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Increasing Chordoma Incidence and Changing Histologic Composition of Primary Osseous Malignancies of the Spine and Pelvis from 2000 to 2023

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Abstract

Purpose

Primary malignant bone tumors of the spine and pelvis are rare and histologically heterogeneous. We evaluated contemporary population incidence trends, changes in histologic composition, and demographic and anatomic correlates of chordoma, chondrosarcoma, osteosarcoma, and Ewing sarcoma using Surveillance, Epidemiology, and End Results (SEER) data.

Methods

Histologically confirmed tumors diagnosed from 2000 through 2023 were identified using prespecified ICD-O-3 topography and histology codes. Age-adjusted incidence trends were evaluated using Joinpoint regression, temporal histologic composition across 3-year intervals, and associations between demographic and anatomic characteristics and histologic family using multivariable multinomial logistic regression.

Results

The cohort included 3,184 tumors: 983 chondrosarcomas, 856 chordomas, 835 Ewing sarcomas, and 510 osteosarcomas. Chordoma was the only histologic family with a significant increase in age-adjusted incidence (APC, 1.94%; 95% CI, 0.65%–3.46%; P = 0.004); no significant incidence trends were observed for the other histologies. Chordoma increased from 20.5% of the cohort in 2000–2002 to 33.4% in 2021–2023, whereas Ewing sarcoma decreased from 30.6% to 19.5% (P < 0.001). In adjusted analyses, later calendar year was associated with lower relative likelihood of chondrosarcoma, osteosarcoma, and Ewing sarcoma versus chordoma.

Conclusion

Chordoma was the only major histologic family with a significant increase in population incidence and became increasingly represented within the analytic cohort. In contrast, the declining proportional representation of Ewing sarcoma occurred without a corresponding population-level incidence decline. These findings identify a contemporary epidemiologic shift in and provide population-level context for the evolving case mix encountered in spine oncology.

Introduction

Primary malignant bone tumors involving the spine and pelvic region are uncommon but clinically consequential neoplasms whose diagnosis and management require integration of oncologic principles with the anatomic constraints of the axial skeleton. Boriani et al. [1] established a widely used surgical-staging framework for primary spinal bone tumors, while Ropper et al. [2] emphasized the distinct epidemiologic, histologic, and imaging characteristics of locally aggressive and malignant vertebral tumors. Primary osseous malignancies of the spine comprise a heterogeneous group of tumors with distinct epidemiologic, histologic, and anatomic characteristics [3]. Population-based studies have demonstrated substantial variation in incidence and survival across histologic and demographic groups [4], while surgical management has been associated with differences in survival [5]. More recently, Elsamadicy et al. [6] identified racial disparities in both management and outcomes, further highlighting the demographic and treatment-related heterogeneity of these rare malignancies.

Chordoma, chondrosarcoma, osteosarcoma, and Ewing sarcoma represent four major malignant osseous histologies encountered in spine oncology, but their biology and clinical behavior differ considerably. Chordoma is a notochord-derived axial malignancy with a predilection for the sacrum and mobile spine [7–11]. Chondrosarcoma is a malignant cartilage-forming neoplasm in which achieving adequate surgical margins remains critical for local disease control [12–15]. Osteosarcoma exhibits distinct age- and demographic-specific patterns of incidence and survival, with recent population-based analyses suggesting a shift from the historically described bimodal age distribution [16–19] whereas Ewing sarcoma is a small round cell sarcoma concentrated in children and young adults, most commonly driven by EWSR1–ETS gene fusions [20–23]. These differences make histologic classification fundamental to prognosis and treatment selection.

The pathologic framework for these tumors has also evolved. Vujovic et al. [24] identified brachyury as a highly characteristic marker of notochordal differentiation, and O'Donnell et al. [25] subsequently illustrated its diagnostic utility in chordoma. For Ewing sarcoma, the seminal work of Delattre et al. [23] demonstrated characteristic chimeric transcripts, establishing a molecular basis for the Ewing family of tumors. More recent work has separated conventional Ewing sarcoma from CIC-rearranged, BCOR-altered, and other molecularly defined round cell sarcomas [26–31].

Prior registry studies have generally focused on a single histology, survival, or treatment. McMaster et al. [8] characterized chordoma incidence and survival using SEER data from 1973 to 1995, and Pan et al. [7] subsequently examined prognostic factors in spinal chordoma. Mukherjee et al. [5] evaluated the association between surgical resection and survival across malignant primary osseous spinal neoplasms, while more recent SEER analyses have examined contemporary epidemiology and disparities [4, 6]. However, changes in the relative distribution of histologic families within a cohort do not necessarily reflect changes in population-level incidence.

We therefore used contemporary SEER data from 2000 through 2023 to characterize chordoma, chondrosarcoma, osteosarcoma, and Ewing sarcoma arising within the vertebral-column and pelvic/sacral topography captured by SEER. We sought to (1) quantify age-adjusted population incidence trends using Joinpoint regression; (2) characterize changes in within-cohort histologic composition over time; and (3) identify demographic, temporal, and anatomic factors independently associated with histologic families.

