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Reviewer A

Comment	**Response**	**Changes to Text**
Overall, excellent paper combining institutional retrospective review and comprehensive systematic review.	Thank you for the kind feedback.	None.
Lines 64-70 – Need to edit epidemiology. Overall – Chondrosarcoma is the most common primary bone sarcoma, followed by osteosarcoma. Could state that osteosarcoma is the most common in pediatric population.	Thank you for this comment. We have made the changes accordingly and provided appropriate references to support this feedback. Epidemiology of Soft Tissue Sarcoma and Bone Sarcoma inItaly: Analysis of Data from 15 Population-Based Cancer Registries (hindawi.com)	Revisions were made to Lines 67-70 in order to address these changes: "Comparatively, CS is the most common primary bone sarcoma, and has a higher occurrence rate amongst elderly patients. Aging populations have contributed to a rising incidence of CS estimated at around 8.8 cases per one million people per year."
I do wonder if the results would have been different if you only included osteosarcoma patients? Only one of the papers included in the systematic review included chondrosarcoma patients.	This is a reasonable point and we were certainly curious if this affected our results for the retrospective case-control. Part of our rationale for performing this study internally was to include chondrosarcoma given the limited amount of data available in the literature for this topic, as reflected in the articles we found through our systematic review. This methodology also allowed us to increase the size of our patient population, and we believe both adding and consolidating information on infection in the setting of chondrosarcoma does not detract from the results reported on osteosarcoma alone.	No changes were made given the rationale outlined.

Reviewer B

Comment	**Response**	**Changes to Text**
Thanks to the authors for providing such an informative and well-formatted manuscript. We believe that the authors' work will be a valuable contribution in this field. To further enhance the quality of the manuscript and improve its impact, the following suggestions are provided for the authors' consideration.	Thank you for the kind feedback.	None.
1. STROBE is for STrengthening the Reporting of OBservational studies in Epidemiology. PRISMA is for transParent ReportIng of Systematic reviews and Meta-Analyses. Given that the manuscript includes two types of studies, observational study and systematic review, two checklists are required to be submitted as supplementary material. A reformatted version has been created for the journal, please download here: (1) STROBE: https://cdn.amegroups.cn/static/public/5-STROBE_Checklist_v4_combined.pdf?/v=1677481091476 (2) PRISMA: https://cdn.amegroups.cn/static/public/12-PRISMA-2020-Checklist.pdf?v=1677481091476 The relevant page/line and section/paragraph number in the manuscript should be stated for each item in the checklist.	Thank you for providing these appropriate materials. We have downloaded both checklists and completed them appropriately.	Both the STROBE and PRISMA checklists were completed with appropriate references to sections of the manuscript satisfying each point of the checklist. These were submitted as supplementary materials attached alongside the revised manuscripts.

2. According to the previous comment, the statement in the Introduction “For the systematic review portion of the study, we present the following article in accordance with the STROBE and PRISMA reporting checklist” is inaccurate. The systematic review portion should follow PRISMA, while the retrospective study portion should follow STROBE.	Thank you for providing this clarification and our description in the Introduction. We corrected this to accurately reflect the guidelines which were followed for each section of the study.	Lines 110-111: Correction was made to specify that “The retrospective review portion of this study was completed in accordance with the STROBE reporting checklist, while the systematic review portion was completed in accordance with the PRISMA reporting checklist.”
Based on the STROBE checklist, we have the following comments: 3. STROBE checklist item 1a Readers should be able to easily identify the design that was used from the Title or Abstract. Thus, please indicate the study type in the Abstract or Title. This should include not only the reported “retrospectively reviewed”, also whether it is a cohort, case-control or cross-sectional study. Kindly take note of the unique characteristics of each type of research design.	Thank you for this suggestion. We changed our Abstract accordingly to reflect that this was a retrospectively reviewed case-control study. We also revised how patients were grouped for clarity while explaining the study design.	Lines 34-40: “Methods” section of the abstract was revised to state “We performed a retrospective case-control study of 192 patients treated between 1/2000 and 12/2015 at a single academic sarcoma referral center (Pittsburgh, PA). Patients with osteosarcoma or chondrosarcoma who underwent operative resection within the treatment period were included in the study. Eligible patients were grouped by metastatic or non-metastatic disease, and survival was then compared between these patients based on presence of a post-operative infection using log-rank analysis.” Line 45: “Results” section was revised to specify this was a “retrospective case-control study”.

