Original Research

The impact of bone metastases and skeletal-related events on healthcare costs in prostate cancer patients receiving hormonal therapy

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Although studies have examined the effect of skeletal-related events (SREs) on healthcare costs in patients with advanced cancer and bone metastases, the effect of bone metastases without SREs on costs has not been studied. To estimate the effects of bone metastases with and without SREs on healthcare costs in men with prostate cancer treated with hormonal therapies, we performed a retrospective cohort study using claims data from large, US health insurance plans between September 2002 and May 2008. The primary measure was total healthcare costs after bone metastases. Secondary measures included components of total healthcare costs and selected measures of healthcare utilization. Of 215,702 patients with prostate cancer, 8,608 had bone metastases, and 1,365 met all inclusion criteria, with 786 (58%) reporting ≥ 1 SRE and 579 (42%) reporting no SRE. The mean duration of follow-up was 14 months. The mean total healthcare costs were $23,047/person-year in the 6 months before bone metastases. After adjustment, the costs increased by $12,780/person-year with bone metastases and no SREs ($P < 0.001$) and by $23,988/person-year with bone metastases and SREs ($P < 0.001$). We concluded that bone metastases are associated with increased total healthcare costs, even in the absence of SREs, in patients with prostate cancer.

Bone is the most common site of metastases in men with advanced prostate cancer, one of the most prevalent cancers in the United States and the second leading cause of cancer death after lung cancer.[1–3] The median survival from diagnosis of bone metastases is 30–40 months.[2] During this time, skeletal-related events (SREs), including pathologic fractures, surgery or radiation to the bone, spinal cord compression, or hypercalcemia of malignancy, can occur. SREs are associated with considerable morbidity, impaired health-related quality of life, reduced survival, and increased costs.[4–10]

Although studies have examined the impact of SREs on costs in patients with advanced cancers and bone metastases,[5–9,11] the effects of bone metastases without SREs on healthcare costs in prostate cancer patients have not been studied. The magnitude of these costs may be important in economic evaluations of treatments to prevent or delay bone metastases in prostate cancer patients. The objective of this study was to estimate the effects on healthcare costs of bone metastases in the presence and absence of SREs in men with prostate cancer who were receiving hormonal therapy.

Materials and methods

Study design

We used a retrospective cohort design drawing on two large US health insurance claims databases (Figure 1). Person-time from the beginning of the history period to the end of the post–bone metastases period was divided into monthly intervals. Costs during person-time with and without bone metastases and with and without SREs were compared using longitudinal multivariate regression analysis.

Data source

The Thomson Reuters MarketScan Commercial Claims and Encounters and Medicare and Coor-

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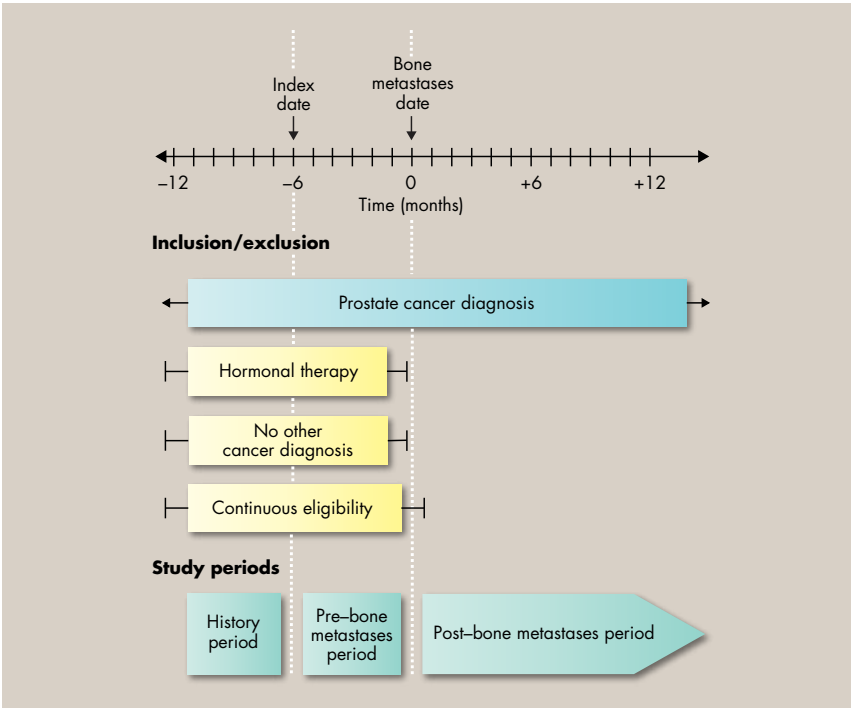