Methods

Study design and data source

This retrospective population-based cohort study used the Surveillance, Epidemiology, and End Results (SEER) Research Data, 17 Registries, November 2025 submission, covering diagnoses from 2000 through 2023. SEER provides deidentified cancer-registry information including year of diagnosis, demographic characteristics, primary site, histology, sequence number, and reporting variables. The study used deidentified registry data and did not involve direct patient contact; institutional review board approval and informed consent were therefore not required under the authors' institutional policy for analyses of deidentified public-use data.

Cohort definition

Tumors were restricted to ICD-O-3 topography codes C41.2 (vertebral column) and C41.4 (pelvic bones, sacrum, coccyx, and associated joints). We subsequently required microscopic confirmation, an eligible sequence number (0 or 1), and an eligible reporting source, excluding cases identified solely by death certificate or autopsy. Prespecified malignant histology codes were then applied to define the final analytic cohort(Fig. 1).

Sequential cohort selection from the SEER source population to the final malignant histologic family cohort.

Chordoma comprised ICD-O-3 codes 9370/3, 9371/3, and 9372/3. Chondrosarcoma comprised 9220/3, 9221/3, 9222/3, 9231/3, 9240/3, 9242/3, and 9243/3. Osteosarcoma comprised 9180/3 through 9187/3 and 9192/3 through 9194/3. Ewing sarcoma comprised 9260/3 and 9364/3. Detailed code-level frequencies are provided in Supplementary Table 1.

Variables

Age was analyzed using SEER age categories collapsed into four groups < 20, 20–39, 40–59, and ≥ 60 years consistent with previously published age stratification of primary bone sarcomas [32]. Sex was categorized as female or male. Race was categorized as White, Black, Asian or Pacific Islander, and Other/Unknown. Ethnicity was categorized as Hispanic or non-Hispanic. Primary site was grouped as vertebral column (C41.2) versus pelvic/sacral (C41.4: pelvic bones, sacrum, coccyx, and associated joints).

Incidence analysis

Age-adjusted incidence rates were generated using SEER*Stat version 9.1.0 standardized to the 2000 U.S. standard population, and expressed as cases per 1,000,000 population. Annual histology-specific incidence rates and corresponding standard errors were analyzed using the National Cancer Institute Joinpoint Regression Program, version 6.1.0. Joinpoint regression was performed using a log-linear model, with model selection used to identify statistically supported changes in temporal slope. For each histologic family, the selected model, number of joinpoints, annual percent change (APC), 95% confidence interval, and two-sided P value were recorded.

Statistical analysis

Categorical characteristics were summarized as counts and percentages within histologic family and compared using Pearson chi-square tests with Cramér V reported to quantify the magnitude of these associations. Temporal histologic composition was evaluated by calculating the proportion of chordoma, chondrosarcoma, osteosarcoma, and Ewing sarcoma within each consecutive 3-year diagnosis interval; the overall association between interval and histologic composition was assessed with Pearson chi-square testing.

A multivariable multinomial logistic regression model was fitted with histologic family as the dependent variable and chordoma as the reference outcome. Predictors included calendar year as a continuous variable scaled to 5-year increments, along with age group, sex, race, Hispanic ethnicity, and primary site. Results are presented as adjusted relative risk ratios (RRRs) with 95% confidence intervals. RRRs quantify relative histologic family among included cases and should not be interpreted as population incidence risk ratios. Statistical significance was defined as two-sided $P < 0.05$.

Results

Cohort characteristics

The final analytic cohort comprised 3,184 tumors: 983 chondrosarcomas (30.9%), 856 chordomas (26.9%), 835 Ewing sarcoma (26.2%), and 510 osteosarcomas (16.0%) (Fig. 1). Demographic and anatomic characteristics according to histologic family are summarized in Table 1. Histologic family differed significantly by age group ($P < 0.001$), with age demonstrating the strongest association among the demographic and anatomic characteristics examined (Cramér V =

0.404). Sex distribution also differed across histologic families (P = 0.028), although the magnitude of the association was small (Cramér V = 0.053).(Table 1)

Ewing sarcoma was concentrated in younger patients: 61.4% occurred before age 20 years and only 2.4% occurred at age 60 years or older. In contrast, 52.6% of chordomas occurred at age 60 years or older. Chondrosarcoma was most concentrated at ages 40–59 years (39.3%), whereas osteosarcoma had a broader age distribution. Black patients constituted 14.1% of osteosarcoma cases but only 4.1% of chordomas and 3.5% of Ewing sarcoma.(Table 1) Pelvic/sacral primary site predominated for all histologies but was most frequent for chondrosarcoma (80.0%) and osteosarcoma (76.1%).(Supplementary Table 5)

