Published in final edited form as:

JCO Oncol Pract. 2024 August ; 20(8): 1064–1074. doi:10.1200/OP.23.00591.

Receipt of Guideline-Concordant Care is Associated with Improved Survival in Patients with Osteosarcoma in California: a Population-Based Analysis

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Abstract

PURPOSE—To examine the relationship between guideline-concordant care (GCC) based on national clinical practice guidelines and survival in children (0–14 years), adolescents and young adults (AYAs, 15–39 years), and adults (≥40 years) with osteosarcoma; and to identify sociodemographic and clinical factors associated with receipt of GCC and survival.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The authors declare no conflict of interest.

METHODS—We used data from the California Cancer Registry (CCR) on patients diagnosed with osteosarcoma during 2004–2019, with detailed treatment information extracted from the CCR text fields, including chemotherapy regimens. Multivariable logistic and Cox proportional hazard regression were used for statistical analyses.

RESULTS—Of 1,716 patients, only 47% received GCC, with variation by age at diagnosis: 67% of children, 43% of AYAs, and 30% of adults. In multivariable models, patients who received part or all care (vs none) at specialized cancer centers were more likely to receive GCC. AYAs and adults were less likely to receive GCC than children ((Odds Ratio (OR)=0.38, 95% Confidence Interval (CI) 0.30–0.50 and OR=0.40, CI 0.28–0.56, respectively). In a model excluding adults, patients treated by pediatric (vs medical) oncologists were more likely to receive GCC (OR=3.44, CI 2.40–4.94). Patients with metastatic osteosarcoma at diagnosis who did not receive GCC had a greater hazard of death (Hazard Ratio (HR)=2.02, CI 1.55–2.63), but no statistical differences were found in those diagnosed at earlier stages (HR=1.15, CI 0.92–1.43).

CONCLUSIONS—GCC was associated with improved survival in patients with metastatic osteosarcoma in California. However, we found disparities in the delivery of GCC, highlighting the need for target interventions to improve delivery of GCC in this patient population.

Keywords

Osteosarcoma; guideline-concordant care; population-based; children; adolescents and young adults; adults; specialized cancer center

INTRODUCTION

Osteosarcoma is the most frequent primary malignancy of the bone[1] and its management requires a multidisciplinary team of specialists, such as pediatric and medical oncologists, and orthopedic oncology surgeons.[2,3] The treatment of osteosarcoma includes resection of the primary tumor and any metastases, and also intensive systemic chemotherapy. Radiation is reserved for selected patients, such as those with unresectable tumors.[3] Over the last 30 years, after the addition of chemotherapy to surgical treatment, survival after osteosarcoma has greatly improved for patients with localized disease, with 5-year event-free survival (EFS) increasing from 20% to approximately 60–70%.[1] However, 5-year EFS remains only 30% or less for those diagnosed with metastatic disease.[1] Clinical practice guidelines based on clinical trials, such as the Children's Oncology Group (COG) and the National Comprehensive Cancer Network (NCCN), were created to help clinicians deliver the best treatment available to their patients[4] and thus improving survival.[5–7]

In the United States (US), receipt of guideline-concordant care (GCC), may vary according to primary tumor site, age at diagnosis, the presence of comorbidities, location of care, and other factors not yet identified.[4–8] However, to our knowledge, no population-based study in the US has assessed GCC patterns or associations with survival for patients diagnosed with osteosarcoma. Much of what is known about the treatment of these patients comes from single institution studies or clinical trials.[9–11] Therefore, we sought to examine factors associated with delivery of GCC in osteosarcoma patients and investigate whether GCC is associated with survival after accounting for clinical and sociodemographic factors.

MATERIAL AND METHODS

Study Setting and Study Population

We conducted a population-based study using data from the California Cancer Registry (CCR). We identified all children (0–14 years), AYAs (15–39 years), and adults (≥40 years) diagnosed with a primary invasive osteosarcoma from January 1st, 2004 to December 31st, 2019. We included morphology codes based on the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) (codes 9180–9187, 9192–9210). Patients with cancer diagnosed by autopsy or death certificate only were excluded (n=11).

Guideline-Concordant Care (GCC) Definition

Treatment data were obtained from the CCR text fields, which contain detailed information on chemotherapy regimens, surgery, and radiotherapy. Initial systemic chemotherapy treatments available in unstructured text fields in CCR were categorized into the following regimens: MAP (methotrexate, adriamycin/doxorubicin and cisplatin), AP (adriamycin, cisplatin), MAP/I +/− E (methotrexate, adriamycin, cisplatin, ifosfamide, etopside), AIM (adriamycin, ifosfamide, mesna), other methotrexate containing regimens, and other. Clinical trial participation was defined based on notation in the text fields indicating that the patient was on a trial and the timeframe corresponded to the trial being open.

GCC was defined based on the NCCN Clinical Practice Guidelines in Oncology for Bone Cancer,[3] COG[10] and European Society for Medical Oncology (ESMO) guidelines.[12] These guidelines recommend that patients with a diagnosis of osteosarcoma undergo definitive local treatment with surgery and also receive systemic chemotherapy. Exceptions include patients with low or intermediate grade parosteal or periosteal osteosarcoma who can be treated with surgery only,[13] and patients with pelvic tumors who can receive radiation treatment and do not undergo surgery.[3] We defined the recommended frontline chemotherapy regimens to include high dose MAP (<40 years) or AP for patients aged ≥40 years. In addition, patients who participated in clinical trials were considered recipients of GCC. The contribution of local control (surgery and radiation) and chemotherapy to GCC, overall and by age group, is shown in Supplemental Table S1.