FIGURE 1 Study design. The date of the first evidence of bone metastases or a skeletal-related event (SRE) was classified as the "bone metastases date." The period beginning with the bone metastases date and ending with disenrollment from the health plan (because of death or another reason) was defined as the "post–bone metastases period." The date 6 months before the bone metastases date was designated the "index date." The 6-month period immediately before the bone metastases date was designated the "pre–bone metastases period." The 6 months before the index date was designated the "history period."

dination of Benefits databases contain information on health insurance claims of employees of large, self-insured corporations and their dependants, along with a few commercial health plans, and for Medicare-eligible persons who are also covered by self-insured employers. Both databases are fully de-identified and compliant with the Health Insurance Portability and Accountability Act of 1996. Data for this study span from September 30, 2002, through May 1, 2008 ("study period"). During this period, the two databases cover more than 50 million people.

Patient selection

The patients were male, had evidence of prostate cancer and bone metastases, and had received hormonal therapy for prostate cancer (luteinizing hormone-releasing hormone [LHRH] agonists, LHRH antagonists, antiandrogens, aminoglutethimide, and estrogens) or orchiectomy during the pre–bone metastases or history periods (Figure 2). The "bone metastases date" was the date of first claim of bone metastases or the date of first claim for an SRE if patients had a claim for an SRE within 1 year before the first bone metastases claim. SREs were identified based on a previously published algorithm and included radiotherapy, pathologic fracture, fracture surgery or stabilization procedure, spinal cord compression, and hypercalcemia.[5,6,8]

Patients were excluded if they had not continuously enrolled in the database during the history or pre–bone metastases period or during the first 30 days post–bone metastases; if they had one or more medical claims with a diagnosis of malignancy (including metastases) other than prostate or squamous or basal cell skin cancer (*International Classification of Diseases, 9th Edition, Clinical Modification [ICD-9-CM]* diagnosis codes 140.XX–172.XX, 175.XX–184.XX, and 186.XX–208.XX) during the history period; were younger than 18 years or older than 90 years as of the index date; and had missing or invalid enrollment or demographic information or date of service or cost information on any claim during the history or pre– or post–bone metastases period.

Patient characteristics

Census region, plan type, and calendar year at index date were assessed for each patient. Beginning with the index date, other characteristics were assessed monthly, including patient age; presence of comorbidities; additional sites of metastases; performance of orchiectomy; and receipt of hormonal therapies, chemotherapy, oral bisphosphonates, and opioids. We calculated the Deyo–Charlson Comorbidity Index monthly beginning with the index date,[12] with all claims during the study period used to identify comorbid conditions (the Charlson Index at the index date and bone metastases date was based on claims during the 6 months preceding the index date and on claims during the 12 months preceding the bone metastases date, respectively). Measures of healthcare utilization and costs during the 6 months before the index date (ie, history period) were calculated for each patient.