Table 1
Characteristics of the analytic cohort by histologic family

Characteristic		Chordoma (n = 856)	Chondrosarcoma(n = 983)	Osteosarcoma (n = 510)	Ewing sarcoma (n = 835)	P value	Cramér V
Age	< 20 years	23 (2.7)	21 (2.1)	111 (21.8)	513 (61.4)	< 0.001	0.404
	20–39 years	120 (14.0)	255 (25.9)	140 (27.5)	237 (28.4)		
	40–59 years	263 (30.7)	386 (39.3)	138 (27.1)	65 (7.8)		
	≥ 60 years	450 (52.6)	321 (32.7)	121 (23.7)	20 (2.4)		
Sex	Female	338 (39.5)	397 (40.4)	236 (46.3)	320 (38.3)	0.028	0.053
	Male	518 (60.5)	586 (59.6)	274 (53.7)	515 (61.7)		
Race	White	715 (83.5)	834 (84.8)	388 (76.1)	729 (87.3)	< 0.001	0.094
	Black	35 (4.1)	65 (6.6)	72 (14.1)	29 (3.5)		
	Asian/Pacific Islander	90 (10.5)	65 (6.6)	42 (8.2)	55 (6.6)		
	Other/Unknown race	16 (1.9)	19 (1.9)	8 (1.6)	22 (2.6)		
Ethnicity	Non-Hispanic	732 (85.5)	804 (81.8)	386 (75.7)	628 (75.2)	< 0.001	0.107
	Hispanic	124 (14.5)	179 (18.2)	124 (24.3)	207 (24.8)		
Primary site	Vertebral column	360 (42.1)	197 (20.0)	122 (23.9)	263 (31.5)	< 0.001	0.191
	Pelvic/sacral	496 (57.9)	786 (80.0)	388 (76.1)	572 (68.5)		

Data are presented as n (% within histologic family). P values were calculated using Pearson χ^2 tests. Cramér V quantifies the magnitude of association between each characteristic and histologic family

Age-adjusted incidence trends

Joinpoint regression selected 0 joinpoints for each histologic family (Supplementary Table 2; Fig. 2). Chordoma was the only histologic family with a statistically significant change in age-adjusted incidence from 2000 through 2023, increasing at an APC of 1.94% per year (95% CI, 0.65% to 3.46%; P = 0.004). Chondrosarcoma incidence did not change significantly (APC, 0.33%; 95% CI, -0.65% to 1.33%; P = 0.451), nor did osteosarcoma (APC, -0.03%; 95% CI, -1.75% to 1.79%; P = 0.985) or Ewing sarcoma (APC, -0.48%; 95% CI, -1.74% to 0.73%; P = 0.388).

Official National Cancer Institute Joinpoint regression output for chordoma, chondrosarcoma, osteosarcoma, and Ewing sarcoma. Rates are age-adjusted and expressed per 1,000,000 population.

Temporal histologic composition

The histologic distribution differed significantly across 3-year diagnosis intervals (P < 0.001), although the overall association was small (Cramér V = 0.074) (Supplementary Table 3; Fig. 3). Chordoma proportion increased from 20.5% of included tumors in 2000–2002 to 33.4% in 2021–2023. Over the same intervals, Ewing sarcoma proportion decreased from 30.6% to 19.5%. Chondrosarcoma proportion remained near one-third of the cohort (33.2% to 34.5%), while osteosarcoma proportion fluctuated and represented 15.6% in 2000–2002 and 12.6% in 2021–2023. These proportions describe case composition among the four selected histologic families and are distinct from population incidence rates.

Proportional distribution of the four included histologic families across 3-year diagnosis intervals.

Adjusted multinomial analysis

After adjustment for age, sex, race, Hispanic ethnicity, and primary site, calendar year remained associated with histologic family(Supplementary Table 4; Fig. 4). For each 5-year increase in diagnosis year, the relative likelihood of chondrosarcoma versus chordoma decreased (RRR, 0.93; 95% CI, 0.86–0.99; P = 0.031), as did osteosarcoma versus chordoma (RRR, 0.89; 95% CI, 0.82–0.97; P = 0.009) and Ewing sarcoma versus chordoma (RRR, 0.90; 95% CI, 0.82–0.98; P = 0.018).

Forest plots from adjusted multinomial logistic regression with chordoma as the reference outcome. Models adjusted for calendar year, age, sex, race, Hispanic ethnicity, and primary site. Points represent adjusted RRRs and horizontal bars represent 95% confidence intervals. Calendar year is modeled per 5-year increase.

Age was strongly associated with histologic family. Compared with patients younger than 20 years, those aged 20–39 years had higher relative representation in chondrosarcoma versus chordoma (RRR, 2.42; 95% CI, 1.29–4.57; P = 0.006), whereas older age groups had markedly lower relative likelihood of osteosarcoma and Ewing sarcoma versus chordoma. Black race was associated with higher osteosarcoma versus chordoma representation (RRR, 3.10; 95% CI, 1.96–4.88; P < 0.001) and lower Ewing sarcoma versus chordoma representation (RRR, 0.45; 95% CI, 0.25–0.82; P = 0.009). Hispanic ethnicity was associated with higher osteosarcoma versus chordoma representation (RRR, 1.50; 95% CI, 1.11–2.04; P = 0.009). Sex was not independently associated with histologic family.

Pelvic/sacral site was independently associated with greater relative likelihood of chondrosarcoma (RRR, 2.93; 95% CI, 2.37–3.62; P < 0.001), osteosarcoma (RRR, 2.27; 95% CI, 1.75–2.93; P < 0.001), and Ewing sarcoma (RRR, 1.51; 95% CI, 1.15–1.97; P = 0.003) versus chordoma.

