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RESEARCH ARTICLE

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Sex, racial/ethnic and socioeconomic disparities in patients with metastatic bone disease

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Abstract

Background: We have analyzed sex, race/ethnicity or socioeconomic disparities in the incidence of metastatic bone disease (MBD).

Methods: Patients with the diagnosis of MBD at presentation for five most common primary anatomical sites was extracted from Surveillance, Epidemiology, and End Results Census tract–level dataset. Mean incidence of MBD for different sex, racial/ethnic and socioeconomic groups were compared.

Results: The five most common anatomical sites with MBD at presentation include "lung: (n = 59 739), "prostate" (n = 19 732), "breast" (n = 16 244), "renal" (n = 7718) and "colon" (n = 3068). There was an increase in incidence of MBD among cancers originating from prostate (annual percentage change [APC] 4.94), renal (APC 2.55), and colon (APC 3.21) ($p < 0.05$ for all). Non-Hispanic Blacks had higher incidence of MBD for prostate and breast primary sites ($p < 0.001$). Non-Hispanic American Indian Alaskan Native had higher incidence of MBD for cancers originating from renal ($p < 0.001$) and colon ($p = 0.049$). A higher incidence of MBD was seen in lower socioeconomic status (SES) groups for the selected sites ($p < 0.001$).

Conclusions: These findings suggest that there are multiple sex-related, racial/ethnic and SES disparities in the incidence of MBD from the 5 most common primary sites. Higher incidence seen among lower SES suggests delay in diagnosis and limited access to screening modalities.

KEYWORDS
bone, dispartiy, metastasis

1 | INTRODUCTION

More than 1.8 million new cases of cancer were expected to be diagnosed in the United States in 2020.[1] The National Cancer Institute (NCI) reported a national expenditure of US$ 150.8 billion in cancer care in 2018.[1] The cost of cancer care is expected to continue to increase with an aging population and expected rising incidence of cancer.[1] Costs are also expected to increase as new and more expensive treatment modalities are adopted as standard of care. The number of cancer survivors is projected to increase to 22.2 million by 2030[1] placing more patients at risk of developing metastatic disease.[2]

Bone is one of the most common sites for cancer metastases.[3,4] Furthermore, the most common malignant process affecting bone is metastatic cancer.[2,5] The prevalence of metastatic bone disease (MBD) in the United States is estimated to be more than 250 000 patients (5.3% of all cancer patients) resulting in an economic burden in excess of 20% of the U.S. cancer care economy.[2,6] Similar MBD prevalence rates (5.13% of prevalent cancer patients) have been reported recently.[3] MBD is associated with significant morbidity and functional compromise. Sarcopenia, cachexia, and pain associated with bony metastases transform a patient's life into one where the primary concern is not only length of life remaining, but the anxiety surrounding the ability to perform simple activities of daily living,[6–8] kinesiophobia and low pain self-efficacy.[9]

Widespread disparities in cancer incidence, prevalence, mortality, survival, morbidity, survivorship, financial burden of disease, screening rates and stage distribution at diagnosis have been reported.[1] However, there are no reports addressing disparities in the incidence of MBD.[10–14] The National Institute of Minority Health and Health Disparities defined health disparities research to encompass health differences in socially disadvantaged populations and specific outcomes, including: (1) higher incidence or prevalence; (2) earlier or higher mortality rate; (3) increased global burden of disease; (4) poorer health behaviors and clinical outcomes related to the previous outcomes; (5) worse outcomes on validated and specific patient reported outcome measures.[15] This report describes sex, racial, and socioeconomic disparities in the incidence of MBD originating from the five most common anatomical sites.

2 | METHODS

Case information was extracted from the NCI's Surveilleance Epidemiology End Results (SEER) program.[1] Presently, SEER collects the data from 22 registries covering approximately 48% of the U.S. population.[1] MBD data was only available after 2010. We utilized the Incidence-SEER 18 Regs Custom Data table (with additional treatment fields), Nov 2018 Sub (2000–2016)' to extract the cases for overall incidence, incidence stratified by gender and gender-socioeconomic status (SES).' The database 'Incidence-SEER 18 Regs excluding AK (with additional treatment fields), Nov 2017 Sub (2000–2015) <Vintage 2015 Pops by Race/Origin Tract 2000/2010 Mixed Geographies>' was used to extract the cases for incidence stratified by race/ethnicity and race/ethnicity-SES. Cases presenting with MBD at diagnosis were analyzed for the most common primary anatomical sites. For this analysis, primary malignancies originating from "trachea and bronchus" were grouped with primary malignancies originating from "lung and pleura." Primary urothelial malignancies ("Urinary collecting system including bladder") were grouped with primaries originating from "kidney and renal pelvis."

Once the most common five primary sites with MBD at the time of diagnosis were determined, incident cases with the selected primaries and MBD at the time of diagnosis were isolated using the SEER*Stat software (version 8.3.8, NCI). Incident cases for each site were further stratified, with respect to gender, race/ethnicity recode and small area-derived SES. To determine the interaction of SES with gender and race/ethnicity, we used two-factor analysis of variance (ANOVA) to determine any modification of effect size. SES was analyzed as a composite index calculated by SEER using the method described by Yost et al.[16] Census tract-level SES indicator variables of median household income, median house value, median rent, percentage of the population below 150% of the poverty line, an education index, percentage of the population with working class occupations and percentage of population older than 16 years in the workforce without a job were utilized.[16] Data are presented as quintiles; Group 1 representing the lowest SES and Group 5 representing the highest SES. Patients diagnosed at the time of death or "autopsy only cases," as well as cases with staging information other than "distant" were also excluded from the analytic cohort.