Sociodemographic and other Clinical Variables

Sociodemographic variables included age group at diagnosis, sex, race/ethnicity (Non-Hispanic (NH) White, NH Black/African American, Hispanic, NH Asian/Pacific Islander, other/unknown), health insurance status at diagnosis (private, public, uninsured, unknown), initial treatment (chemotherapy, surgery, radiation), neighborhood socioeconomic status (nSES) at diagnosis, and area of residence (rural/urban). For health insurance, we analyzed patients with public and no insurance combined, as patients newly diagnosed with cancer in California who are uninsured are often eligible for Medicaid insurance at time of diagnosis. Neighborhood SES (nSES) is a composite measure of seven indicators of education, poverty, and unemployment rate at the census block-group level, and was categorized as high, middle or low.[14]

Clinical variables included cancer stage at diagnosis (metastatic or non-metastatic (localized/regional)), tumor size (0–5, 5.1–10, >10 cm or unknown), anatomic site (extremity, pelvis, other bone, extraskeletal osteosarcoma), Charlson comorbidity index (yes, no, unknown), treatment at a specialized cancer center (SCC), and treating specialty. We categorized patients as receiving all, part or no treatment at SCCs, which were defined as COG member institutions and National Cancer Institute-Designated Comprehensive Cancer Centers (NCI-CCCs) for patients aged up to 21 years and NCI-CCCs for those older than 21 years. Treating specialty was defined by the primary specialty of the physicians treating each patient (pediatric oncology, medical oncology, orthopedic oncology, surgical oncology, radiation oncology). Pediatric oncology specialty was restricted to the analyses of children and AYAs because no older adults were treated by this specialty.

Statistical Analysis

We estimated overall (all-cause) survival using the Kaplan Meier method and used the log-rank test to compare differences in survival between groups. We used multivariable logistic regression to evaluate factors associated with receipt of GCC and multivariable Cox proportional hazard regression to investigate factors related to overall survival. Survival time was calculated from the date of osteosarcoma diagnosis to the date of death from any cause, loss to follow-up or end of the study (April, 2022), whichever occurred first. We assessed proportional hazard assumptions by inspection of the survival curves for all variables in the model. None of the variables violated proportional hazards assumption, thus all were included in the models. We tested for interactions between receipt of GCC and treatment at SCCs and between receipt of GCC and stage at diagnosis with survival. Results are reported as odds ratios (OR) or hazard ratios (HR) and corresponding 95% confidence intervals (CI). All statistical analyses were performed using SAS 9.4 (SAS, Cary, NC). All p-values were two-sided. Results with p-values<0.05 were considered statistically significance. All analyses were overseen by the Institutional Review Board of the University of California, Davis.

RESULTS

Patient Sociodemographic and Clinical Characteristics

Of 1,716 patients diagnosed with osteosarcoma, 515 (30%) were children, 768 (45%) were AYAs, and 433 (25%) were adults (Table 1). Most patients were male (57%), lived in urban areas (88%), and had private insurance at diagnosis (55%). The highest proportion of patients were of Hispanic race/ethnicity (43%) and resided in the lowest nSES (37%) category. Most patients were diagnosed with non-metastatic disease and had tumors larger than 5cm (72% and 71% respectively). Osteosarcoma of the extremity was the most common anatomic site across all age groups (73%). Few children (11%) and AYAs (15%) had comorbidities at diagnosis, with a higher proportion occurring among adults (35%).

Overall, approximately 10% of patients participated in clinical trials, with participation varying by age group (Table 1). A total of 807 (47%) patients received GCC, with a higher proportion of children receiving GCC (67%) compared to AYAs (43%) and adults (30%). Most patients received part or all treatment at SCCs (63%), but this also differed by age

group (79% children, 66% AYAs, and 41% adults). Most children (62%) were treated by pediatric oncologists, compared with only 27% of AYAs.

Factors Related to Receipt of GCC

In multivariable models, patients who received part of their treatment (OR=2.53, CI 1.93–3.33) or all treatment (OR=1.56, CI 1.19–2.04) at SCCs were more likely to have received GCC than those who received no treatment at these centers (Table 2). Patients of NH Asian/Pacific Islander (vs. NH White) race/ethnicity (OR=1.45, CI 1.03–2.11) and those residing in the highest (vs lowest) sociodemographic neighborhoods (OR=1.59, CI 1.17–2.14) or rural (vs urban) regions (OR=1.66, CI 1.18–2.32) were also more likely to receive GCC. In a cohort restricted to children and AYAs, we found that patients treated by pediatric oncologists (vs medical oncologists) were more likely to receive GCC (OR= 3.44, CI 2.40–4.94) (Figure 1).

Factors associated with decreased receipt of GCC included patients with metastatic osteosarcoma (vs localized/regional disease, OR=0.66, CI 0.51–0.86) and non-extremity disease (e.g., pelvis, OR=0.53, CI 0.34–0.82) (Table 2). Further, we observed that, compared with children, AYAs (OR=0.38, CI 0.30–0.50) and adults (OR=0.40, CI 0.28–0.56) were less likely to receive GCC. Sex, health insurance, tumor size, and presence of comorbidities were not associated with receipt of GCC in our cohort.

Factors Associated with Survival

The median follow-up time after osteosarcoma diagnosis was 3.6 years (interquartile range 1.5–8.8). At the end of study follow-up, 29% of children, 38% of AYAs, and 62% of adults had died. Overall, 5-year overall survival was higher among patients who received GCC, though for children the result was not statistically significant (Figure 2A–C): 74.1% vs 69.3%, p=0.224 for children; 65.2% vs. 58.1%, p=0.023 for AYAs; and 50.9% vs 30.9%, p<0.001 for adults.