Discussion

In this population-based analysis of 3,184 primary malignant osseous tumors of the SEER vertebral-column and pelvic/sacral topography codes, three findings were most notable. First, chordoma was the only histologic family with a significant population-level increase in age-adjusted incidence between 2000 and 2023. Second, the relative composition of the analytic cohort shifted toward chordoma and away from Ewing sarcoma, even though Ewing sarcoma population incidence did not significantly decline. Third, demographic and anatomic distributions remained strongly histology

-specific, and the relative predominance of chordoma in later calendar years persisted after multivariable adjustment.

Chordoma

The principal finding of this study was that chordoma was the only histologic family with a significant increase in age-adjusted incidence from 2000 through 2023. Chordoma also accounted for an increasing proportion of the study cohort over time, a pattern that persisted after adjustment for demographic and anatomic factors.

The observed chordoma APC of 1.94% per year extends earlier epidemiologic work into a contemporary period. McMaster et al. [8], analyzing 400 microscopically confirmed chordomas in SEER from 1973 to 1995, reported an age-adjusted incidence of 0.08 per 100,000, with higher incidence in males and increasing occurrence with age; approximately one-third of tumors each arose in cranial, spinal, and sacral locations. Median survival was 6.3 years, with 5- and 10-year relative survival rates of 67.6% and 39.9%, respectively. Pan et al. [7] subsequently evaluated 808 primary spinal chordomas in SEER through 2014 and found that 56.6% occurred in patients aged ≥ 60 years and 62.6% occurred in males. Older age, distant metastasis, and nonsurgical management were independently associated with worse overall survival, whereas survival did not differ significantly between vertebral and sacral/pelvic tumors. Bakker et al. [10], in a systematic review, reported chordoma incidence rates ranging from 0.18 to 0.84 per million persons per year, with diagnosis typically occurring in the late 50s and a male predominance. Across included studies, older age, larger tumor size, greater tumor invasion, incomplete resection, metastasis, local recurrence, and dedifferentiated histology were among the factors associated with poorer progression-free or overall survival. Our study adds a different dimension to this literature by formally demonstrating a significant increase in age-adjusted incidence within the selected vertebral/pelvic-sacral topography through 2023.

Improved diagnostic recognition is one plausible contributor to this trend, although SEER cannot establish the mechanism. Vujovic et al. [24] demonstrated that brachyury, a transcription factor essential to notochordal development, is a highly characteristic biomarker for chordoma. O'Donnell et al. [25] subsequently showed how brachyury can aid the diagnosis of chordoma in diagnostically challenging extra-axial disease. Together with broader advances in chordoma biology, these developments may have improved distinction of chordoma from morphologic mimics and increased diagnostic ascertainment. However, because SEER does not record immunohistochemical testing, molecular confirmation, or referral pathways, the contribution of improved recognition to the observed incidence increase cannot be quantified.

Chondrosarcoma

Chondrosarcoma demonstrated no significant population incidence trend and remained approximately one-third of the analytic cohort at both the beginning and end of the study period. Fisher et al. [12], in a multicenter analysis of spinal chondrosarcoma, highlighted the importance of surgical management and oncologic principles in this anatomically challenging disease. More broadly, Gazendam et al. [13] reviewed the clinical heterogeneity of chondrosarcoma, while contemporary molecular studies have further distinguished dedifferentiated and mesenchymal variants [14, 15]. In our cohort, chondrosarcoma was strongly associated with pelvic/sacral rather than vertebral-column topography relative to chordoma, underscoring the importance of anatomic site when comparing axial sarcoma populations.

Osteosarcoma

Osteosarcoma likewise showed no significant change in age-adjusted incidence from 2000 through 2023. Mirabello et al. [17], analyzing 3,482 osteosarcoma cases in SEER from 1973 to 2004, demonstrated marked age-related differences in incidence, tumor characteristics, and survival, with the highest incidence occurring in adolescents and a second incidence peak among adults aged ≥ 60 years. Older patients more frequently had osteosarcoma associated with Paget disease or a prior malignancy, and survival varied substantially by age, disease stage, and anatomic site, without significant improvement from 1984 to 2004. Cole et al. [18], in an updated SEER analysis of 5,016 cases diagnosed from 1975 to 2017, similarly demonstrated substantial variation in osteosarcoma incidence and survival across age and racial/ethnic groups; notably, Black individuals had the highest overall incidence, and incidence increased significantly over time among Black individuals and children aged 0–9 years. A multicenter study of spinal osteosarcoma similarly highlighted the importance of local tumor control and surgical management in determining outcomes [33]. More recently, Kar et al. [19], analyzing 5,129 SEER cases from 2000 to 2021, found a persistent incidence peak during the second decade of life but no consistent second peak among adults aged ≥ 35 years, challenging the traditionally described bimodal age distribution of osteosarcoma in the contemporary United States. Osteosarcoma likewise showed no significant change in age-adjusted incidence from 2000 through 2023. Our anatomically restricted cohort similarly demonstrated a broad age distribution, while the adjusted model showed strong age, race, ethnicity, and site associations with osteosarcomas.