Incidence rates were age adjusted and normalized using the 2000 U.S. Standard Population. Annual percentage change (APC) was calculated. Student's *t*-tests were used to statistically compare the means of two groups male versus female incidence. "Single factor" and "two-factor with replication" ANOVA was used to compare the means for more than two groups. Two-sided significance levels of ≤0.05 was considered statistically significant.

The study was deemed to be exempt from approval by institutional review board (IRB) at University of California, Davis.

3 | RESULTS

3.1 | Demographics

The five most common anatomical sites with MBD include (1) "lung and pleura" ($n = 56\,534$, 46.3%) and "trachea and bronchus" ($n = 3205$, 2.6%) (total: $n = 59\,739$, 48.9%) (2) "prostate" ($n = 19\,732$, 16.1%) (3) breast ($n = 16\,244$, 13.3%) (4) "kidney and renal pelvis" ($n = 5618$, 4.6%) and "urinary collection system including bladder" ($n = 2100$, 1.7%) (total: $n = 7718$, 6.3%) and (5) "colon" ($n = 3068$, 2.5%). Details of histopathological diagnoses for each of the primary sites are summarized in Table S1.

3.2 | Trends in overall incidence

There has been a statistically significant secular increase in patients presenting with bone metastasis with primary malignancy originating from prostate (APC 4.94; $p < 0.05$ for trend), renal and urothelium (APC 2.55; $p < 0.05$), and colon (APC 3.21; $p < 0.05$) (Figure 1A–C). No statistically significant increase in overall incidence was observed in MBD among patients with lung and breast primaries. All the rates presented are per 100 000 persons.

3.3 | Sex-related disparities

For lung cancer patients with bone metastasis, higher incidence is observed for men compared to women ($p < 0.001$) (Figure 2A).

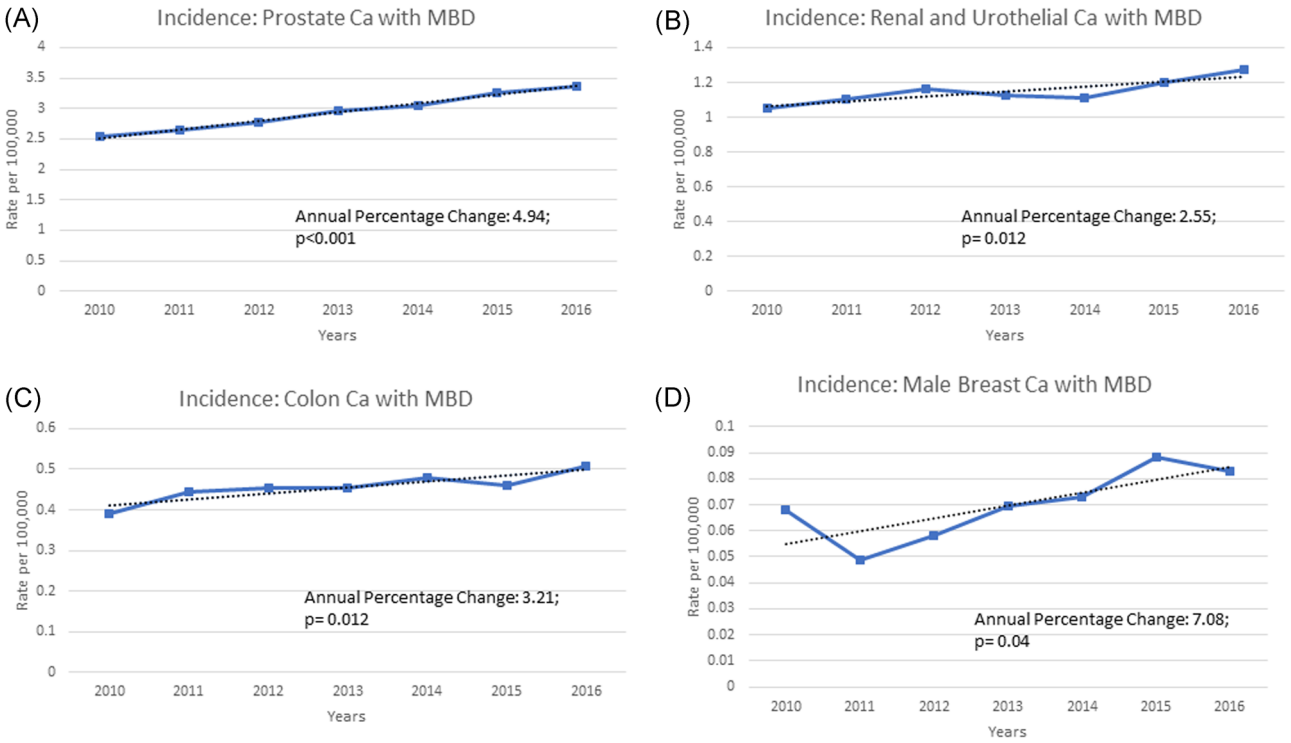

FIGURE 1 Incidence over time: (A) Prostate Ca with metastatic bone disease (MBD), (B) Renal and Urothelial Ca with MBD, (C) Colon Ca with MBD showing statistically significant increase over time (2010–2016), (D) Male breast cancer with MBD showing statistically significant increase over time (2010–2016)