4. STROBE checklist item 1b (1) Please add the key element of the observational study design in the methods section of the abstract, such as the exact dates (including the month), location (city, country) of the enrollment period, primary eligibility criteria of participants, and statistical methods. (2) Please present the total number of participants included in the analysis (n=104) and the number of participants in each group (not just as percentages) in the Results section of the abstract.	Key elements of the observational study design were further specified in the Methods section in response to comment (1). We also presented the number of participants in the Results section in response to comment (2).	Lines 34-40: "Methods" section of the abstract was revised. Changes made for comment (1) - "We performed a retrospective case-control study of 192 patients treated between 1/2000 and 12/2015 at a single academic sarcoma referral center (Pittsburgh, PA). Patients with osteosarcoma or chondrosarcoma who underwent operative resection within the treatment period were included in the study. Eligible patients were grouped by metastatic or non-metastatic disease, and survival was then compared between these patients based on presence of a post-operative infection using log-rank analysis." Lines 45-47: "Results" section was revised to specify "Within our retrospective case-control study, 104 patients were included in the analysis, with 85 without infection (26 metastatic, 59 non-metastatic) and 19 with infection (10 metastatic, 9 non-metastatic)."
5. STROBE checklist item 4 Similar to the Comment 3, please describe the study design at the beginning of the Methods. This should include not only the reported "a retrospective study" in the Methods, but also whether the article is a cohort or a case-control or a cross-sectional study.	We acknowledge this feedback and have changed our Methods accordingly to accurately reflect the study design to be a retrospective case-control study.	In Methods section, we updated lines 120-122 to reflect details of the study: "A retrospective case-control study was performed of 192 patients treated for primary OS or CS at a large academic sarcoma referral center in Pittsburgh, PA, USA from January 2000 to December 2015."

6. STROBE checklist item 5 Please provide the exact dates (including the month) and location (city and country) of the recruitment period.	We updated our Methods accordingly to specify the recruitment period to the exact dates and location.	In Methods section, the first sentence in lines 120-122 was updated: “A retrospective case-control study was performed of 192 patients treated for primary OS or CS at a large academic sarcoma referral center in Pittsburgh, PA, USA from January 2000 to December 2015.”

7. STROBE checklist item 6 Please provide clear eligibility criteria in the Methods section, for example, inclusion criteria: patients diagnosed with osteosarcoma/chondrosarcoma according to the diagnostic criteria of a certain institution. Regarding to the exclusion criteria - “patients with insufficient medical record information, insufficient follow-up, or death within six months of diagnosis”, what duration of follow-up will be considered insufficient? Will patients with other serious underlying diseases be included in the study?	Thank you for providing this feedback. We reviewed the inclusion criteria and further specified the diagnostic details of our institution to clarify the diagnosis of osteosarcoma or chondrosarcoma had to be made based on biopsy pathology results. Furthermore, we clarified insufficient follow-up to be within six months, as patients who were lost to follow-up could not be adequately followed during their post-operative course. Certainly, we agree that patients with other serious underlying diseases may have responded differently to a diagnosis of osteosarcoma/ chondrosarcoma and possibly concomitant infection. We did not assess the effect of these underlying conditions, but they certainly could have contributed to susceptibility to developing and recovering from an infection. For any underlying diseases acutely affecting patient survival we hoped to mitigate these effects by excluding patients who died with six months of diagnosis.	Inclusion and exclusion criteria were updated in the Methods section in lines 122-134: “Information from each patient was collected from the electronic medical record regarding biopsy results, sarcoma, survival status, presence of post-operative wound infection, metastasis, and infectious organism grown on surgical culture. Only patients with 1) a diagnosis of osteosarcoma or chondrosarcoma made via biopsy and 2) were undergoing surgical resection for their malignancy were included in the study. Post-operative wound infections can occur at different time-points, with early infections occurring within 30 days of surgery and late infections developing more than 3 months following surgery, In 2017, the CDC recommended surveillance of 30 days or 90 days following operation for a surgical site infection depending on if any implants were utilized. In order to capture the broad range of infections that could occur, postoperative wound infects were defined as surgical culture-confirmed infection occurring within six months of surgery. After excluding patients with insufficient medical record information, insufficient follow-up under six months (e.g. due to loss to follow-up), or death within six months of diagnosis, an analysis of 104 patients took place.”

8. STROBE checklist item 7 Please specify the criteria used to determine metastasis in patients with osteosarcoma/ chondrosarcoma, and provide the sources or references for defining “postoperative wound infection”.	Criteria for metastasis in this patient population were further clarified. Additional references for defining postoperative wound infection were provided, namely to justify the time frame of within six months to be considered a postoperative infection. Furthermore the use of surgical culture-confirmed infection was an additional measure utilized to define postoperative wound infection. References cited included Peel & Taylor, 1991 and Berrios-Torres et al, 2017	Criteria for metastasis were clarified in lines 137-138: “Patients with metastasis were defined based on presence of disease found in any organ distinct from the primary osteosarcoma or chondrosarcoma site.” Definition of a postoperative infection were further justified with references and clarification in lines 122-132: “Information from each patient was collected from the electronic medical record regarding biopsy results, sarcoma survival status, presence of post-operative wound infection, metastasis, and infectious organism grown on surgical culture. Only patients with 1) a diagnosis of osteosarcoma or chondrosarcoma made via biopsy and 2) were undergoing surgical resection for their malignancy were included in the study. Post-operative wound infections can occur at different time-points, with early infections occurring within 30 days of surgery and late infections developing more than 3 months following surgery. In 2017, the CDC recommended surveillance of 30 days or 90 days following operation for a surgical site infection depending on if any implants were utilized. In order to capture the broad range of infections that could occur, post-operative wound infections were defined as surgical culture-confirmed infection occurring within six months of surgery.”