In the multivariable survival analysis, we found and interaction between receipt of GCC and stage at diagnosis (p<0.001). Therefore, the analysis was stratified by stage. Patients with metastatic disease who did not receive GCC had worse overall survival than those who were treated according to clinical guidelines (HR=2.02, CI 1.55–2.63) (Table 3), but results did not reach statistical significance for patients with non-metastatic disease (HR=1.15, CI 0.92–1.43). This finding was similar across age groups (data not shown). Among patients diagnosed with non-metastatic disease, other clinical factors associated with worse survival were anatomic site other than extremity osteosarcoma, tumor size >5cm, and the presence of comorbidities. When we evaluated the relation of age with survival, we found that AYAs diagnosed with both metastatic and non-metastatic disease, as well as adults diagnosed with non-metastatic disease, were more likely to die than children. In addition, publicly or uninsured patients (vs privately insured) with non-metastatic osteosarcoma, and those with metastatic disease living in the low or middle (vs high) SES neighborhoods experienced worse survival. Survival was markedly better among patients who received all initial treatment at SCCs compared to those who did not receive treatment at these centers (HR=0.61, CI 0.43–0.86 for patients with metastatic disease and HR=0.61, CI 0.46–0.80 for

those with non-metastatic disease at diagnosis). There was no interaction between receipt of GCC and treatment facility (p=0.208). We did not find differences in survival by sex, race/ethnicity or area of residence (rural/urban). In children and AYAs, we found no associations between medical specialty and survival (Supplemental Table S2).

DISCUSSION

In this large population-based study, we identified that GCC was associated with improved survival among patients with metastatic osteosarcoma at diagnosis, but results did not reach statistical significance for patients diagnosed at earlier stages. Despite this survival advantage with GCC, we found that patients with metastatic disease were less likely to receive GCC. Management of patients with osteosarcoma is complex, particularly for those diagnosed with metastatic disease. For example, patients with unresectable metastatic disease should undergo chemotherapy, radiation, and be reassessed as appropriate for local control. Those with resectable metastatic disease need preoperative chemotherapy followed by metastasectomy or stereotactic radiation or ablation (if pulmonary metastasectomy is not feasible).[3] However, disparities in the delivery of GCC exist. The majority of patients with osteosarcoma did not receive GCC in California, with GCC varying by age at diagnosis, nSES, and location of care. Specifically, we observed that only 43% of AYAs and 30% of adults received GCC compared to 67% of children. In addition, patients who resided in the lower SES neighborhoods and those who did not receive care at SCCs were less likely to receive GCC. These findings are concerning and may contribute to disparities in survival we observed in patients with osteosarcoma.[15–17] To our knowledge, this is the first population-based study to provide information on the delivery of osteosarcoma clinical guidelines in the US and to compare the results across age groups.

Our findings of 47% of patients with osteosarcoma receiving GCC is lower than a single institution study in the US that found 67% of AYAs with osteosarcoma or Ewing sarcoma received GCC,[18] but higher than a French study on patients with soft tissue sarcoma (STS).[8] The French study examined 127 patients ages 0–25 diagnosed with STS and observed that only 41% of patients were treated according to international guidelines. Importantly, STS event-free survival was superior when the 5 guideline criteria were followed compared to ≤ 4 criteria were met.[8] Although not on osteosarcoma, other studies reporting on treatment according to NCCN guidelines found that this varied from 80%–97% depending on the cancer site, age at diagnosis, comorbidities, and reporting facility for patients with lung, anal, rectum, cervical, and nasopharynx cancer.[4] Our findings highlight the need for cancer care delivery interventions to improve compliance to clinical practice guidelines, especially for older patients.

We observed that patients aged less than 40 treated by medical (vs pediatric) oncologists were less likely to receive GCC, underscoring the importance of collaboration between medical and pediatric oncologists in the treatment of AYAs. A national study in France examined the impact of compulsory patient case presentation before treatment to a multidisciplinary tumor board (MDTB) on survival of patients aged >14 years diagnosed with STS and visceral sarcoma.[19] The MDTB included, among others, pediatric and medical oncologists. The study found that presentation to a MDTB before treatment was associated

with increased adherence to clinical guidelines and improved relapse-free survival. A more recent French study included patients with osteosarcoma and emphasized the need for presentation of patients to a MDTB that include both pediatric and medical oncologists in the diagnostic phase, before any treatment is delivered.[20] Our findings suggest that involvement of pediatric oncologists in the care of AYA patients with osteosarcoma could improve delivery of GCC and presentation at a MDTB inclusive of both pediatric and medical oncologists could be one way to approach this.

We demonstrated that patients who received treatment at SCCs were more likely to receive GCC. Interestingly, this finding was more pronounced among patients who received part (vs all) of their treatment at these centers. Our findings may relate to care at SCCs focusing on specific services, such as surgery or specialized diagnostics, with local facilities overseen by SCCs administering radiation and/or chemotherapy to optimize the overall treatment plan. Receiving care closer to the patient's home may enhance adherence to GCC. In Europe[13] and in the US[3], national guidelines recommend referral of patients with osteosarcoma to SCCs. At these centers, tumor-specific cancer treatment can be delivered by a highly specialized team of clinicians. It has been shown that pre-treatment tumor biopsy, pre-treatment imaging, and neoadjuvant chemotherapy were performed more often in specialized sarcoma centers.[20] In addition, established treatment guidelines that are based on the results of collaborative clinical trials or established treatment protocols are more often followed at SCCs.[13] SCCs also provide comprehensive supportive care, which include modern and innovative intensive care units, specialist nurses, and psychologists, that has been shown to be associated with improved survival.[2,21,22] Efforts should be made to increase early referral of osteosarcoma patients to SCCs in order to help improve survival outcomes in this patient population.