Ewing sarcoma

Conversely, the proportion of Ewing sarcoma decreased within the cohort from 30.6% in 2000–2002 to 19.5% in 2021–2023, and later calendar years was independently associated with lower Ewing sarcoma-versus-chordoma family. Nevertheless, Joinpoint regression demonstrated no significant population-level decline in Ewing sarcoma incidence. Esiashvili et al.[21], using SEER data spanning three decades, similarly reported relatively stable incidence despite temporal improvements in outcome.

The demographic distribution in our study is also consistent with established Ewing sarcoma epidemiology. Jawad et al.[20], in an analysis of 1,631 SEER cases, demonstrated pronounced racial disparities in Ewing sarcoma incidence and outcome. In our cohort, Ewing sarcoma was overwhelmingly concentrated in younger patients and was relatively less frequent among Black patients. Charest-Morin et al. [34] found that Enneking-appropriate surgery was associated with improved survival in spinal Ewing sarcoma, whereas intralesional margins were associated with increased local recurrence. Berger et al. [35] reported 1, 2, and 5-year survival rates of 82%, 75%, and 57%, respectively.

Evolving molecular classification may also affect longitudinal registry composition. Delattre et al. [23] established the defining role of specific chimeric transcripts in the Ewing family of tumors. Machado et al. [26]described genetically distinct sarcomas that can resemble Ewing sarcoma but are now recognized as separate tumor entities. Dehner et al. [27] further described how contemporary classification separates Ewing sarcoma from these small round cell mimics, and successive molecular and WHO classification updates have formalized these distinctions [28–31]. These changes provide a biologically plausible framework for temporal shifts in coding or diagnostic assignment, but the absence of tumor-level molecular data in SEER prevents direct testing of this hypothesis.

Interpretation of the multinomial model

The multinomial analysis provides an assessment of changes in histologic composition over time. The lower calendar-year RRRs for chondrosarcoma, osteosarcoma, and Ewing sarcoma indicate that these histologies became relatively less common than chordoma within the study cohort over time. Demographic associations also differed **by histologic family**. Increasing age was strongly associated with lower relative **likelihood of** Ewing sarcoma versus chordoma,

consistent with their markedly different age distributions. Osteosarcoma was relatively more common than chordoma among Black and Hispanic individuals, consistent with previously reported demographic variation in bone sarcoma epidemiology [17, 18, 20]. These associations describe differences within the study cohort and should not be interpreted as incidence changes at the population-level.

Clinical and research implications

Our findings also highlight the importance of aligning cancer registry classification with evolving molecular definitions of bone tumors. Contemporary classifications increasingly distinguish tumor entities using characteristic molecular alterations **[27–31]**. Linking population-based registries with pathologic, genomic, treatment, and longitudinal outcome data may help determine whether future changes in observed incidence reflect true epidemiologic trends, improved detection, or changes in tumor classification.

Strengths and limitations

This study has several strengths. It uses a large population-based registry spanning 24 diagnosis years, applies a prespecified ICD-O-3 histologic codebook, distinguishes population incidence from within-cohort composition, incorporates Joinpoint modeling of age-adjusted rates, and uses multivariable multinomial regression to characterize adjusted histologic family. Joinpoint regression is a well-established approach for evaluating changes in cancer incidence trends; Kim et al. [36] described major methodological enhancements to the program, and Irimata et al. [37] provided guidance for model-option selection. The present analysis also retains detailed ICD-O-3 subtype information, allowing transparent reconstruction of the four broad histologic families.

Likewise, there are several limitations. First, SEER is observational and subject to coding error, incomplete clinical detail, and temporal changes in registry practice. Second, C41.4 does not isolate the sacrum from other pelvic bones, so the cohort should not be interpreted as a purely vertebral-and-sacral series. Third, SEER does not consistently capture central pathology review, molecular testing, surgical margins, local recurrence, detailed systemic therapy, radiation dose or modality, or multidisciplinary referral patterns. Fourth, changes in WHO classification and molecular diagnostics may have altered histologic assignment during the study period, particularly among small round cell sarcomas [26–31]. Fifth, multinomial RRRs describe the relative distribution of histologic families within the study cohort rather than population-level disease risk. Finally, although Joinpoint regression is appropriate for population trend analysis [36, 37], estimates for rare tumors remain dependent on annual case counts and the precision of registry-derived rates.

Conclusion

From 2000 through 2023, chordoma was the only major histologic family in this SEER cohort with a significant increase in age-adjusted incidence. Chordoma also represented an increasing proportion of the analytic cohort, whereas Ewing sarcoma represented a decreasing proportion despite no significant decline in population incidence. These findings demonstrate changing histologic composition among primary osseous malignancies of the vertebral column and pelvic/sacral region and highlight the importance of distinguishing population incidence from relative case composition.

