Trends in Skeletal-Related Event Hospitalization and Use of Bone-Targeting Agents in Older Patients with Bone Metastases from Solid Tumors in the United States: 1994-2015

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Disclosures

Introduction

◆ Skeletal-related events (SREs) are associated with bone metastasis (BMs) from solid tumors,[1] leading to decreased quality of life and increased healthcare resource utilization, particularly hospitalizations.[2,3]

◆ Clinical trials have shown the efficacy of bone-targeting agents (BTAs) in reducing SRE incidence.[4-6]

◆ In this study, we characterized trends in BTA use and SRE-related hospitalization rates over time (1994-2015) in a population-based cohort of elderly Medicare patients with BMs from solid tumors.

Methods

◆ **Data source:** Medicare 5% (1993-2007) and 20% (2007-2015) sample data.

◆ **Inclusion criteria:** We assembled yearly prevalent cohorts of patients with BMs 1994-2015 with the following eligibility criteria:
  ◆ Evidence of BMs from solid tumors in the cohort year (the BM index date is the BM diagnosis date) or in the prior year and alive on January 1 of the cohort year (BM index date is January 1).
  ◆ Age ≥66 years at BM index date.
  ◆ Continuously enrolled in Medicare Part A and B without enrollment in a health maintenance organization for ≥12 months before BM index date.

◆ **Exclusion criteria:** Evidence of ≥2 solid tumors.

◆ **Baseline period:** 12 months before BM index date.

◆ **Follow-up period:** from BM index date to the earliest of death, change of enrollment status, or December 31 of the cohort year (September 30 for the 2015 cohort) to define BTA use and SRE-related hospitalization.

Definitions:

◆ **Evidence of BM:** ≥1 inpatient (IP) claim or ≥2 outpatient (OP) claims on different days within a 12-month interval carrying the ICD-9-CM code for BM (198.5) during a 2-year period from January 1 of the year before the cohort year to December 31 of the cohort year.

◆ **BM diagnosis date:** earliest of the discharge date for IP claim or the service date of the second OP claim with the qualifying code.

◆ **Solid tumor types**: assigned using the ICD-9-CM diagnosis codes on ≥1 IP claim or ≥2 OP claims on different days during the baseline period. Breast (female), lung, or prostate, or other cancers combined.

◆ **BTA use:** defined using the HCPCS codes for pamidronate, zoledronic acid, or denosumab from OP claims.

◆ **SRE-related hospitalization:** identified through ICD-9-CM diagnosis or procedure codes for spinal cord compression, pathologic fracture, surgery to bone, or radiation to bone from IP claims.[7] If a patient had multiple SRE-related hospitalizations, only the first one was counted for the analyses.

Statistical Analyses:

◆ Baseline characteristics were reported using descriptive statistics.

◆ We described trends in proportions of patients receiving BTAs and observed and adjusted (with 2014 cohort as the reference) rates of SRE-related hospitalization over the years.

◆ We evaluated trends in first SRE-related hospitalization rates using a Poisson regression model with spline curve of calendar year adjusting for patient age, dual eligible status, baseline hospital days, baseline SREs, and cancer type.

Results

Table 1. Patient characteristics for select years from 1994 to 2015

Characteristics	Medicare 5% Sample			Medicare 20% Sample		
	1994	2001	2007	2008	2014	2015
Total patients, n	4,121	3,709	4,504	17,774	19,260	18,354
Age category, %						
66-69 years	19.1	16.2	17.0	16.9	18.8	18.9
70-74 years	26.2	24.0	22.4	23.3	24.3	23.9
75-79 years	23.3	25.7	25.0	23.0	21.7	21.4
≥80 years	31.4	34.2	35.6	36.8	35.3	35.8
Female, %	40.4	43.8	45.1	45.9	42.4	44.2
Race, %						
White	87.8	87.8	88.7	87.9	86.9	86.8
Black	9.8	9.1	7.8	8.6	8.6	8.7
Other	2.3	3.1	3.5	3.5	4.4	4.5
Medicare-Medicaid dual eligible, %	9.6	11.2	11.7	12.1	12.1	11.1
History of all-cause hospitalization						
Length of stay, mean (SD), days	9.1(14.4)	5.9(9.4)	4.7(8.3)	5.0(9.9)	3.7(8.3)	3.7(9.4)
Length of stay categories						
0 day	27.6	36.9	46.0	45.9	55.0	57.0
1-7 days	33.8	36.2	33.1	32.5	29.1	27.1
≥ 8 days	38.6	26.9	21.0	21.7	15.9	15.9
Charlson Comorbidity Index category, %						
≤ 4	14.3	16.3	16.6	16.3	15.9	13.1
5-8	48.3	43.9	42.4	41.6	41.6	43.4
≥ 9	37.4	39.8	41.0	42.1	42.5	43.5
History of SREs[a]	38.0	36.6	32.7	30.7	27.0	27.9
Tumor type, %						
Breast cancer	23.9	26.8	27.4	27.1	25.2	27.0
Prostate cancer	42.3	35.5	35.3	34.2	38.3	37.3
Lung cancer	18.6	20.9	20.8	22.0	19.1	18.4
Other cancer	15.2	16.8	16.5	16.8	17.5	17.3