Our study additionally demonstrated that several sociodemographic factors influenced delivery of GCC. For example, patients of NH Asian/Pacific Islander race/ethnicity and those who resided rural areas or in higher SES neighborhoods were more likely to receive GCC. Our race/ethnicity findings differ from a study using data from the NCI-Surveillance Epidemiology and End Results (SEER) Program, which found that NH Black/African American and NH Asian/Pacific Islander patients with osteosarcoma were less likely to undergo primary surgery than NH Whites.[23] However, our study also considered radiation and systemic chemotherapy for GCC. In addition, our results are consistent with studies that found that cancer patients residing in rural areas are more likely to receive GCC ("the urban-rural paradox"), when distance to the treating facility is not consistently associated with care delivered.[24] This paradox has been partially explained by patients living in rural more commonly traveling longer distances[25] and more often have their own transportation. Further, this study demonstrated lower delivery of GCC among patients living in low and middle SES neighborhoods, which is consistent with previous reports that observed lower delivery of GCC among patients living in neighborhoods of lower SES. These findings indicate that there are factors beyond stage at diagnosis that continue to impact delivery of optimal care for patients with osteosarcoma.[26]

Our study has several limitations. We did not have information on whether pre-treatment imaging and pre-treatment tumor biopsy were performed. We also did not have detailed

data on microscopically residual disease or on the quality of surgery performed (complete resection or not). Further, treating specialty was defined by hospital first admission, therefore we may not have captured some encounters with additional specialists. This could potentially explain why a higher than anticipated proportion of patients under the age of 15 years were not recorded as being treated by a pediatric oncologist. The strengths of our study include a large population-based cohort, detailed information on first-line chemotherapy, primary surgery, and radiation data available in the CCR text fields. In addition, we examined the associations between treating physicians, location of care, and receipt of GCC and survival. Furthermore, CCR has sociodemographic data that allowed us to identify disparities in the receipt of GCC.

In conclusion, to our knowledge, this is the first population-based study to provide information on the “real world” delivery of GCC for patients with osteosarcoma in the US. Our study revealed that less than half of patients received GCC for osteosarcoma in the large and diverse state of California and confirmed that receipt of GCC was associated with improved survival for patients diagnosed with metastatic disease. However, patients with metastatic disease were less likely to receive GCC. AYAs, adults and patients residing in lower SES neighborhoods had less access to GCC, highlighting areas for interventions to improve delivery of GCC. Importantly, we reinforced the importance of referring patients newly diagnosed with osteosarcoma to SCCs, where GCC treatment is more likely to be delivered by a highly specialized multidisciplinary team.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENT

This study was funded in part by The Doris Duke Charitable Foundation COVID-19 Fund to Retain Clinical Scientists (EMA) awarded to UC Davis School of Medicine by the Burroughs Wellcome Fund and the UC Davis Comprehensive Cancer Center (P30CA093373) and Keaton’s Child Cancer Alliance (EMA). The collection of cancer incidence data used in this study was supported by the California Department of Public Health pursuant to California Health and Safety Code Section 103885; Centers for Disease Control and Prevention’s (CDC) National Program of Cancer Registries, under cooperative agreement 5NU58DP006344; the NCI’s Surveillance, Epidemiology and End Results (SEER) Program under contract HHSN261201800032I awarded to the University of California, San Francisco, contract HHSN261201800015I awarded to the University of Southern California, and contract HHSN261201800009I awarded to the Public Health Institute. The ideas and opinions expressed herein are those of the authors and do not necessarily reflect the opinions of the State of California, Department of Public Health, the NCI, and the CDC or their Contractors and Subcontractors.

Financial support:

Elysia Alvarez

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Context Summary

Key objective

We sought to examine factors associated with receipt of guideline-concordant care (GCC) and impact of GCC on survival of children, adolescents and young adults (AYAs), and older adults with osteosarcoma.

Knowledge generated

Using statewide data from California, we found that less than 50% of patients with osteosarcoma received GCC, with children (vs adults), patients residing in higher socioeconomic neighborhoods, and those treated at specialized cancer centers (SCCs) being more likely to receive GCC. Patients <40 years treated by pediatric compared to medical oncologists were more likely to receive GCC. GCC was associated with increased survival among patients diagnosed with metastatic disease.

Relevance:

Our study underscores the need for interventions to improve delivery of GCC. Additionally, we highlight the importance of referring osteosarcoma patients to SCCs, where treatment can be delivered by a highly specialized multidisciplinary team, and collaborations between medical and pediatric oncologists in the treatment of AYAs.