Declarations

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Author contributions: Bhargavi R. Budihal: Conceptualization, Methodology, Data curation, Formal analysis, Investigation, Software, Validation, Visualization, Project administration, Writing - original draft, Writing - review & editing. Matthew Carr: Conceptualization, Methodology, Validation, Writing - review & editing. Jeremy Steinberger: Conceptualization, Methodology, Validation, Writing - review & editing. Konstantinos Margetis: Conceptualization, Methodology, Supervision, Project administration, Validation, Writing - review & editing.

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Figures

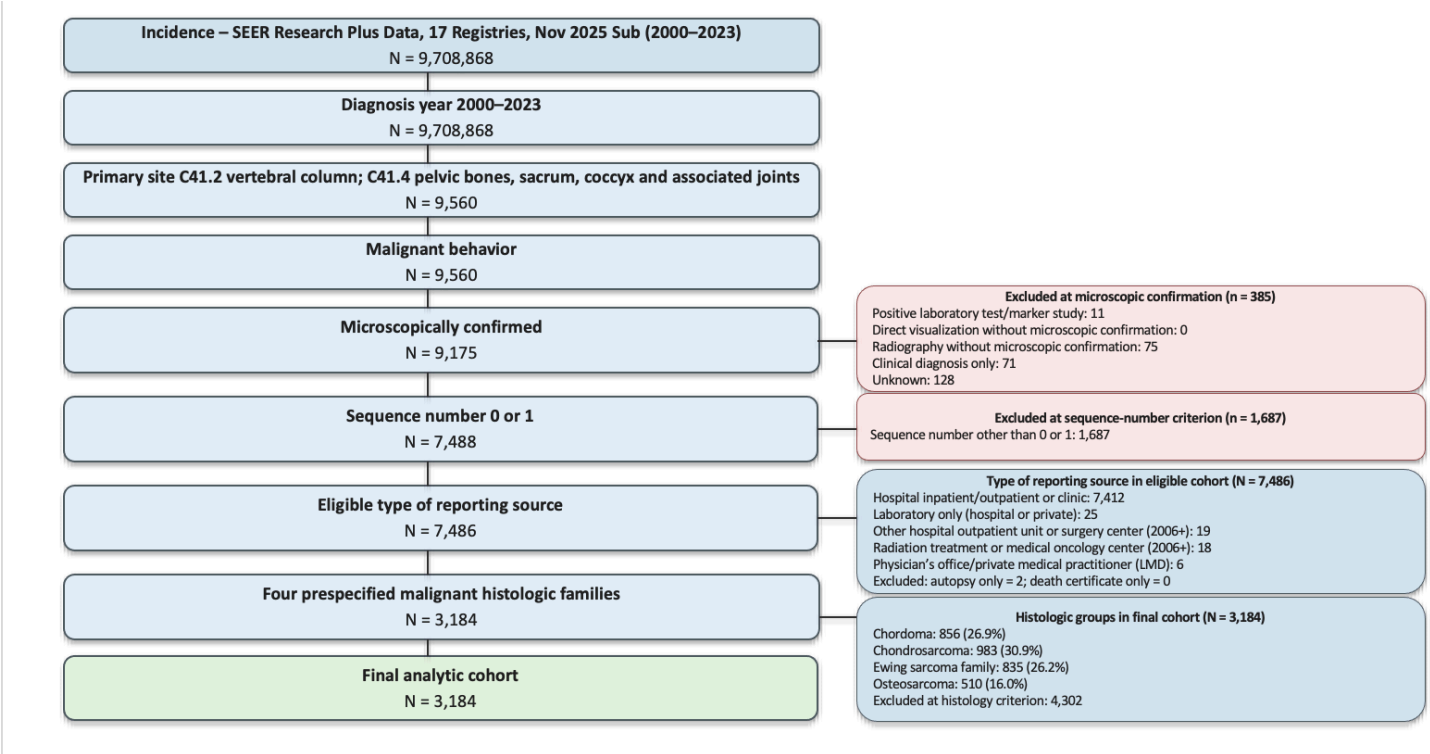

Figure 1

Cohort Selection Flow Diagram

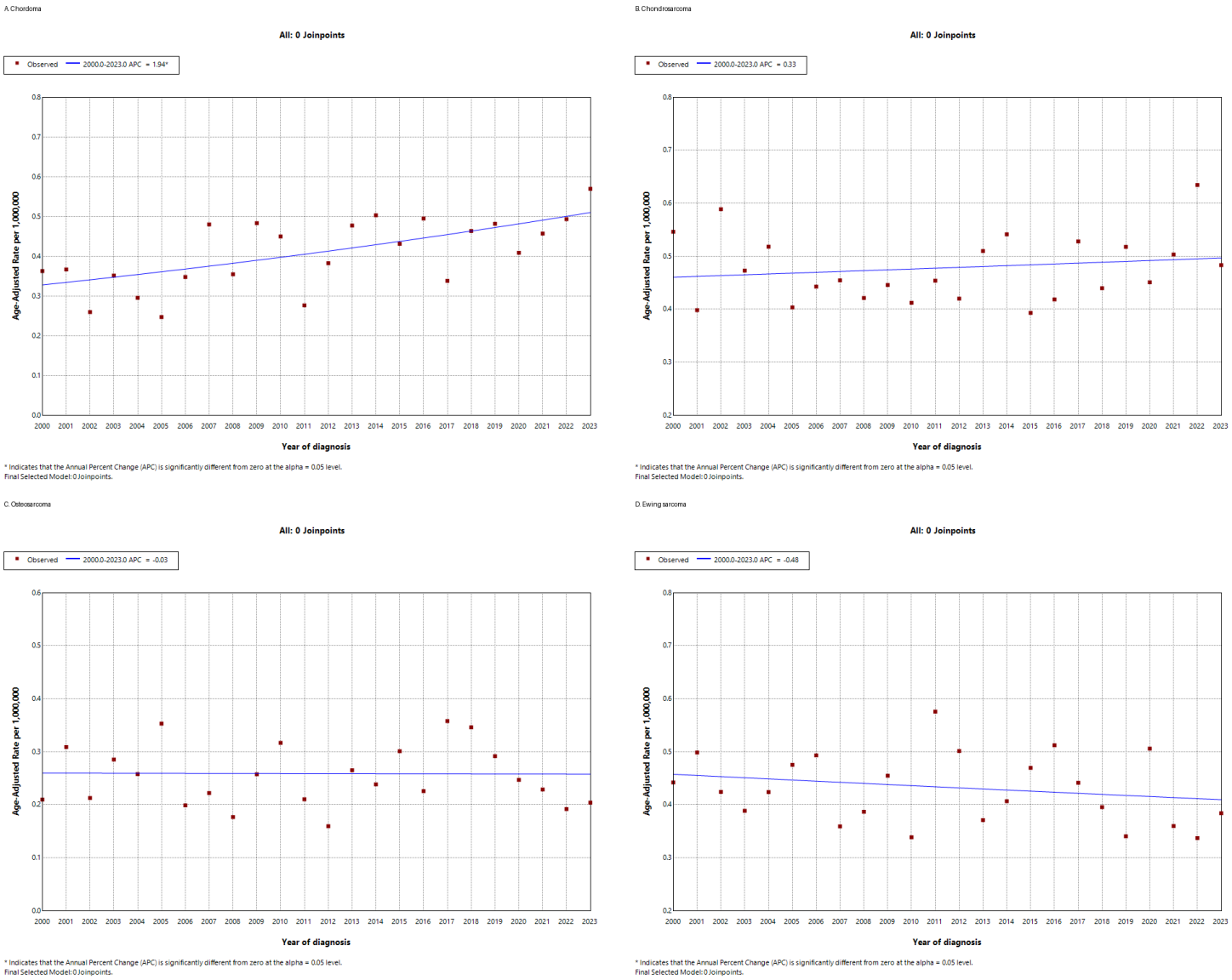