SRE, skeletal-related events; SD, standard deviation. [a]Defined by SRE episodes using the algorithm by Aly et al[7].

◆ Yearly cohorts of eligible patients ranged from 3599 to 4559 in 1994-2007 and from 17,774 to 19,423 in 2008-2015. Proportion of patients aged ≥80 years ranged from 31% to 37% (**Table 1**).

Use of BTAs, overall and by type of agent
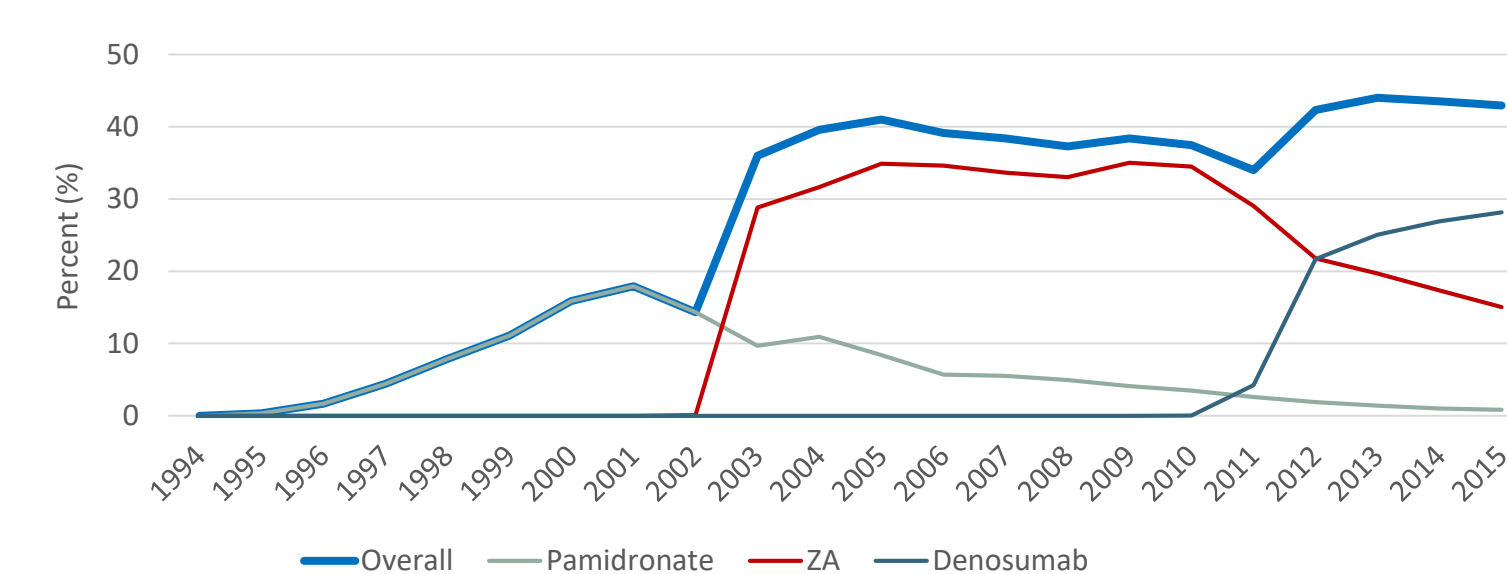
BTAs, bone-targeting agents; ZA, zoledronic acid.

◆ Proportions receiving BTAs were <1% in 1994-1995, steadily increased to 18% in 2001, and dramatically increased to 34%-44% in 2003-2015, mainly due to introduction of zoledronic acid in 2002 and denosumab in 2010.