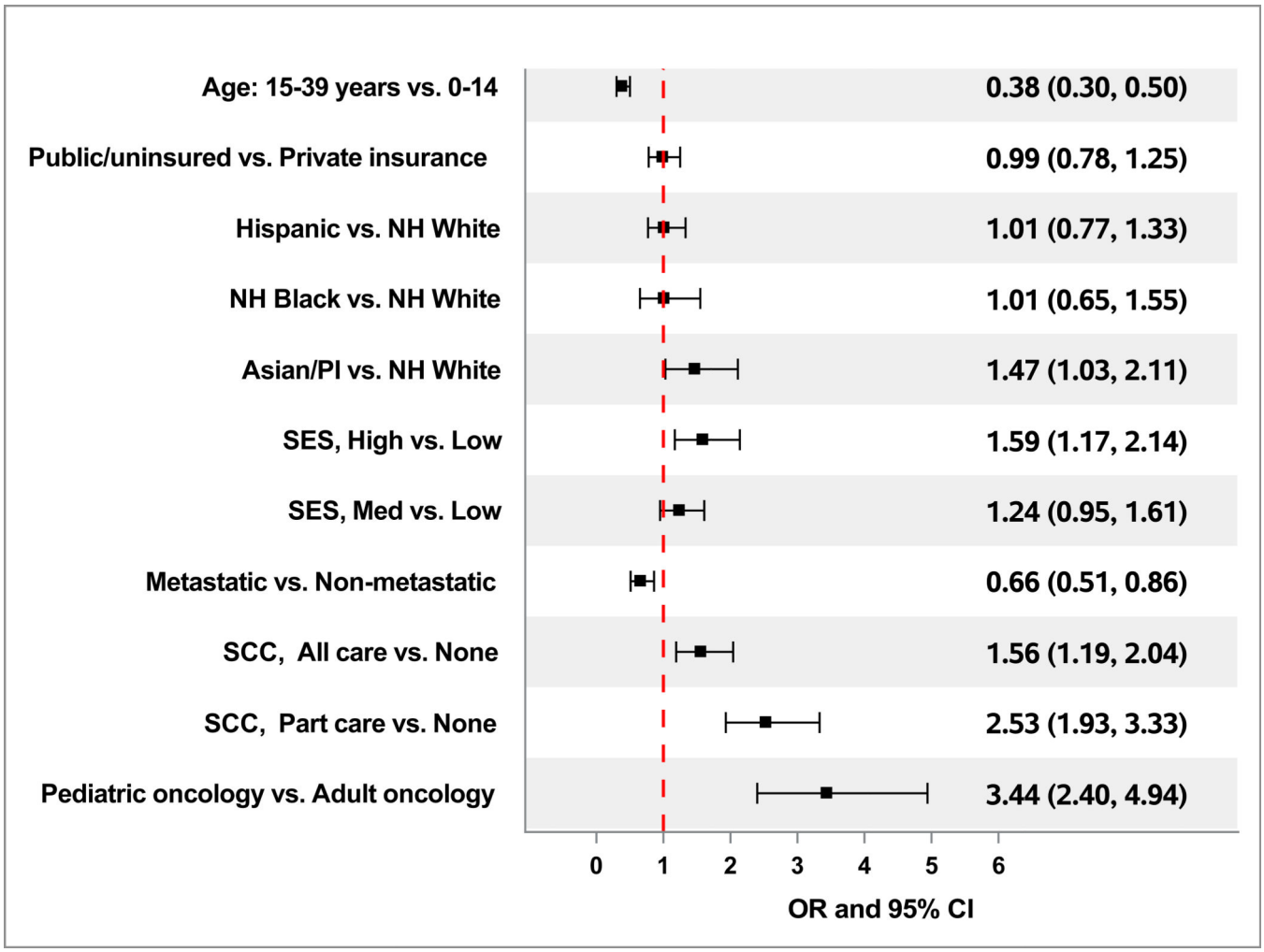
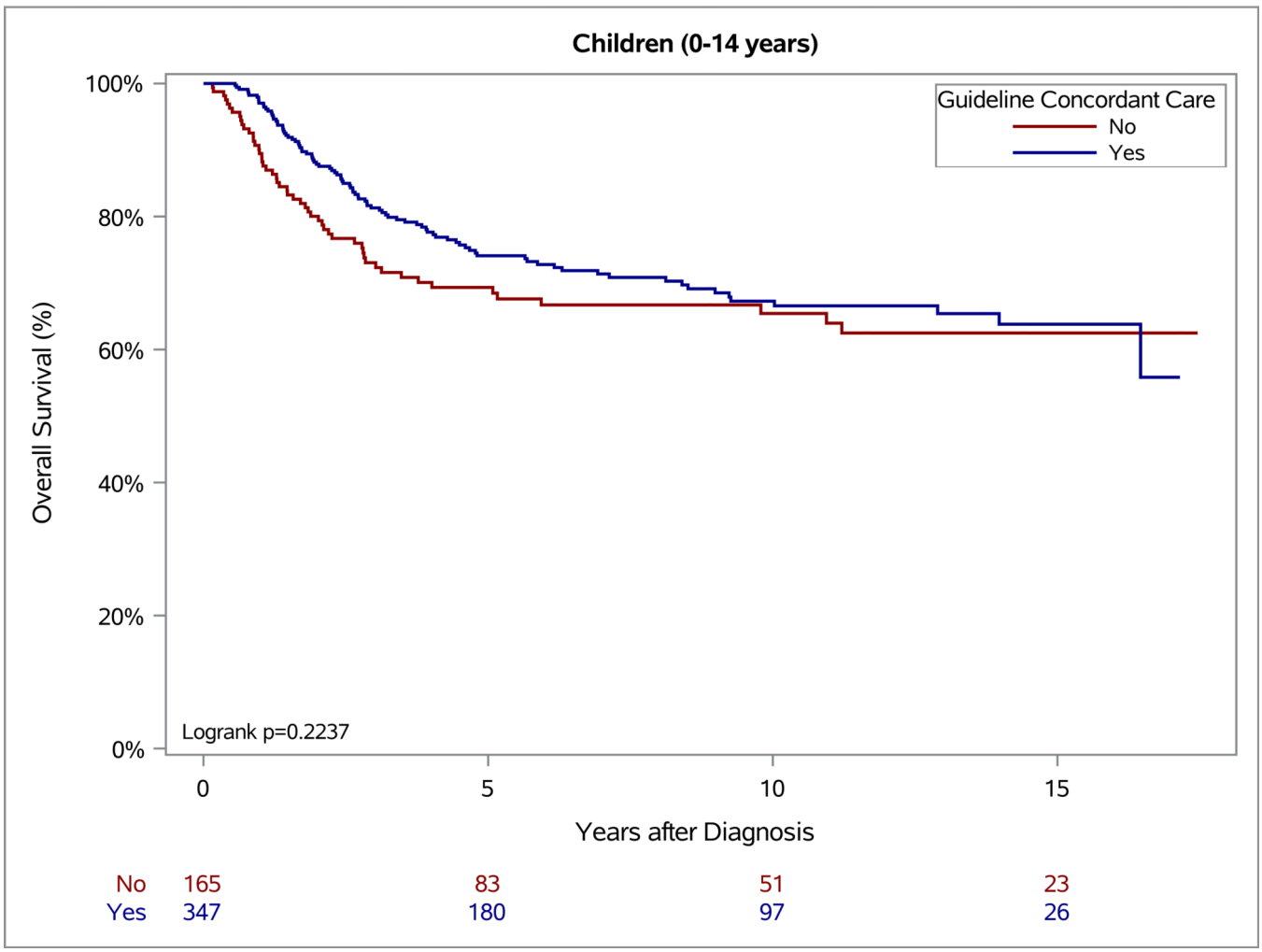


Figure 1.