In addition, healthcare utilization and costs were determined monthly following the index date. Utilization measures included whether the patient had visited an oncologist/hematologist or urologist, the number of prescriptions written, physicians' office visits, outpatient visits, inpatient visits (including length of inpatient stay), and emergency department (ED) visits. Cost measures were estimated based on reimbursed

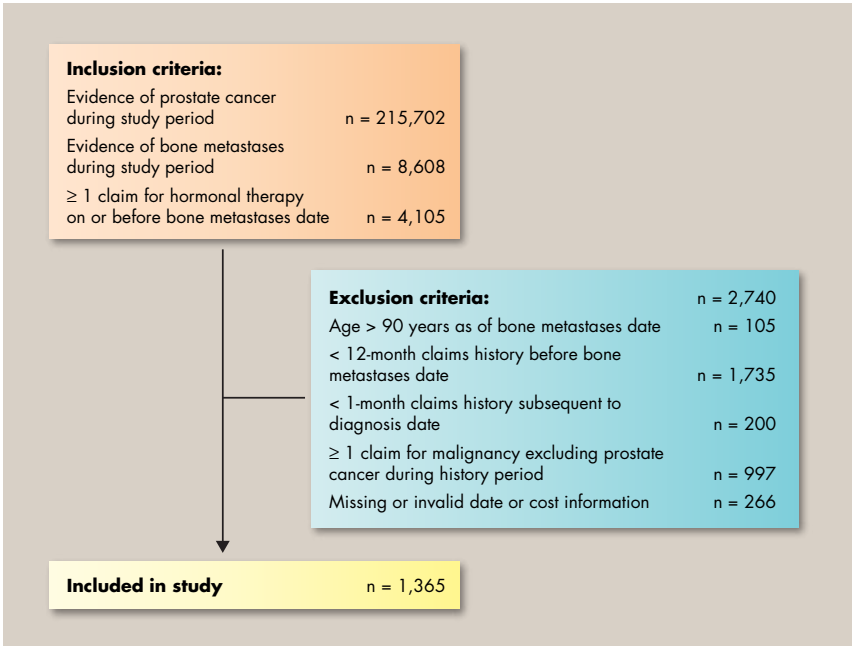

FIGURE 2 Selection of study subjects. Evidence of prostate cancer was defined as one or more inpatient or two or more outpatient medical claims more than 30 days apart with any diagnosis (ie, in the primary or secondary position) of "primary prostate cancer" (*International Classification of Diseases, 9th edition,* Clinical Modification [ICD-9-CM] diagnosis code 185.XX). Evidence of bone metastases was defined as one or more inpatient or two or more outpatient medical claims more than 30 days apart with a diagnosis of "malignant neoplasm of bone and articular cartilage" (ICD-9-CM diagnosis code 170.XX) or "secondary malignant neoplasm of bone and bone marrow" (ICD-9-CM diagnosis code 198.5X).

amounts (including patient contributions) normalized to the calendar year 2008[13] and included inpatient, outpatient medical (ED, outpatient, and physician's office visits), outpatient pharmacy, and total healthcare costs. Professional services and other care received during hospitalization were "rolled up" into the cost of each hospitalization.

Study outcomes

Study outcomes were assessed monthly, beginning with the first month after the index date through the end of the post–bone metastases period. The primary study outcome measure was total healthcare cost. Secondary outcomes included inpatient costs, outpatient medical costs, outpatient pharmacy costs; hospitalization (yes or no); and the number of outpatient visits (physician's office, hospital outpatient, or ED visits on different days).

Statistical analysis

Descriptive statistics on patient characteristics at the index date were reported for patients with bone metastases with and without SREs. The number and percentage of patients who developed SREs during the post–bone metastases period were calculated. The time to first SRE was calculated using Kaplan-Meier methods, with patients censored at disenrollment or the end of the study period.

Independent effects of bone metastases and SREs on healthcare utilization and costs were estimated using multivariate generalized estimating equation (GEE) regression, an extension of generalized linear model (GLM) regression for longitudinal data.[14–16] The GLM/GEE regressions were performed to relate costs (and other study outcomes), in any given interval, to the history of bone metastases with and without SREs and all patient characteristics as previously described (covariates were dropped from the models only as necessary to obtain model convergence). For each interval, the history of an event (bone metastases or SRE) was defined as an occurrence of the event during the interval or some prior interval.