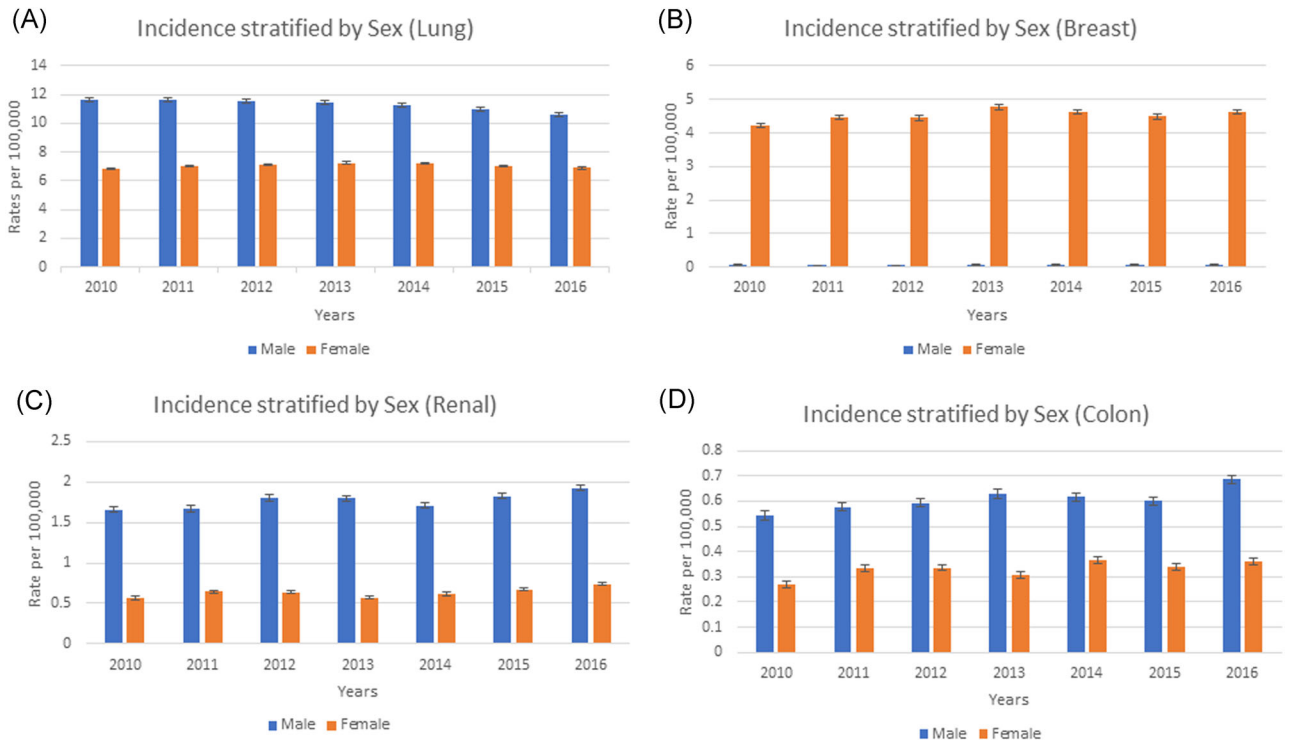

FIGURE 2 Incidence of primary cancers with metastatic bone disease (MBD) over time stratified by sex. (A) Lung cancer with MBD: Statistically significant higher incidence among males as compared to females, *t*-test $p < 0.001$. (B) Breast cancer with MBD: Statistically significant higher incidence among females as compared to males, *t*-test $p < 0.001$. (C) Renal and urothelial cancer with MBD: Statistically significant increase in incidence among males as compared to females, *t*-test $p < 0.001$. (D) Colon cancer with MBD: Statistically significant increase in incidence among males as compared to females, *t*-test $p < 0.001$

However, there has been a decrease in incidence observed among men (APC −1.47; $p < 0.004$). No statistically significant change is observed among women. For breast cancer patients with bone metastasis, higher incidence is observed in females as expected ($p < 0.001$) (Figure 2B), however, there has been a statistically significant increase in incidence among men over time (APC 7.08; $p < 0.05$) (Figure 1D). Increased incidence among men was observed for renal and urothelium ($p < 0.001$), and colon cancer ($p < 0.001$) primaries (Figure 2C,D, respectively). In addition, there was a increase in incidence of MBD among male patients with renal and urothelium (APC 2.09, $p = 0.02$) and colon cancer (APC 3.01, $p = 0.013$).

3.4 | Racial/ethnic disparities

The highest incidence of MBD was observed among Non-Hispanic Blacks (NHB) for primaries originating from lung (average incidence of 10.07 from 2010 to 2015, $p < 0.001$), prostate (average incidence 5.33, $p < 0.001$), and breast (average incidence 3.61, $p < 0.001$) (Figure 3A–C). A statistically significant increase in incidence was seen for Non-Hispanic Whites (NHW) (APC 6.03, $p < 0.001$) and Non-Hispanic Asian/Pacific Islanders (NHAPI) (APC 4.76, $p = 0.049$) with primaries originating from prostate. Highest incidence was observed among Non-Hispanic American Indian Alaskan Native (NHAIAN) for primaries originating from renal and urothelium (1.69 in 2014, $p < 0.001$), and colon (1.01 in 2015, $p = 0.049$) (Figure 3D,E, respectively). On the other hand, NHAIAN (APC −12.28, $p < 0.05$) and Hispanics (APC −2.21, $p < 0.05$) showed a statistically significant decrease in incidence of MBD with breast cancer primaries.

