteoarthritis, and stroke). All dollar amounts were adjusted for inflation and are expressed in 2019 US dollars. The error bars represent 95% confidence intervals. Spending in the Medicare supplement sample in 2019 was excluded because of a substantial drop in the average price per claim compared with the previous years. USD indicates US dollars.

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## TABLE 1

Characteristics of beneficiaries with metastatic prostate cancer and control beneficiaries: MarketScan commercial and Medicare supplemental databases, 2009–2019.

	Commercial, I	Vo. (%)	Medicare supp	olement, No. (%)
	Cases	Controls	Cases	Controls
Characteristics measured at the person level				
No. of individuals	9011	44,934	17,899	87,884
Age on index date: Mean $\pm$ SD, years	$58.5 \pm 4.8$	$58.5 \pm 4.8$	77.8 ± 7.5	$77.8 \pm 7.5$
Metastatic disease at diagnosis	1571 (17.4)	NA	3252 (18.2)	NA
Characteristics measured at the person-year level				
No. of person-years	20,433	101,795	37,098	181,398
Prescription drug coverage	17,795 (87.1)	88,917 (87.4)	31,777 (85.7)	155,894 (85.9)
Enrollment in a (partially) capitated health plan	2194 (10.7)	12,418 (12.2)	4237 (11.4)	22,966 (12.7)
Comorbidities				
Acute myocardial infarction	269 (1.3)	972 (1.0)	1316 (3.6%)	3333 (1.8)
Alzheimer disease	5 (0.02)	22 (0.02)	699 (1.9)	2955 (1.6)
Anemia	5509 (27.0)	4195 (4.1)	16,148 (43.5)	22,419 (12.4)
Atrial fibrillation	749 (3.7)	1638 (1.6)	5578 (15.0)	14,548 (8.0)
Chronic kidney disease	4083 (20.0)	2956 (2.9)	12,856 (34.7)	18,900 (10.4)
Chronic obstructive pulmonary disease	1136 (5.6)	1287 (1.3)	5588 (15.1)	12,293 (6.8)
Colorectal cancer	797 (3.9)	461 (0.5)	2492 (6.7)	2567 (1.4)
Congestive heart failure	907 (4.4)	1602 (1.6)	6593 (17.8)	16,014 (8.8)
Depression	1693 (8.3)	1708 (1.7)	3303 (8.9)	6485 (3.6)
Diabetes	3246 (15.9)	7117 (7.0)	8980 (24.2)	26,064 (14.4)
Ischemic heart disease	2770 (13.6)	7457 (7.3)	13,293 (35.8)	42,597 (23.5)
Lung cancer	974 (4.8)	196 (0.2)	3634 (9.8)	1731 (1.0)
Rheumatoid arthritis or osteoarthritis	2035 (10.0)	4586 (4.5)	5751 (15.5)	16,395 (9.0)
Stroke	576 (2.8)	917 (0.9)	2899 (7.8)	7490 (4.1)
Receipt of opioids	9420 (46.1)	17,277 (17.0)	15,861 (42.8)	34,205 (18.9)

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# TABLE 2

Annual spending among beneficiaries with metastatic prostate cancer and control beneficiaries: MarketScan commercial and Medicare supplemental databases, 2009–2019.<sup>a</sup>