In primary analyses, regression models included independent variables representing bone metastases with SREs and bone metastases without SREs. The coefficients on these two independent variables measured average effects, compared with no bone metastases, of bone metastases with and without SREs over the entire post–bone metastases period. Because effects of bone metastases and SREs on cost might vary over time, models that included variables representing effects of events by time since occurrence (months 1, 2–12, 13–24, and 25+ post–SRE and post–bone metastases [for person-time with no previous SRE]) were estimated. Because costs might increase prior to bone metastases, a variable representing the three monthly periods before the bone metastases date also was included. In addition, a covariate was included for the month before death or disenrollment. Analyses were conducted using SAS Proprietary Software, Release 9.1.3 (SAS Institute Inc., Cary, NC).

Results

Study sample

Among 215,702 patients in the database with a diagnosis of prostate cancer, 8,608 (4%) had evidence of bone metastases, including 4,105 who were receiving hormonal therapy in the year before bone metastases (Figure 2). Of those, 1,365 met all inclusion criteria, including 786 (58%) with one or more SRE and 579 (42%) with no SRE. All but three patients had a diagnosis of prostate cancer on or before the bone metastases date; the three patients had a first prostate cancer diagnosis within 3 months of the bone metastases date. The most

TABLE 1

Characteristics of study subjects

Characteristic	No SREs (n = 579)	≥ 1 SREs (n = 786)	Total (N = 1,365)
Age, years			
Range	47–90	43–90	43–90
Mean (SD)	74.4 (9.6)	74.0 (9.3)	74.2 (9.4)
Comorbidities			
Diabetes	82 (14)	120 (15)	202 (15)
Hypertension	179 (31)	237 (30)	416 (30)
Coronary artery disease	93 (16)	143 (18)	236 (17)
Chronic obstructive pulmonary disease	41 (7.1)	61 (7.8)	102 (7.5)
Mean (SD) Charlson index	1.4 (1.4)	1.4 (1.4)	1.4 (1.4)
Medications during pre–index period			
Hormonal therapies for prostate cancer			
LHRH agonists	331 (57)	494 (63)	825 (60)
Antiandrogens	208 (36)	294 (37)	502 (37)
LHRH antagonists	0 (0)	1 (0)	1 (0)
Orchiectomy	4 (1)	4 (1)	8 (1)
Chemotherapy	32 (6)	50 (6)	82 (6)
Oral bisphosphonates	18 (3.1)	27 (3.4)	45 (3.3)
Opioids	152 (26)	229 (29)	381 (28)
Systemic corticosteroids	128 (22)	193 (25)	321 (24)
Diabetes medications	92 (16)	140 (18)	232 (17)
Hyperparathyroidism medications	93 (16)	154 (20)	247 (18)
Cardiovascular medications	433 (75)	579 (74)	1,02 (74)
Healthcare utilization during history period			
Visit to oncologist (years/n)	33 (5.7)	46 (5.9)	79 (5.8)
Visit to urologist (years/n)	308 (53.2)	434 (55.2)	742 (54.4)
Number of office, outpatient, and emergency department visits, mean (SD)	8.9 (8.5)	9.4 (8.6)	9.2 (8.5)
Number of inpatient days, mean (SD)	0.5 (2.2)	0.4 (1.6)	0.4 (1.9)
Mean (SD) healthcare costs during history period, $			
Hospital inpatient care	1,50 (7,16)	1,34 (8,23)	1,43 (7,79)
Physician's office, hospital outpatient, and emergency department visits	4,42 (8,26)	4,98 (7,90)	4,79 (8,05)
Outpatient pharmacy	2,03 (2,08)	2,15 (2,05)	2,06 (2,07)
Other care	285 (1,58)	357 (2,50)	326 (2,16)
Mean (SD) duration of follow-up, months	13.2 (10.1)	14.9 (10.7)	14.2 (10.5)

LHRH = luteinizing hormone-releasing hormone; SD = standard deviation; SRE = skeletal-related event

Note: Unless otherwise noted, all values are n (%).

common reasons for study exclusion were that a patient had less than 12 months of claims history before the bone metastases date (1,735 patients), one or more claims for malignancy other than prostate cancer during the history period (997 patients), and a missing or invalid date or cost information (266 patients).