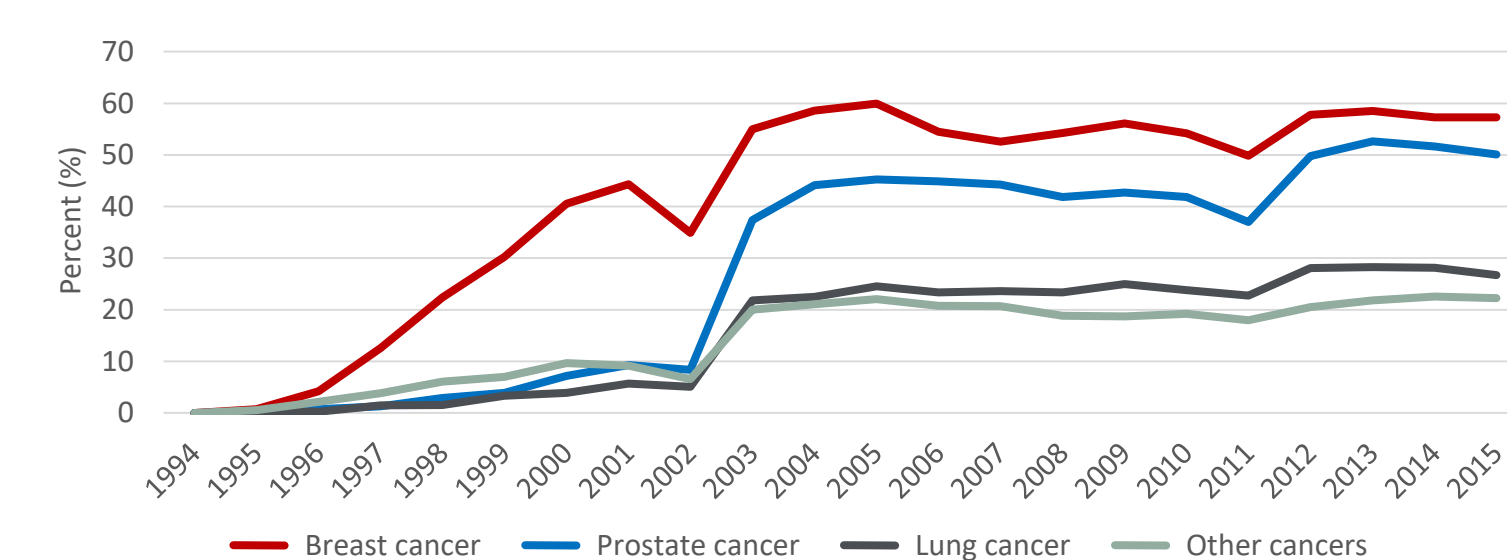### Overall unadjusted and adjusted incidence rate of SRE-related hospitalization
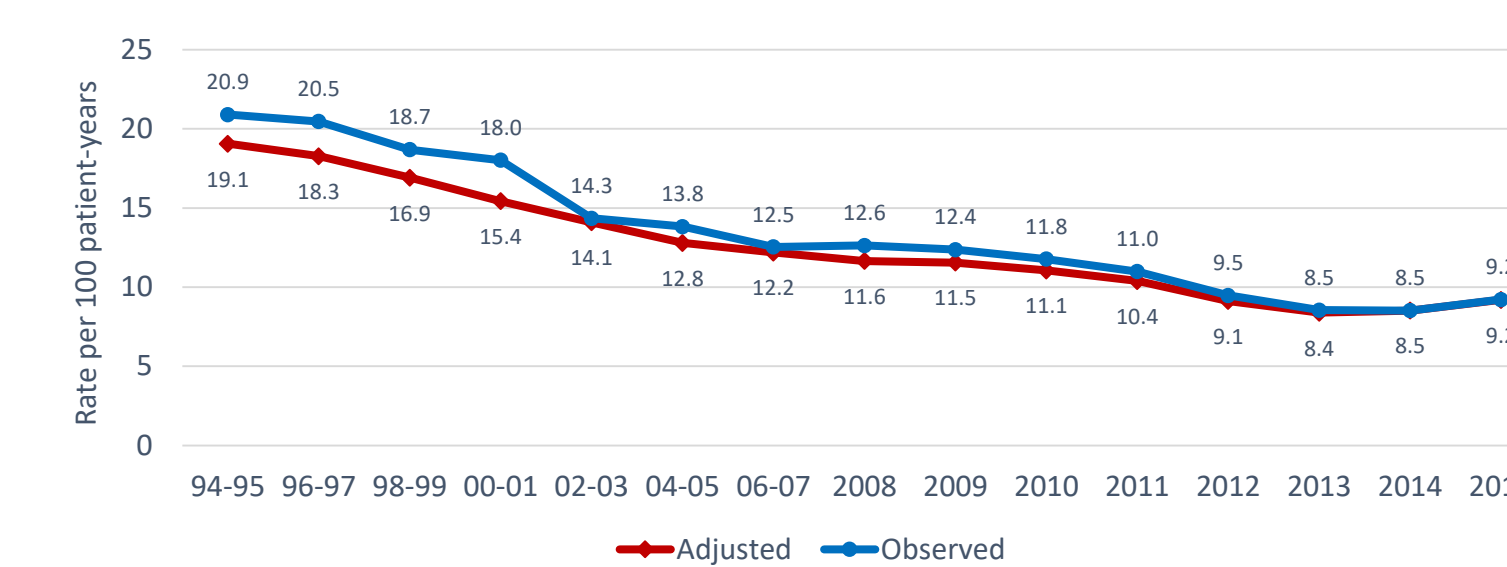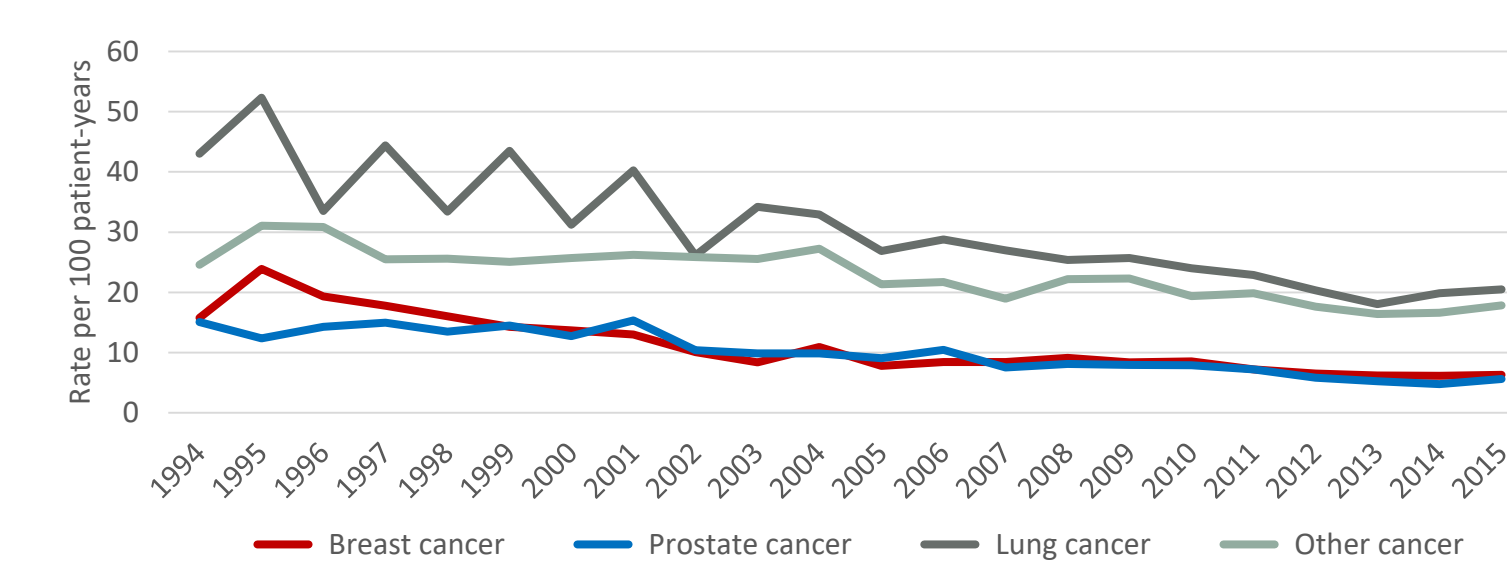

SRE, skeletal-related events.

◆ Overall, crude rates of first SRE-related hospitalization decreased from 20.9 per 100 patient-years in 1994-1995 to 9.2 in 2015.

◆ After adjustment for baseline patient characteristics, incidence rates of SRE-related hospitalization decreased, on average, 3% each year before 2008 and 4.3% per year from 2008.

Use of BTAs and unadjusted incidence rate of SRE-related hospitalization by cancer type

3A. Use of BTAs

3B. Incidence rate of SRE-related hospitalization

BTAs, bone-targeting agents; SRE, skeletal-related events.

◆ In general, patterns of BTA use and the unadjusted incidence rate of SRE-related hospitalization over the years were similar across cancer types. BTA use occurred most often in patients with BMs from breast cancer, while incidence of SRE-related hospitalization was lowest in patients with BMs from breast or prostate cancer.

Conclusions

◆ BTA use increased substantially after 2002 among elderly Medicare patients with BMs from solid tumors.

◆ Rates of SRE-related hospitalization decreased over the same time period, with a more rapid decrease from 2008.

◆ Further studies are needed to better understand SRE management among patients with BMs in the real-world setting.

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