3.5 | SES disparities

Socioeconomic disparities were observed for each of the top five primary MBD sites. For patients with lung cancer, higher incidence was observed among patients belonging to the lower SES groups (9.35 for Group 1 vs. 7.05 for Group 5 in 2016, $p < 0.001$) (Figure 4A). A statistically significant decrease in incidence was observed in SES Group 4 (APC −0.945, $p = 0.029$) over time. For patients with primary prostate carcinoma there is a higher incidence of bone metastasis among patients belonging to lower SES (3.56 for Group 1 vs. 3.07 for Group 5) with p value <0.001 (Figure 4B). All prostate SES groups show statistically significant increases in incidence with highest rate of increase in incidence among the highest SES group with APC = 7.82, $p < 0.001$ for Group 5 versus APC = 2.82, $p < 0.001$ for Group 1. For patients with breast cancer primaries presenting with MBD, a higher incidence was observed in the lowest SES as compared to highest SES (2.59 for Group 1 vs. 2.15 for Group 5 in 2016, $p < 0.001$)

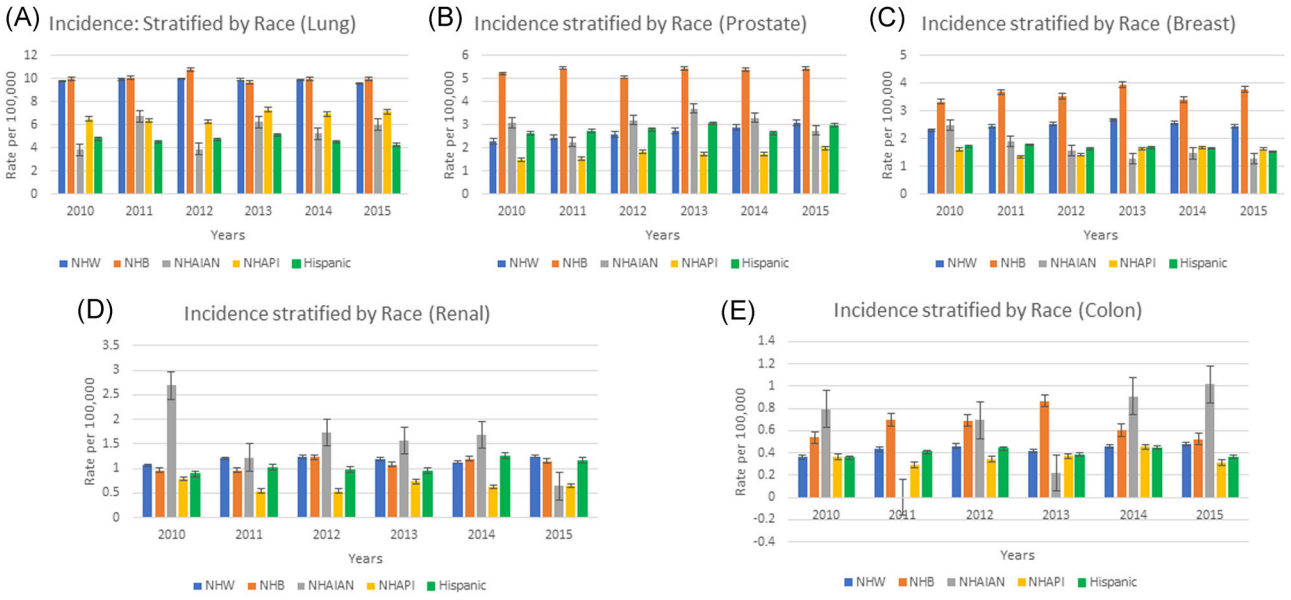

FIGURE 3 Incidence of primary cancers with metastatic bone disease (MBD) over time stratified by race/ethnicity. NHW: Non-Hispanic White, NHB: Non-Hispanic Black, NHAIAN: Non-Hispanic American Indian Alaskan Native, NHAPI: Non-Hispanic Asian Pacific Islanders, Hispanics. (A) Lung cancer with MBD: Statistically significant differences in incidence among patients of different racial ethnic backgrounds (NHW, NHB, NHAIAN, NHAPI, Hispanic), One way ANOVA $p < 0.001$. (B) Prostate cancer with MBD: Statistically significant differences in incidence among patients of different racial ethnic backgrounds (NHW, NHB [highest incidence], NHAIAN, NHAPI, Hispanic), One way ANOVA $p < 0.001$. (C) Breast cancer with MBD: Statistically significant differences in incidence among patients of different racial ethnic backgrounds (NHW, NHB [highest incidence], NHAIAN, NHAPI, Hispanic), One way ANOVA $p < 0.001$. (D) Renal and urothelial cancer with MBD: Statistically significant differences in incidence among patients of different racial ethnic backgrounds (NHW, NHB, NHAIAN [highest incidence], NHAPI, Hispanic), One way ANOVA $p < 0.001$. (E) Colon cancer with MBD: Statistically significant differences in incidence among patients of different racial ethnic backgrounds (NHW, NHB, NHAIAN, NHAPI, Hispanic). One way ANOVA $p = 0.049$. ANOVA, analysis of variance