Patient characteristics at index date

Among the 1,365 patients included in the study, the mean age at index date was 74.2 (standard deviation [SD], 9.4) years; 81% of the patients were 65 years or older (Table 1). Most of the patients were insured by comprehensive plans (59%) and resided in the midwestern (38%) and southern (32%) regions of the United States. Common comorbid conditions included hypertension (30%), coronary artery disease (17%), and diabetes (15%). Sixty percent of patients received LHRH agonists; 37% received antiandrogens. The mean duration of follow-up from the bone metastases date was 14.2 months (SD, 10.5). Patients who subsequently experienced one or more SREs (786 patients, 58%) were generally similar to those who did not experience SREs (579 patients, 42%) in terms of baseline characteristics at the index date.

Incidence of SREs

Of the 1,365 patients, radiotherapy was the most frequent SRE (679 patients, 49.7%), followed by fracture (238 patients, 17.4%), fracture surgery or stabilization procedure (107 patients, 7.8%), spinal cord compression (38 patients, 2.8%), and hypercalcemia (18 patients, 1.3%). The median time to first SRE was 8 months post–bone metastases and to radiotherapy, 14 months. The median time to an event for other SREs was not reached. The incidence of first SRE was 0.487 per person-year.

Healthcare utilization and costs

The mean total healthcare costs were $23,047 per person-year in the 6 months before bone metastases, $43,251 per person-year with bone metastases and no SREs, and $60,162 per person-year with bone metastases and SREs (Table 2). The occurrence of bone metastases without SREs was associated with an increase of 95% in annual total healthcare costs, and the occurrence of bone metastases with SREs was associated with an increase of 173% in healthcare costs. Adjusting for patient characteristics, total healthcare costs increased by 55% with bone

TABLE 2

Regression analyses of the association between diagnosis of bone metastases and occurrence of skeletal-related events (SREs) vs healthcare costs in patients with prostate cancer

Outcome	Cost, $	Person-years	Cost per person-year, $	Univariate (unadjusted) regression			Multivariate (adjusted) regression		
				e^B	(95% CI)	*P*	e^B	(95% CI)	*P*
Costs									
Hospital inpatient car									
Pre–bone metastases	2,527,586	684	3,696	1.00	–	–	1.00	–	–
Bone metastases and no SRE	7,189,784	857	8,391	–	–	–	–	–	–
Bone metastases and SRE	11,118,930	806	13,790	–	–	–	–	–	–
Outpatient care									
Pre–bone metastases	9,098,765	684	13,304	1.00	–	–	1.00	–	–
Bone metastases and no SRE	23,318,193	857	27,213	2.03	(1.83–2.25)	< 0.001	1.62	(1.47–1.79)	< 0.001
Bone metastases and SRE	29,788,688	806	36,946	3.03	(2.72–3.38)	< 0.001	2.29	(2.02–2.60)	< 0.001
Outpatient pharmacy									
Pre–bone metastases	3,283,450	684	4,801	1.00	–	–	1.00	–	–
Bone metastases and no SRE	4,162,827	857	4,858	1.00	(0.93–1.08)	0.900	0.78	(0.7 –0.85)	< 0.001
Bone metastases and SRE	4,390,635	806	5,446	1.12	(1.04–1.21)	0.004	0.90	(0.82–0.98)	0.021
Other care									
Pre–bone metastases	852,071	684	1,246	1.00	–	–	1.00	–	–
Bone metastases and no SRE	2,389,940	857	2,789	2.23	(1.82–2.73)	< 0.001	1.78	(1.40–2.27)	< 0.001
Bone metastases and SRE	3,209,092	806	3,980	3.33	(2.74–4.05)	< 0.001	2.20	(1.68–2.87)	< 0.001
Total care									
Pre–bone metastases	15,761,873	684	23,047	1.00	–	–	1.00	–	–
Bone metastases and no SRE	37,060,744	857	43,251	1.95	(1.75–2.17)	< 0.001	1.55	(1.40–1.73)	< 0.001
Bone metastases and SRE	48,507,345	806	60,162	2.73	(2.47–3.02)	< 0.001	2.04	(1.82–2.29)	< 0.001