Associations between receipt of guideline-concordant care and sociodemographic and clinical factors among patients aged 0–39 years diagnosed with osteosarcoma in California (2004–2019).



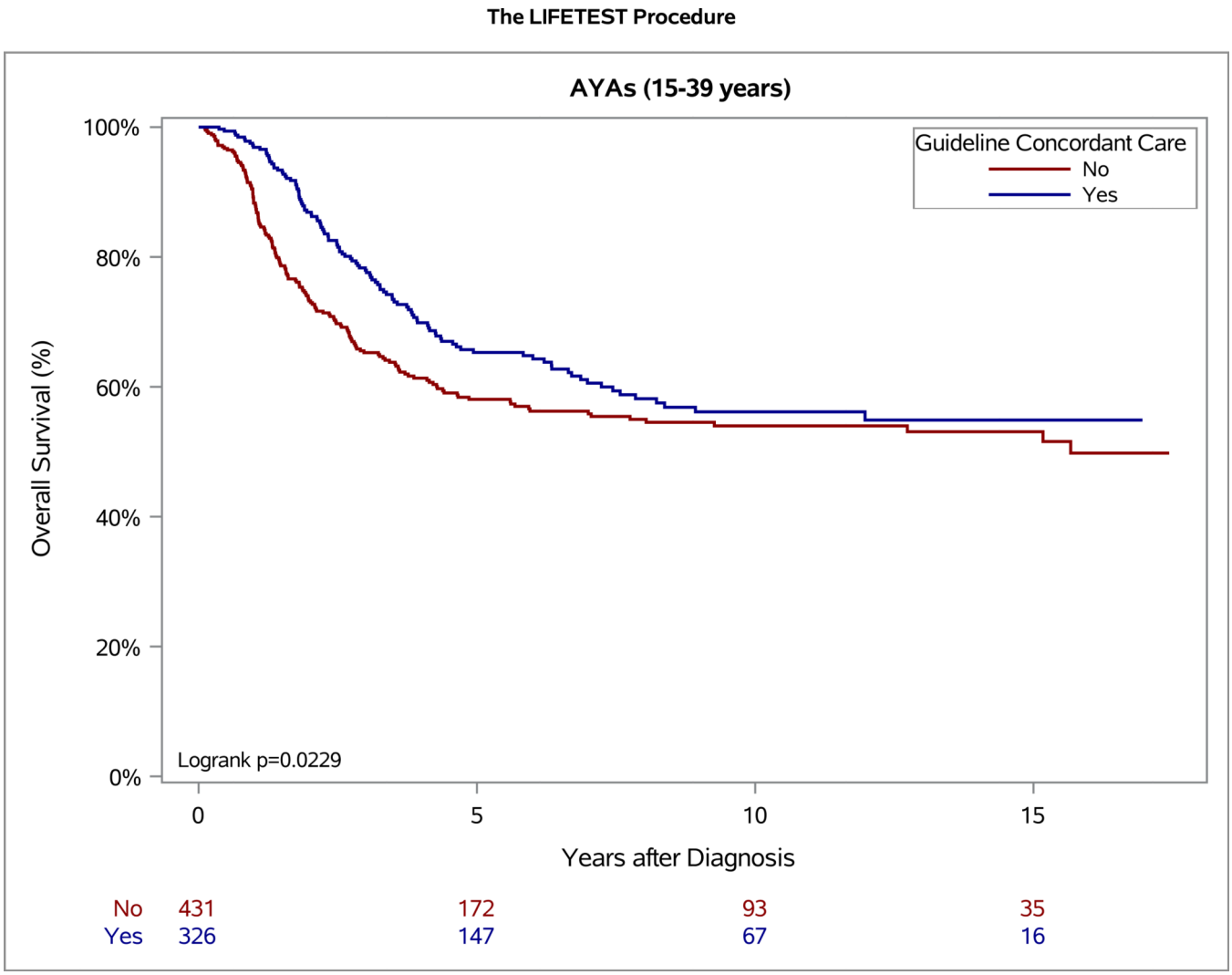


Figure 2.

Overall survival by receipt of guideline-concordant care among patients diagnosed with osteosarcoma in California (2004–2019): Children (0–14 years), Adolescents and young adults (15–39 years), Adults (40 years and over).

Table 1:

Sociodemographic and Clinical Characteristics of Patients with Osteosarcoma, 2004–2019, California, by Age Group