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	Commercial				Medicare supple	$ment^b$		
	Cases ( <i>n</i> = 20,433 person- years)	Controls ( <i>n</i> = 101,795 person- years)	Difference	Adjusted difference attributable to metastatic prostate cancer [95% CI]	Cases (n = 37,098 person- years)	Controls ( <i>n</i> = 181,398 person- years)	Difference	Adjusted difference attributable to metastatic prostate cancer [95% CI]
Annual health care spending, total $c$	85,597	8822	76,775	55,949 [54,074–57,825]	75,897	16,286	59,611	43,682 [42,022–45,342]
By spending type								
Physician	20,027	2388	17,639	13,966 [13,407–14,525]	18,276	4198	14,077	11,160 [10,776–11,544]
Outpatient facility	34,089	2269	31,820	24,725 [23,748–25,701]	25,139	4646	20,493	14,112 [13,179–15,045]
Inpatient facility	18,559	1908	16,651	7011 [6514–7508]	17,511	4228	13,283	6027 [5581–6473]
Prescription drugs <sup><math>c</math></sup>	12,493	2174	10,319	8720 [8136–9305]	14,760	2896	11,864	11,150 [10,662–11,638]
Antineoplastic drugs <sup>c</sup> ,d	13,805	4	13,801	12,761 [11,984–13,539]	13,120	12	13,108	13,620 [13,031 - 14,208]
Opioids <sup>c</sup>	224	40	184	97 [71–124]	161	37	124	89 [68–111]
By disease stage at prostate cancer	diagnosis and spen	ding type						
Men with a diagnosis code for metastatic disease within 7 days of the first claim listing a diagnosis code for prostate cancer <sup>C</sup>	85,169	8822	76,347	57,062 [52,702–61,423]	66,874	16,286	50,588	36,840 [33,517-40,163]
Physician	22,274	2388	19,886	16,305 [14,943–17,667]	18,246	4198	14,048	11,571 [10,662–12,481]
Outpatient facility	29,596	2269	27,327	19,927 [17,693–22,160]	18,221	4646	13,575	7705 [6068–9341]
Inpatient facility	21,822	1908	19,914	6790 [5672–7908]	18,065	4228	13,837	7264 [6431–8097]
Prescription drugs <sup><math>c</math></sup>	11,885	2174	9711	7994 [6781–9208]	12,165	2896	9269	8379 [7453–9305]
Men with a diagnosis code for metastatic disease $>7$ days after the first claim listing a diagnosis code for prostate cancer <sup>C</sup>	85,685	8822	76,862	56,725 [54,662–57,787]	77,773	16,286	61,488	44,933 [43,083–46,782]
Physician	19,558	2388	17,170	13,585 [12,981–14,188]	18,282	4198	14,084	11,021 [10,602–11,440]
Outpatient facility	35,027	2269	32,758	25,782 [24,702–26,861]	26,627	4646	21,981	15,268 [14,221–16,315]
Inpatient facility	17,877	1908	15,970	6520 [5995–7046]	17,391	4228	13,164	5550 [5059–6040]

	Commercial				Medicare supple	mentb		
	Cases (n = 20,433 person- years)	Controls ( <i>n</i> = 101,795 person-years)	Difference	Adjusted difference attributable to metastatic prostate cancer [95% CI]	Cases (n = 37,098 person- years)	Controls ( <i>n</i> = 181,398 person-years)	Difference	Adjusted difference attributable to metastatic prostate cancer [95% CI]
Prescription drugs $^{\mathcal{C}}$	12,617	2174	10,443	8836 [8189–9482]	15,300	2896	12,404	11,658 [11,108–12,208]
By prescription drug coverage (no	on-Rx spending)							
$\operatorname{Enrolled}^{\mathcal{C}}$	73,104	6648	66,456	47,013 [45,375–48,651]	61,137	13,390	47,746	32,329 [30,828–33,830]
Not enrolled	69,780	5988	63,792	45,740 [42,577–48,904]	59,692	11,171	48,521	34,646 [32,123–37,169]
By calendar years								
$2010-2013^{\mathcal{C}}$	83,204	7822	75,382	54,871 [52,416–57,326]	65,342	13,094	52,248	37,559 [35,806–39,311]
$2014-2019^{C}$	86,918	9374	77,545	56,556 [54,130–58,981]	86,058	17,637	65,041	48,721 [46,275–51,167]
By health plan type								
Traditional	85,324	8870	76,454	55,768 [53,777–57,759]	77,333	16,960	60,374	43,917 [42,100–45,734]
(Partially) capitated $^{\mathcal{C}}$	87,857	8489	79,368	57,426 [52,079–62,773]	64,327	11,500	52,827	40,359 [36,968–43,749]
Abbreviations: CI, confidence inter	val; Rx, prescription							

kidney disease, chronic obstructive pulmonary disease, colorectal cancer, congestive heart failure, depression, diabetes, ischemic heart disease, lung cancer, rheumatoid arthritis or osteoarthritis, and stroke) multivariable model that controlled for patient's age, length of enrollment in the given calendar year, and comorbidities (acute myocardial infarction, Alzheimer disease, anemia, atrial fibrillation, chronic <sup>a</sup>All dollar amounts in this table were adjusted for inflation and are expressed in 2019 US dollars. The columns for cases, controls, and adjusted difference are adjusted for inflation, but not for any other spending factors (e.g., age, comorbidity). The adjusted difference attributable to metastatic prostate cancer is the difference in total annual spending between cases and controls obtained from a two-part,

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 $b^{b}$  Spending in the Medicare supplement sample in 2019 was excluded because of a substantial drop in the average price per claim compared with the previous years.

 $^{\mathcal{C}}$ Restricted to beneficiaries with prescription drug coverage.

d. The antineoplastic drug category includes physician-administered drugs; therefore, the average spending may be higher than that on all prescription drugs.

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