CI = confidence interval; e^B = exponentiated coefficient from regression model; *P* = probability value

Notes: Multivariate models for hospital inpatient care did not converge. Adjusted model included all covariates reported in Table 1. CI is based on the Wald method. P is based on chi-squared distribution. For cost measures, log link and gamma error term distributions were used. For measures representing counts, log link and negative binomial error term distributions were used. For binary outcomes, logit link and binomial error term distributions were used. Autoregressive correlation structures were specified. Standard errors of coefficient estimates were based on empirical robust estimators.

TABLE 3

Regression analyses of the association between diagnosis of bone metastases and occurrence of skeletal-related events (SREs) vs healthcare utilization in patients with prostate cancer

Outcome	Cost, $	Person-years	Cost per person-year, $	Univariate (unadjusted) regression			Multivariate (adjusted) regression		
				e^B	(95% CI)	*P*	e^B	(95% CI)	*P*
Hospitalizations									
Pre–bone metastases	207	684	0.30	1.00	–	–	1.00	–	–
Bone metastases and no SRE	599	857	0.70	2.39	(2.03–2.82)	< 0.001	2.69	(2.21–3.26)	< 0.001
Bone metastases and SRE	804	806	1.00	3.50	(3.00–4.09)	< 0.001	4.04	(3.30–4.95)	< 0.001
Outpatient visits									
Pre–bone metastases	17,127	684	25	1.00	–	–	1.00	–	–
Bone metastases and no SRE	27,706	857	32	1.40	(1.33–1.47)	< 0.001	1.46	(1.38–1.55)	< 0.001
Bone metastases and SRE	38,519	806	48	2.29	(2.17–2.42)	< 0.001	2.52	(2.35–2.71)	< 0.001

CI = confidence interval; e^B = exponentiated coefficient from regression model; *P* = probability value

Notes: Adjusted model included all covariates reported in Table 1. CI is based on the Wald method. *P* is based on chi-squared distribution.

metastases and no SREs ($P < 0.001$) and by 104% with bone metastases and SREs ($P < 0.001$). Inpatient costs increased by $4,695 per person-year with bone metastases and no SREs and by $10,095 per person-year with bone metastases and SREs (GEE models for inpatient costs did not converge because of the high number of months with zero costs). Adjusted outpatient costs increased by 62% with bone metastases and no SREs and by 129% with bone metastases plus SREs. Outpatient pharmacy costs declined with the occurrence of bone metastases (with or without SREs).

On an adjusted basis, bone metastases without SREs were associated with a 169% increase in hospitalization risk, whereas bone metastases with SREs were linked to a 304% increase in hospitalization risk (Table 3). Bone metastases were associated with a 46% increase in the frequency of physician's office, outpatient, and ED visits. Bone metastases with SREs were associated with a 152% increase in the frequency of such encounters.

Mean monthly total healthcare costs increased from $1,298 per patient 12 months before the bone metastases diagnosis to $2,584 per patient 1 month before bone metastases (Figure 3). In the month after the diagnosis of bone metastases, total healthcare costs were $12,720 per patient among persons with SREs and $6,958 per person among those without SREs. Monthly total healthcare costs generally declined after the first month post–bone metastases but also were generally higher than before the bone metastases.