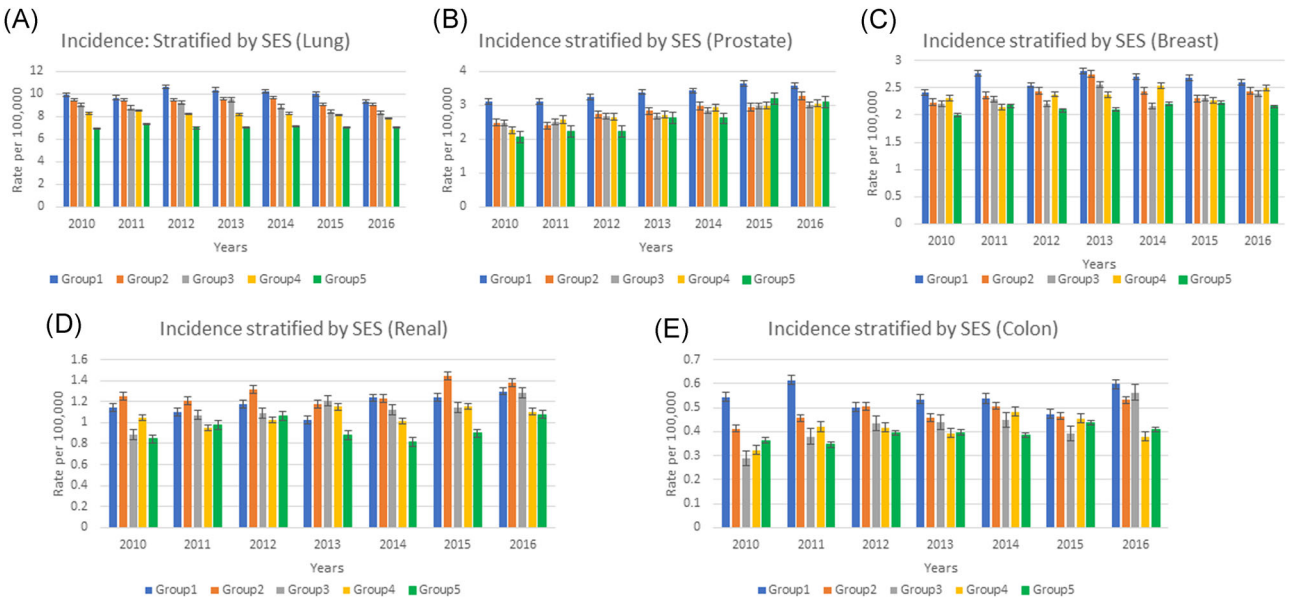

FIGURE 4 Incidence of primary cancers with metastatic bone disease (MBD) over time stratified by socioeconomic status (SES). Group 1 (Lowest) through Group 5 (Highest). (A) Lung cancer with MBD: Statistically significant differences in incidence among patients of different SES groups (higher incidence in lower SES and lower incidence in higher SES), One way ANOVA $p < 0.001$. (B) Prostate cancer with MBD: Statistically significant differences in incidence among patients of different SES groups (higher incidence in lower SES and lower incidence in higher SES), One way ANOVA $p < 0.001$. (C) Breast cancer with MBD: Statistically significant differences in incidence among patients of different SES groups (higher incidence in lower SES and lower incidence in higher SES), One way ANOVA $p < 0.001$. (D) Renal and urothelial cancer with MBD: Statistically significant differences in incidence different SES groups (higher incidence in lower SES and lower incidence in higher SES), One way ANOVA $p < 0.001$. (E) Colon cancer with MBD: Statistically significant differences in incidence among patients of different SES groups (higher incidence in lower SES and lower incidence in higher SES). One way ANOVA $p < 0.001$. ANOVA, analysis of variance; SES, socioeconomic status

(Figure 4C). Among patients with renal and urothelium (1.29 for Group 1 vs. 1.08 for Group 5) and colon (0.6 for Group 1 vs. 0.4 for Group 5) primaries a higher incidence of MBD was seen among patients with lower SES with $p < 0.001$ (Figure 4D,E, respectively). For colon cancer patients presenting with MBD a statistically significant increase was observed in SES Group 3 (APC = 4.34 and $p = 0.02$) and Group 5 (APC = 2.88 and $p = 0.028$).

3.6 | Sex/SES disparities

For patients with lung cancer presenting with MBD, a statistically significant higher incidence was observed with male sex and lower SES. Two-factor ANOVA revealed statistically significant differences for sex, SES and a sex*SES interaction ($p < 0.001$ for each) (Figure 5A). A statistically significance interaction term suggests effect modification for sex by SES. For breast cancer primaries with MBD at diagnosis, higher incidence was seen with female sex and a lower SES. Statistically significance differences ($p < 0.001$) were observed for sex, SES and sex*SES (Figure 5B). For patients with primary tumors originating from renal and urothelium, higher incidence was seen for male sex and lower SES. Statistical significance ($p < 0.001$) was observed for gender and SES on two-factor ANOVA. However, sex*SES interaction did not achieve statistical significance (Figure 5C). Patients with colon cancer presenting with MBD showed increased incidence for male sex and lower SES. Significant colon cancer differences were observed on two-factor ANOVA ($p < 0.001$ for sex, SES and sex*SES) (Figure 5D). Of note, SES Group 3 (APC 7.55, $p = 0.03$) and Group 5 (APC 2.88, $p = 0.03$) showed statistically significant increase in overall incidence of MBD among patients with colon cancer over 2010–2016. Males in Group 3 SES (APC 9.30, $p = 0.03$) with colon cancer also showed a statistically significant increase in MBD over the study period.

3.7 | Racial/ethnic*SES disparities

Lung cancer patients with MBD had higher incidence among NHW and lower SES group (Figure 6A). Statistical significance was achieved on two-factor ANOVA with $p < 0.001$ for race/ethnicity, SES and race/ethnicity*SES. Patients with primary cancer originating from prostate demonstrated racial/ethnic ($p < 0.001$) and SES disparities ($p = 0.027$) with higher incidence among NHB and lower SES strata (Figure 6B). Of note, NHW demonstrated statistically significant increase in incidence of MBD among patients with prostate cancer across all SES strata (Group 1: APC 6.34, $p = 0.002$; Group 2: APC 5.84, $p = 0.02$; Group 3: APC 3.65, $p = 0.007$; Group 4: APC 5.75, $p = 0.033$; Group 5: APC 8.80, $p = 0.003$). NHAPI patients with prostate cancer showed a statistically significant increase in MBD among patients with the highest SES group