Figure 2

Age-Adjusted Incidence Trends by Histologic Family, 2000–2023

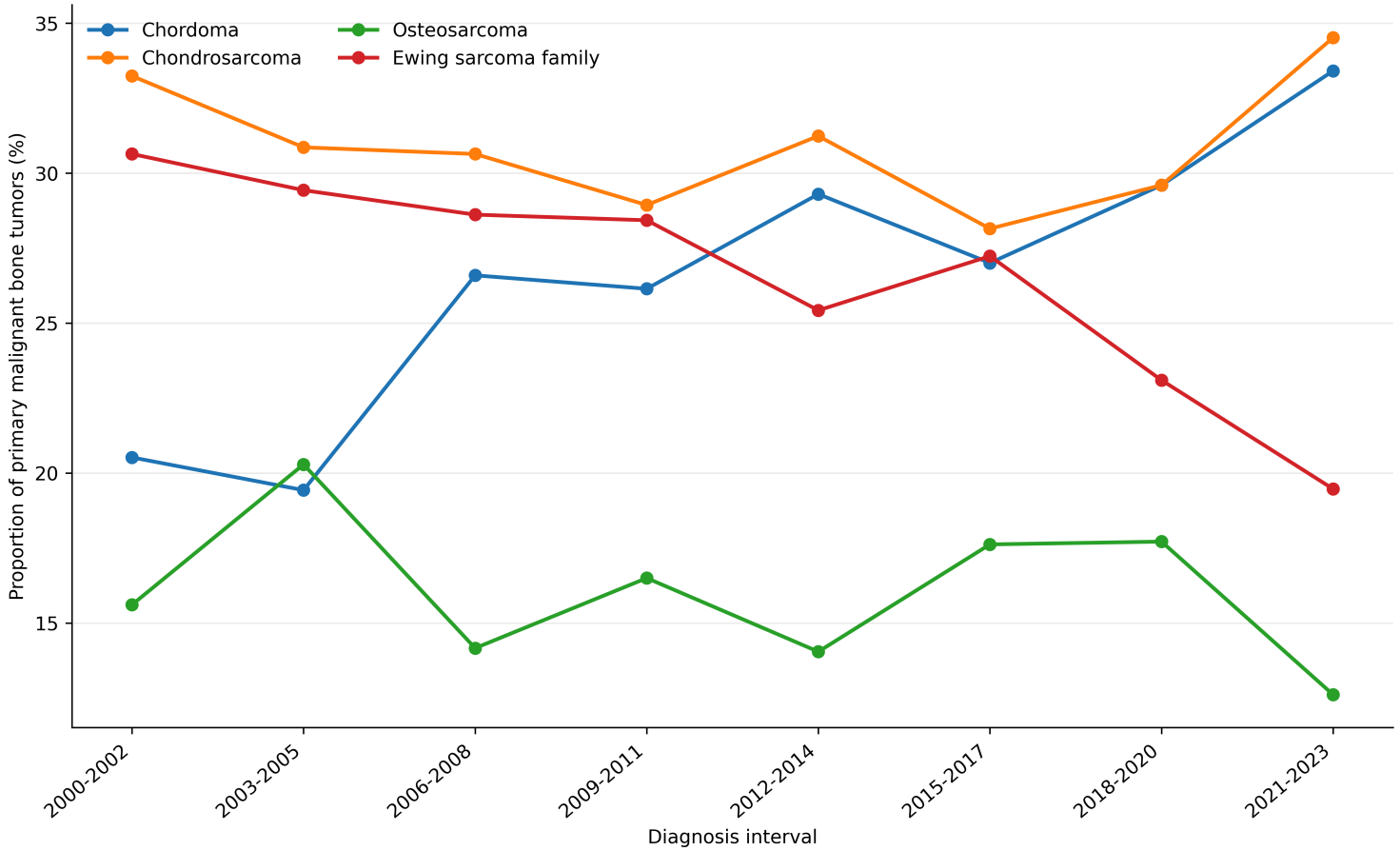

Figure 3

Temporal Changes in Histologic Composition of the Analytic Cohort, 2000–2023

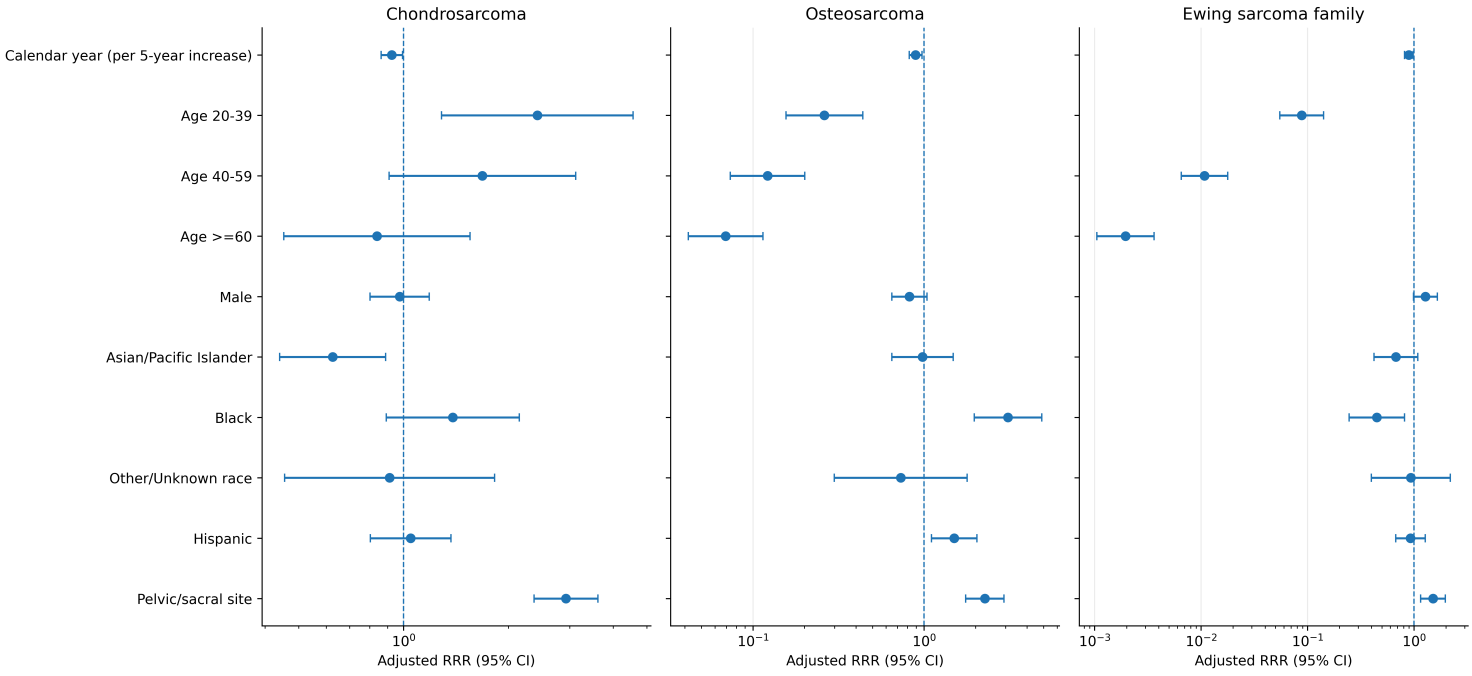

Figure 4

Adjusted Relative Risk Ratios for Histologic Family

Supplementary Files

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