Based on multivariate longitudinal regression analysis, compared with the period 4 to 6 months before the bone metastases, there was a 20% increase in the total healthcare costs in the 3 months before the bone metastases (Table 4). Bone metastases without SREs were associated with a 276% increase in costs in the month after the diagnosis of bone metasta-

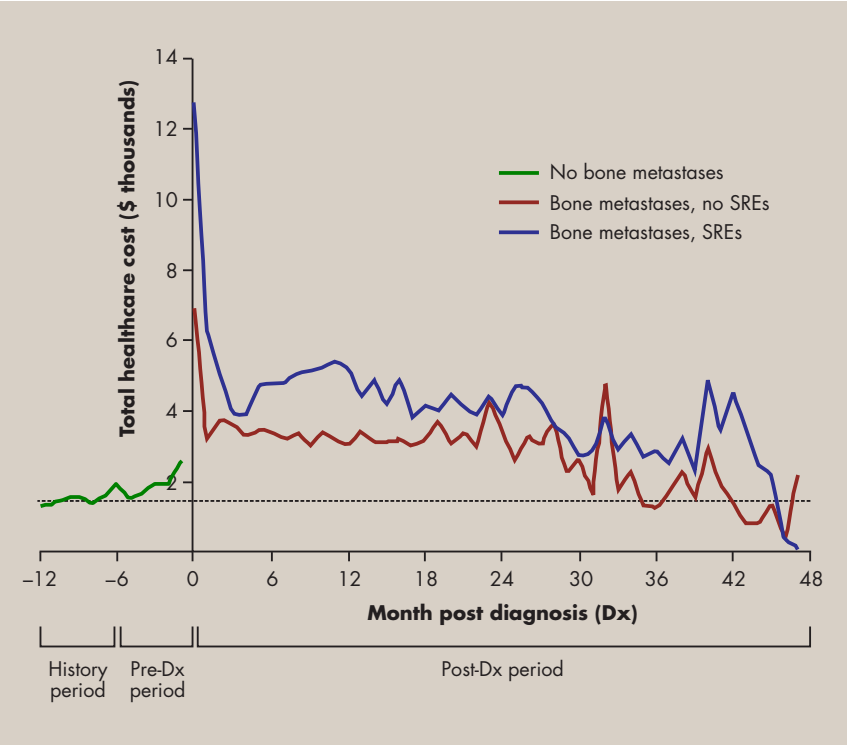

FIGURE 3 Mean total healthcare costs per month by history of bone metastases and/or skeletal-related events (SREs). Patients were censored at disenrollment or the end of the study period. Average costs for each interval were calculated as the sum of costs during the interval divided by the number of persons at risk at the beginning of the interval. The dotted line shows the mean monthly costs in the history period ($1,453).

TABLE 4

Regression analyses of the association between time since diagnosis of bone metastases and time since occurrence of skeletal-related events (SREs) vs total healthcare costs in patients with prostate cancer

Variable	e^{β}	(95% CI)	*P*
Number of bone metastases			
4–6 months pre–bone metastases	1.00	–	–
1–3 months pre–bone metastases	1.20	(1.05–1.38)	0.008
Bone metastases and no SRE			
Month 1 post–bone metastases	3.76	(3.14–4.50)	< 0.001
Months 2–12 post–bone metastases	1.17	(1.01–1.36)	0.039
Months 13–24 post–bone metastases	1.02	(0.86–1.21)	0.836
Months > 24 post–bone metastases	0.87	(0.67–1.13)	0.310
Bone metastases and SRE			
Month 1 post–SRE	5.52	(4.66–6.53)	< 0.001
Months 2–12 post–SRE	1.50	(1.30–1.74)	< 0.001
Months 13–24 post–SRE	1.10	(0.93–1.30)	0.245
Months > 24 post–SRE	0.87	(0.67–1.14)	0.317
Month of death	0.26	(0.20–0.34)	< 0.001

CI = confidence interval; e^{β} = exponentiated coefficient from regression model; *P* = probability value

Notes: Models included all covariates reported in Table 1. CI is based on the Wald method. *P* is based on chi-squared distribution.

ses and a 17% increase in months 2 to 12 after the diagnosis of bone metastases, whereas bone metastases with SREs were associated with a 452% increase in total healthcare costs in the month of the SRE diagnosis and a 50% increase in costs in months 2 to 12 after the SRE diagnosis.