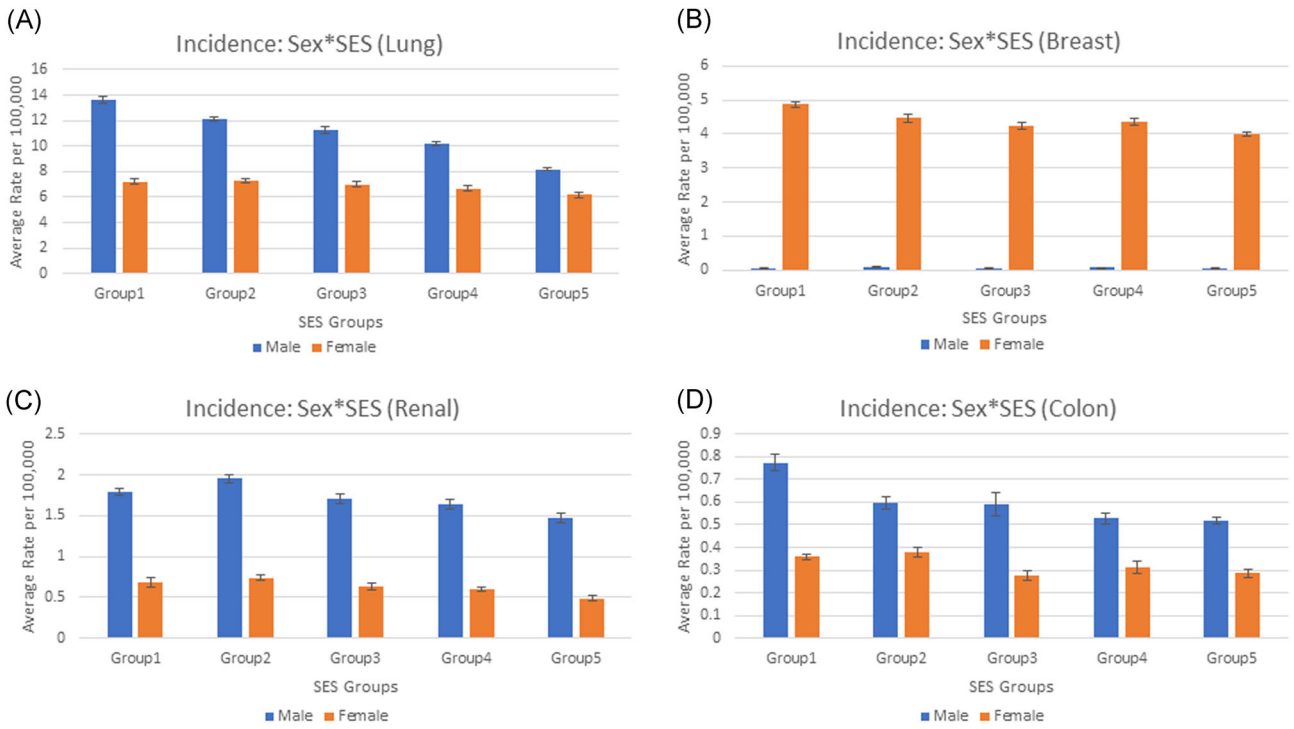

FIGURE 5 Incidence of primary cancer with metastatic bone disease over time stratified by sex and SES. (A) Lung cancer with MBD: Two-factor ANOVA revealed a significant effect of sex ($p < 0.001$) and effect of SES ($p < 0.001$) on incidence. There was a statistically significant interaction between effect of sex and effect of SES on incidence was also observed ($F(4, 60) = 45$, $p < 0.001$). (b) Breast cancer with MBD: Two-factor ANOVA revealed a significant effect of sex ($p < 0.001$) and effect of SES ($p < 0.001$) on incidence. There was a statistically significant interaction between effect of sex and effect of SES on incidence was also observed ($F(4, 60) = 10.9$, $p < 0.001$).(C) Renal and urothelial cancer with MBD: Two-factor ANOVA revealed a significant effect of sex ($p < 0.001$) and effect of SES ($p < 0.001$) on incidence. (D) Colon cancer with MBD: Two-factor ANOVA revealed a significant effect of sex ($p < 0.001$) and effect of SES ($p < 0.001$) on incidence. There was a statistically significant interaction between effect of sex and effect of SES on incidence was also observed ($F(4, 60) = 4.9$, $p = 0.002$). ANOVA, analysis of variance; SES, socioeconomic status

(APC 8.79, $p = 0.03$). Patients with breast cancer presenting with MBD at diagnosis demonstrated statistical significance only for the effect of race/ethnicity when co-factored with SES on two-factor ANOVA (Figure 6C). A statistically significant interaction between the effects of race/ethnicity and the effect of SES on breast cancer with MBD was also observed ($F(16, 125) = 1.79$, $p = 0.038$). NHB have the highest average incidence of all racial/ethnic groups. Among different NHB SES groups a statistically significant increase in incidence over time was observed for SES Group 4 (APC 6.92, $p < 0.05$) and statistically significant decrease over time was observed for for NHB SES Group 5 (APC −9.22, $p < 0.05$). Patients with renal and bladder cancer presenting with MBD demonstrated racial/ethnic ($p < 0.001$), SES ($p = 0.001$) and disparities in incidence (Figure 6D). There was significant interaction between effect of race/ethnicity and effect of SES on incidence ($p < 0.001$). NHW demonstrated statistically significant increase in incidence over 2010–2105 for SES Group 3 (APC 7.02, $p < 0.05$). Similar increase was observed among Hispanics for SES Group 1 (APC 12.1, $p < 0.05$) and Group 5 (APC 6.24, $p < 0.05$). Analysis of patients with colon cancer presenting with MBD demonstrated only SES disparities with highest incidence in lowest SES group ($p = 0.003$) (Figure 6E).