Characteristics	Total N (%)	0–14 years N (%)	15–39 years N (%)	≥ 40 years N (%)
All	1,716 (100)	515 (30.0)	768 (44.8)	433 (25.2)
Sex				
Female	746 (43.5)	247 (48.0)	298 (38.8)	201 (46.4)
Male	970 (56.5)	268 (52.0)	470 (61.2)	232 (53.6)
Health Insurance at Diagnosis				
Private	943 (55.0)	273 (53.0)	421 (54.8)	249 (57.5)
Public/uninsured	704 (41.0)	224 (43.5)	317 (41.3)	163 (37.6)
Unknown	69 (4.0)	18 (3.5)	30 (3.9)	21 (4.8)
Race/Ethnicity				
Non-Hispanic White	606 (35.3)	150 (29.1)	242 (31.5)	214 (49.4)
Non-Hispanic Black	135 (7.9)	39 (7.6)	62 (8.1)	34 (7.9)
Hispanic	743 (43.3)	265 (51.5)	354 (46.1)	124 (28.6)
Non-Hispanic Asian/Pacific Islander	202 (11.8)	50 (9.7)	98 (12.8)	54 (12.5)
Other	30 (1.7)	11 (2.1)	12 (1.6)	7 (1.6)
Neighborhood Socioeconomic Status				
Low	631 (36.8)	213 (41.4)	284 (37.0)	134 (30.9)
Middle	575 (33.5)	151 (29.3)	260 (33.9)	164 (37.9)
High	510 (29.7)	151 (29.3)	224 (29.2)	135 (31.2)
Residence				
Urban	1505 (87.7)	442 (85.8)	680 (88.5)	383 (88.5)
Rural	211 (12.3)	73 (14.2)	88 (11.5)	50 (11.5)
Stage at Diagnosis				
Metastatic	407 (23.7)	122 (23.7)	173 (22.5)	112 (25.9)
Non-Metastatic (Localized, Regional)	1228 (71.6)	378 (73.4)	571 (74.3)	279 (64.4)
Unknown	81 (4.7)	15 (2.9)	24 (3.1)	42 (9.7)
Tumor Size				
0–5 cm	212 (12.4)	45 (8.7)	92 (12.0)	75 (17.3)
5.1–10 cm	604 (35.2)	205 (39.8)	273 (35.5)	126 (29.1)
>10 cm	620 (36.1)	193 (37.5)	296 (38.5)	131 (30.3)
Unknown	280 (16.3)	72 (14.0)	107 (13.9)	101 (23.3)
Anatomic Site				
Extremity	1250 (72.8)	476 (92.4)	604 (78.6)	170 (39.3)
Pelvis	128 (7.5)	16 (3.1)	56 (7.3)	56 (12.9)
Other Bone	224 (13.1)	20 (3.9)	86 (11.2)	118 (27.3)
Other *	114 (6.6)	3 (0.6)	22 (2.9)	89 (20.6)
Guideline-Concordant Care				
Yes	807 (47.0)	347 (67.4)	328 (42.7)	132 (30.5)

Characteristics	Total N (%)	0–14 years N (%)	15–39 years N (%)	≥ 40 years N (%)
No	909 (53.0)	168 (32.6)	440 (57.3)	301 (69.5)
Radiation				
Yes	172 (10.0)	16 (3.1)	63 (8.2)	93 (21.5)
No	1542 (89.9)	499 (96.9)	704 (91.7)	339 (78.3)
Unknown	2 (0.1)	0.0 (0)	1 (0.1)	1 (0.2)
Chemotherapy				
Yes	1384 (80.7)	488 (94.8)	659 (85.8)	237 (54.7)
No	312 (18.2)	26 (5.0)	101 (13.2)	185 (42.7)
Unknown	20 (1.2)	1 (0.2)	8 (1.0)	11 (2.5)
Surgery				
Yes	1420 (82.8)	469 (91.1)	654 (85.2)	297 (68.6)
No	273 (15.9)	43 (8.3)	102 (13.3)	128 (29.6)
Unknown	23 (1.3)	3 (0.6)	12 (1.6)	8 (1.8)
Comorbidities				
No	844 (49.2)	221 (42.9)	431 (56.1)	192 (44.3)
Yes	328 (19.1)	58 (11.3)	117 (15.2)	153 (35.3)
Unknown	544 (31.7)	236 (45.8)	220 (28.6)	88 (20.3)
Cancer Treatment at SCC				
All	577 (33.6)	236 (45.8)	262 (34.1)	79 (18.2)
Part	512 (29.8)	170 (33.0)	244 (31.8)	98 (22.6)
None	623 (36.3)	108 (21.0)	260 (33.9)	255 (58.9)
Unknown	4 (0.2)	1 (0.2)	2 (0.3)	1 (0.2)
Chemotherapy Agents				
MAP	671 (39.1)	329 (63.9)	313 (40.8)	29 (6.7)
AP	330 (19.2)	65 (12.6)	143 (18.6)	122 (28.2)
MAP/I +/− E	111 (6.5)	40 (7.8)	65 (8.5)	6 (1.4)
AIM	50 (2.9)	8 (1.6)	23 (3.0)	19 (4.4)
Other containing Methotrexate	52 (3.0)	14 (2.7)	32 (4.2)	6 (1.4)
Other	178 (10.4)	32 (6.2)	89 (11.6)	57 (13.2)
Did not receive chemotherapy	324 (18.9)	27 (5.2)	103 (13.4)	194 (44.8)
Clinical Trial				
Yes	164 (9.6)	94 (18.3)	68 (8.9)	2 (0.5)
No	1552 (90.4)	421 (81.7)	700 (91.1)	431 (99.5)
Treating Specialty				
Pediatric Oncology **	524 (30.5)	319 (61.9)	205 (26.7)	0 (0)
Medical Oncology **	462 (26.9)	40 (7.8)	230 (29.9)	192 (44.3)
Hematology/Oncology &	323 (18.8)	82 (15.9)	172 (22.4)	69 (15.9)
Other	187 (10.9)	7 (1.4)	67 (8.7)	113 (26.1)
Unknown	220 (12.8)	67 (13.0)	94 (12.2)	59 (13.6)

Abbreviations: SCC, specialized cancer center; MAP, methotrexate, adriamycin/doxorubicin and cisplatin; AP, Adriamycin, cisplatin; I, ifosfamide; E, etoposide; AIM; adriamycin, ifosfamide, mesna.

*Refers to extraskeletal osteosarcoma

**Pediatric or Medical Oncology category alone or with surgery and/or radiation.

&Unknown if Pediatric or Medical Oncology, with surgery, with or without radiation.

#Fifty-five patients had low or intermediate paraosteal sarcoma and 23 patients had periosteal osteosarcoma

Table 2.