Discussion

In this retrospective observational health insurance claims-based study of prostate cancer patients, bone metastases in the absence of SREs were associated with a 55% increase in total monthly healthcare costs ($12,780 per person-year), whereas bone metastases with SREs were associated with a 104% increase in total monthly healthcare costs ($23,988 per person-year), compared with costs in the 6 months before bone metastases ($23,047 per person-year). Most of the increase in costs associated with bone metastases, with or without SREs, occurred in the outpatient setting, predominantly during the months immediately after the diagnosis of bone metastases. Claims for zoledronic acid (Zometa), bone scans, and chemotherapy (medications and administration) were among the most frequently observed claims in the immediate post–bone metastases period, suggesting that these services may have contributed most to the increase in costs.

Lage and colleagues analyzed the costs of SREs in patients with prostate cancer using health insurance claims data[9]; they estimated the mean costs associated with SREs in the year after the initial diagnosis of an SRE to be $12,469. We estimated that among patients with bone metastases, the total healthcare cost per person-year is about $17,000 higher in those with SREs than in those with no SREs. Assuming a median post-SRE survival of 8.5 months,[9] our results are consistent with those reported by Lage and colleagues. However, whereas they focused only on the costs of SREs, our study also documents the costs of bone metastases in the absence of SREs. Our results suggest that although the costs of SREs are substantial, the costs of treating bone metastases in the absence of SREs also may be an important contributor to increased healthcare costs. Consequently, preventing or delaying the occurrence of bone metastases in patients with prostate cancer may result in substantial reduction of healthcare utilization costs.

Limitations of this study should be noted. To begin, a control group was not included because of the difficulties in identifying prostate cancer patients without bone metastases who could be compared with those with bone metastases. Instead, we used longitudinal regression analysis to compare person-time before and after bone metastases and SREs in the same set of patients, with patients serving as their own controls. Although this comparison is less likely to be confounded by differences across patients, factors that are temporally associated with the occurrence of bone metastases were not controlled for in our analysis. In particular, bone metastases may occur contemporaneously with metastases to other sites, and some of the increase in costs that we observed could be associated with treatment of other sites. We did not control for other sites because treatment of metastases is not specific to bone or other metastases.

Because patients with asymptomatic bone metastases may be less likely to have insurance claims with diagnoses of bone metastases than would those with symptomatic disease, the study sample may be weighted toward patients with more severe bone metastases, who may have higher costs. The SREs identified in this study may not be comparable to those evaluated in clinical trials of denosumab (Xgeva) and zoledronic acid.[17,18] In those trials, patients underwent regular radiologic assessment to identify asymptomatic fractures. Such regular assessments may not occur in typical clinical practice. This finding may explain the relatively low proportion of SREs that were fractures in the current study, compared with that in reported trials of zoledronic acid and denosumab (17% and 39%, respectively).[17,18] The fractures identified in this study are more likely to represent symptomatic events, which may have higher costs than asymptomatic fractures.

Hypercalcemia was included in the definition of SRE in this study, consistent with the definition used in at least one previous study of zoledronic acid,[19] whereas the recent trial of denosumab in hormone-resistant prostate cancer did not count hypercalcemia in the definition of SREs. Hypercalcemia accounted for 1.3% of all SREs, however, and its inclusion in the definition of SREs likely had little impact on the estimated costs of SREs.

Because procedural codes for radiotherapy do not determine the site of therapy, it was not possible to identify with specificity radiotherapy to bone. All claims for therapeutic radiotherapy were assumed to be to bone. Although this is likely a reasonable assumption for men with hormone-refractory prostate cancer and bone metastases, it is possible that some claims for radiotherapy were for non-bone metastases, which might have biased the comparison of SRE and non-SRE patients.

This study included only patients with medical and prescription benefit coverage and may not be generalizable to other populations. Information on patient mortality was not available, except for hospital discharge disposition, and the validity of this field for assessing mortality is unknown. Therefore, it was not feasible to assess the effects of SREs on mortality or to estimate expected lifetime costs.

Conclusion

Bone metastases in patients with prostate cancer are associated with

increased total healthcare costs, even in the absence of SREs. Therapies that prevent or the delay occurrence of bone metastases in patients with prostate cancer may reduce healthcare utilization costs.

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