4 | DISCUSSION

The current study highlights multiple sex-related, racial/ethnic, and SES disparities in the most common malignant process affecting bone. There are a number of inferences that can be made in light of these results. A higher incidence of MBD largely observed among lower SES suggests that those who are relatively disadvantaged have limited access to primary screening modalities, delay in diagnosis related to health care costs, possible differences in subsequent cancer care delivery and advanced stage at presentation. Sex and racial/ethnic disparity trends are more variable and appear to be specific to the site of primary cancer.

To our knowledge, this is the largest and most detailed account of disparities in MBD, to date. Among common sites for distant metastases, for example, lung, liver, bone and brain, metastatic lesions often appear first in the bone.[4] Recent evidence suggests a substantial proportion of metastases in other organs arise from initial metastases to bone.[4,17,18] If clinically confirmed, recognition and strategies to address disparities in MBD would have far reaching impact on all patients with metastatic disease.

The findings should prompt a high degree of suspicion and screening among at risk strata to facilitate earlier diagnosis and

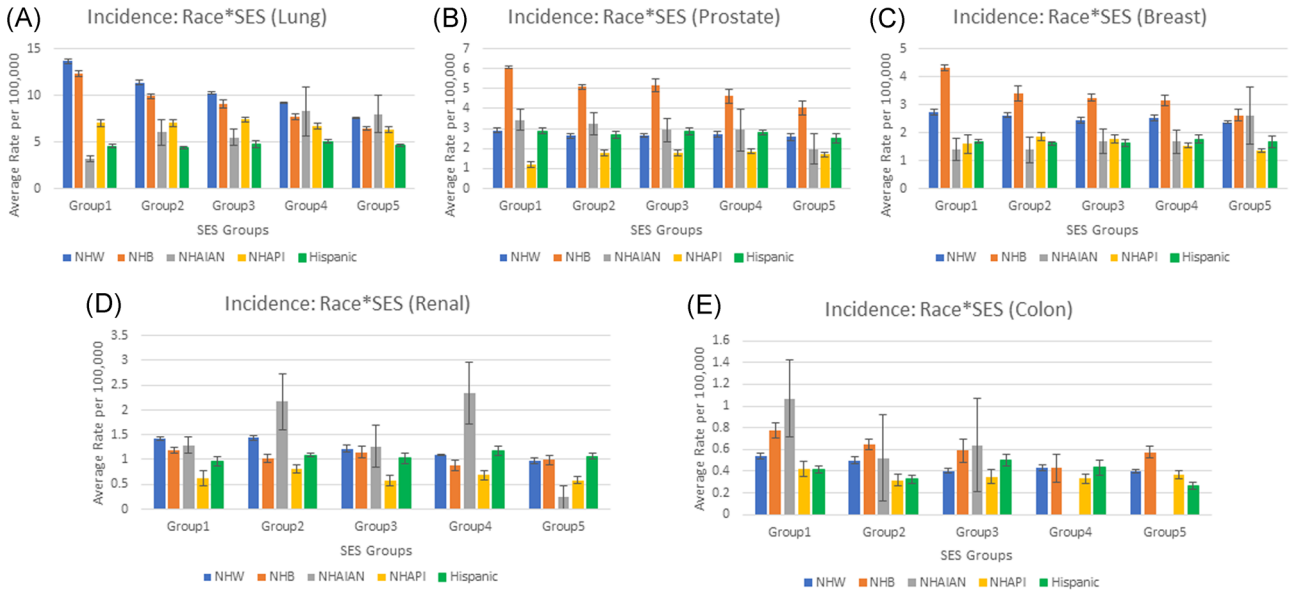

FIGURE 6 Incidence of primary cancer with metastatic bone disease over time stratified by race and SES. (A) Lung cancer with MBD: Two-factor ANOVA revealed a significant effect of race ($p < 0.001$) and effect of SES ($p = 0.031$) on incidence. There was a statistically significant interaction between effect of race and effect of SES on incidence was also observed ($F(16, 125) = 5.4$, $p < 0.001$). (B) Prostate cancer with MBD: Two-factor ANOVA revealed a significant effect of race ($p < 0.001$) and effect of SES ($p = 0.027$) on incidence. (C) Breast cancer with MBD: Two-factor ANOVA revealed a significant effect of race ($p < 0.001$) on incidence. There was a statistically significant interaction between effect of race and effect of SES on incidence was also observed ($F(16, 125) = 1.79$, $p = 0.038$). (D) Renal and urothelial cancer with MBD: Two-factor ANOVA revealed a significant effect of race ($p < 0.001$) and effect of SES ($p < 0.001$) on incidence. There was a statistically significant interaction between effect of race and effect of SES on incidence was also observed ($F(16, 125) = 3.18$, $p < 0.001$). (E) Colon cancer with MBD: Two-factor ANOVA revealed a significant effect of SES ($p < 0.001$) on incidence. ANOVA, analysis of variance; SES, socioeconomic status

subsequent earlier access to care. The findings are also important for public health policy. Policy level changes are stipulated to mandate resource allocation towards early detection and treatment for patients in the lower socioeconomic strata and certain sex and racial/ethnic groups for specific primary cancers. Considering the sentinel role of orthopaedic oncologists for managing bone metastases, impending and pathologic fractures, it is important information for focusing clinical evaluation and management to prioritize identification of metasis in at-risk groups.