Factors Associated with Receipt of Guideline-Concordant Care in California, 2004–2019

Characteristics	Odds Ratio (95% CI)	P-value
Age (years)		
0–14	Reference	
15–39	0.38 (0.30, 0.50)	<0.001
≥ 40	0.40 (0.28, 0.56)	<0.001
Sex		
Female	Reference	
Male	1.02 (0.82, 1.27)	0.850
Health Insurance Status[&]		
Private	Reference	
Public/uninsured	0.99 (0.78, 1.25)	0.913
Race/Ethnicity		
Non-Hispanic White	Reference	
Non-Hispanic Black	1.01 (0.65, 1.55)	0.980
Hispanic	1.01 (0.77, 1.33)	0.933
Non-Hispanic Asian/Pacific Islander	1.45 (1.03, 2.11)	0.036
Other	0.52 (0.21, 1.24)	0.139
Neighborhood Socioeconomic Status		
Low	Reference	
Middle	1.24 (0.95, 1.61)	0.113
High	1.59 (1.17, 2.14)	0.003
Residence		
Urban	Reference	
Rural	1.66 (1.18, 2.32)	0.003
Stage at Diagnosis[&]		
Non-Metastatic (Localized, Regional)	Reference	
Metastatic	0.66 (0.51, 0.86)	0.002
Tumor Size[&]		
0–5 cm	Reference	
5.1–10 cm	1.01 (0.70, 1.44)	0.967
>10 cm	1.14 (0.79, 1.66)	0.484
Anatomic Site		
Extremity	Reference	
Pelvis	0.53 (0.34, 0.82)	0.005
Other Bone	0.54 (0.37, 0.77)	0.001
Other [*]	0.27 (0.16, 0.46)	<0.001
Comorbidities[&]		
No	Reference	
Yes	1.01 (0.75, 1.35)	0.959

Characteristics	Odds Ratio (95% CI)	P-value
Cancer Treatment at a Specialized Cancer Center		
None	Reference	
All	1.56 (1.19, 2.04)	0.001
Part	2.53 (1.93, 3.33)	< 0.001

*Refers to extraskeletal osteosarcoma.

&Unknown categories not shown.

Table 3.

Factors Associated with Survival in Patients with Osteosarcoma by Stage at Diagnosis, California, 2004–2019

	Metastatic Disease at Diagnosis		Non-Metastatic Disease at Diagnosis	
Characteristics	**Hazard Ratios (95% CI)**	**P-value**	**Hazard Ratios (95% CI**	**P-value**
Guideline-Concordant Care				
Yes	Reference		Reference	
No	2.02 (1.55, 2.63)	< 0.001	1.15 (0.92, 1.43)	0.224
Age at Diagnosis (years)				
0–14	Reference		Reference	
15–39	1.51 (1.08, 2.09)	0.015	1.23 (0.93, 1.62)	0.149
≥40	4.69 (3.08, 7.13)	< 0.001	2.25 (1.62, 3.13)	< 0.001
Sex				
Female	Reference		Reference	
Male	1.07 (0.83, 1.38)	0.594	1.21 (0.98, 1.49)	0.071
Health Insurance Status[&]				
Private	Reference		Reference	
Public/uninsured	1.08 (0.83, 1.41)	0.577	1.31 (1.04, 1.65)	0.020
Race/Ethnicity				
Non-Hispanic White	Reference		Reference	
Non-Hispanic Black	0.81 (0.53, 1.26)	0.355	0.93 (0.61, 1.41)	0.722
Hispanic	1.08 (0.79, 1.47)	0.624	1.00 (0.77, 1.30)	0.985
Non-Hispanic Asian/Pacific Islander	0.89 (0.58, 1.35)	0.574	1.13 (0.81, 1.56)	0.471
Other	0.94 (0.39, 2.26)	0.896	1.33 (0.53, 3.32)	0.545
Neighborhood SES				
Low	1.42 (1.01, 1.98)	0.043	1.19 (0.89, 1.61)	0.244
Middle	1.42 (1.03, 1.94)	0.030	1.25 (0.95, 1.64)	0.105
High	Reference		Reference	
Residence				
Urban	Reference		Reference	
Rural	1.39 (0.95, 2.04)	0.088	0.96 (0.70, 1.30)	0.783
Tumor size[&]				
0–5 cm	Reference		Reference	
5.1–10 cm	1.07 (0.59, 1.97)	0.819	1.71 (1.20, 2.44)	0.003
>10 cm	1.31 (0.73, 2.36)	0.368	2.10 (1.45, 3.03)	< 0.001
Anatomic Site				
Extremity	Reference		Reference	
Pelvis	1.34 (0.93, 1.93)	0.111	1.78 (1.22, 2.59)	0.003
Other Bone	0.91 (0.61, 1.37)	0.658	1.48 (1.06, 2.08)	0.023
Other	0.93 (0.57, 1.52)	0.771	1.63 (1.10, 2.41)	0.014
Comorbidities[&]				
No	Reference		Reference	
Yes	1.26 (0.93, 1.71)	0.134	1.65 (1.29, 2.12)	< 0.001

	Metastatic Disease at Diagnosis		Non-Metastatic Disease at Diagnosis	
Characteristics	**Hazard Ratios (95% CI)**	**P-value**	**Hazard Ratios (95% CI**	**P-value**
Cancer Treatment at a SCC				
None	Reference		Reference	
All	0.61 (0.43, 0.86)	0.005	0.61 (0.46, 0.80)	< 0.001
Part	0.78 (0.59, 1.03)	0.084	1.18 (0.91, 1.52)	0.206

*Refers to extraskeletal osteosarcoma.

&Unknown categories not shown.

Abbreviations: SCC, Specialized Cancer Center; CI, Confidence Interval.