Other studies have highlighted the disparity in incidence of carcinomas originating in the most common primary sites contributing to MBD.[19–25] Zhang et al.[18] recently reported sex-related and racial/ethnic disparities in the incidence of lung cancer from 1974 to 2015.[22] They reported a higher incidence among men, with a decreasing gender gap over time. The decrease in the incidence of lung cancer over time was observed among men and, in a delayed fashion, among women. In the current study, a higher incidence of lung cancer with MBD was seen among men with a statistically significant decrease from 2010 to 2016. No significant changes were observed in the incidence of lung cancer with MBD among women, thus decreasing the gender gap. Zhang et al.[18] further reported a higher incidence of lung cancer among blacks, a finding also observed in lung cancer patients presenting with MBD.[22] The current study highlights the impact of lower SES on incidence of lung cancer presenting with MBD. In addition, we have demonstrated the mutual interaction of gender/SES and race/ethnicity/SES.

Badal et al have highlighted the racial/ethnic disparity in prostate cancer and proposed possible SES disparities.[23] The current investigation reports the highest overall incidence of prostate cancer with MBD among NHB. However, there is also a significant increase in incidence seen among NHW from 2010 to 2015. The present study further highlights the important association between SES and incidence of disease with MBD. This could potentially represent a disparity in allocation of health care resources by SES for detection of bone metastasis. Another important finding of the current investigation is the lack of association between SES on incidence of prostate cancer with MBD among NHB, raising the possibility that underlying biological mechanisms may at least partially explain racial/ethnic disparities.[23] A significant increase in incidence of prostate cancer with MBD was seen among all SES strata for NHW and for highest SES stratum for NHAPI.

Paradoxical racial disparities in incidence and outcomes for breast cancer have been reported with higher incidence among whites and higher mortality among blacks despite having a lower incidence.[21,24,26] DeSantis et al.[26] reported an observed increase seen in the incidence of breast cancer from 2012 to 2016.[26] The increase in incidence was largely attributed to increase in incidence of "local" stage disease. The incidence of "distant" stage disease was stable since 2011.[26] The current analysis confirms their findings among breast cancer patients presenting with MBD. DeSantis et al.[26] also reported highest incidence of breast cancer among NHW women followed by NHB women. The rate of increase in incidence

was similar among NHW and NHB women. An analysis of the incidence of different stages of breast cancer stratified by race/ethnicity, however, was lacking. This investigation demonstrates that NHB have the highest incidence of breast cancer with MBD. This finding highlights the possible role of delay in diagnosis and treatment and provides a potential explanation for the high mortality rate observed. However, other factors such as reluctance to accept aggressive treatment regimens, and more aggressive cancer biology in a racial/ethnic minority cannot be ruled out. Hendrick et al.[27] have shown that a higher proportion of minority women are diagnosed with breast cancer at a younger age and advanced stage. The current study also demonstrated the highest incidence for the lowest SES and the lowest incidence for the highest SES for breast cancer with MBD on simple effect analysis. There appeared to be effect modification of the associations between race/ethnicity and SES with respect to the incidence of breast cancer with MBD, with only race/ethnicity retaining an effect. An interaction between the effect of SES and the effect of race/ethnicity was also observed.

Lucca et al.[20] reported a sex-related paradoxical disparity in incidence and outcomes, where renal and urothelial cancers had higher incidence among men but had higher mortality among women. The current investigation showed a higher incidence of renal and urothelial malignancies with MBD among men, which was consistent with the prior study by Lucca et al.[20] Male patients continued to have higher incidence for each SES stratum. The current investigation also demonstrated racial/ethnic disparity in incidence of kidney and urothelial malignancies with MBD. The highest incidence was seen was NHAIAN. An interaction between the effect of SES and the effect of race/ethnicity on incidence of kidney and urothelial malignancies with MBD was also observed.

Racial disparities have been implicated in the incidence of colon cancer and distant stage at diagnosis.[19,25] The current investigation showed sex-related (M > F) disparity in the incidence of colon cancer presenting with MBD. A higher incidence was also observed among the lowest SES group. The analysis of gender-related and SES disparities showed statistical significance for gender, SES and their interaction. On the other hand, a higher incidence was observed among NHB, but when analyzed with SES, racial/ethnic disparities were not statistically significant. This finding indicates that observed racial/ethnic disparities in incidence of advanced stage colon cancer are attributable to other underlying factors.

A limitation of the current study is the lack of incident data for primary sites without MBD. It is beyond the scope of the investigation to assess incidence data for all the primary sites stratified by sex, race/ethnicity and SES for direct comparison. The incidence data reported here is collected from less than 50% of the U.S. population, based upon the SEER reporting.[1] This data is only representing the patients that present with MBD at the time of initial diagnosis. The data does not cover the patients who develop metastasis after the initial diagnosis. So, the data presented here is a conservative estimate.

Nonetheless, this data can be used to direct allocation of public health funds towards awareness and screening among high-risk patient groups to facilitate early diagnosis and access to care. This analysis of sex-related, racial/ethnic and SES disparities in the incidence of MBD is novel and clinically relevant for multiple medical subspecialities and policy groups.

FUNDING INFORMATION

Funding information is not available.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

R. Lor Randall, Steven W. Thorpe, Brad H. Pollock, and Barton L. Wise: conception and editing. **Amy Cizik and Betty Ferrell**: data extraction. **Lauren N. Zeitlinger, Edmond F. O' Donnell, and Janai R. Carr-Ascher**: analysis. **Muhammad Umar Jawad**: manuscript prepration.

DATA AVAILABILITY STATEMENT

Availability of Data and Material: Available at https://seer.cancer.gov/data-software/

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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