9. STROBE checklist item 13 We strongly recommend the authors provide a flow chart illustrating the numbers of participants at each stage, including the number of recruited OS and CS patients, the number of patients excluded, the final number of participants included in the analysis, and with reasons for inclusion and exclusion. Here is an example for your reference: The figure 1 in this report (https://academic.oup.com/fampra/article/20/6/696/530870) is here for authors' information.	Thank you for this feedback, we included a figure illustrating the participants recruited and ultimately included in the study in order to improve understanding of our methods.	Additional figure was included illustrating process for including patients in study. This is now labeled as Figure 1 at the end of the manuscript. Figure 1 was also cited in the Methods section in Line 156.
10. STROBE checklist item 14a It is important to give characteristics of study participants (e.g., demographic, clinical, social) and information on potential confounders. Readers need descriptions of study participants and their exposures to judge the generalizability of the findings. We advise authors to include a baseline table summarizing continuous variables for each study group by giving the mean and standard deviation, or when the data have any asymmetrical distribution, as is often the case, the median and percentile range (e.g. 25th and 75th percentiles).	Thank you for this feedback, we agree and reassessed our patient population data to provide sufficient demographic information for context.	An additional table (now table 1) was included in order to provide the demographics of our patient population, based on the data that was collected we were able to provide demographics on age, gender, sarcoma type, survival in months, and survival percentage at end follow-up by each group. This table was referenced in the Results section in lines 211-213: "Overall, patients were 45.1 ± 24.1 years old, were 45.2% male, had 64.4% osteosarcoma, and had an overall survival of 103.8 ± 63.3 months with 65.4% of surviving patients at end follow-up (Table 1)."

11. STROBE checklist item 15 Please report the number of patients in each group and the number of patients who survived at the end of follow-up in the Results section. Also, please specify the number of years of follow-up for which the survival rates presented here are calculated.	We agree and further added to our table of demographics to specify the percentage and number of patients who survived by end of follow-up, and also elaborated on this in the results section. Additionally, we specified in our results section that follow-up was performed for a minimum of five years for the surviving patient cohort.	In the Methods section for lines 138-139: "For surviving patients, follow-up was performed for a minimum of five years from the date of diagnosis." Our new table 1 (please see the response in the row above) also now specifies the surviving percentage and number of patients at end follow-up, and a discussion of these results was elaborated on in the Results section in lines 165 - 174: "Overall, patients were 45.1 ± 24.1 years old, were 45.2% male, had 64.4% osteosarcoma, and had an overall survival of 103.8 ± 63.3 months with 65.4% of surviving patients at end follow-up (Table 1). Overall survival ranked from greatest to lowest in the order of the following groups: 1) Non-metastatic disease with infection (88.9%), 2) Non-metastatic disease without infection (78.0%), 3) Metastatic disease with no infection (42.3%), and 4) Metastatic disease with infection (30.0%), respectively (Figure 1). Five-year survival was greatest in the group who experienced a post-operative wound infection and did not develop metastasis (100.0%), followed by patients who developed neither infection nor metastasis (89.8%). Five-year survival was lowest in patients with post-operative infection and metastasis (30.0%), followed by patients with metastasis and no post-operative infection (61.5%)."

Based on the PRISMA checklist, we have the following comments: 12. PRISMA for abstracts checklist item 2 Since the search strategy includes the term “postoperative infection”, we suggest that the authors change “perioperative infection” used in the title, abstract, and introduction to “postoperative infection”.	Thank you for this feedback, we changed our terminology used accordingly.	All sections utilizing the term “perioperative infection” were changed to “postoperative infection” within the title, abstract, and introduction.
13. PRISMA for abstracts checklist item 3 The authors stated in the abstract that “prospective studies” were retrieved, however, the search strategy provided in the main text does not reflect this. Please verify and ensure consistency.	The terminology “prospective” was not used as intended and this was removed accordingly in the abstract.	In the Abstract line 42: “prospective studies” was corrected to ”published studies”.
14. PRISMA for abstracts checklist item 5 Please specify the methods used to assess risk of bias in the included studies.	The method uses to assess risk of bias for the included studies was the Cochrane ROBINS-I (Risk of Bias in Non-randomized Studies – of Interventions) risk of bias assessment tool.	Risk of bias assessment method was updated in the Abstract in lines 43-44: “Risk of bias assessment was performed utilizing the Cochrane ROBINS-I (Risk of Bias in Non-randomized Studies – of Interventions) assessment tool.”
15. PRISMA for abstracts checklist item 7 Please give the total number of participants of the included studies, and summarize relevant characteristics of studies (publish year, location, setting, and study design, etc.).	Our Results and Figures (now Table 2) were updated accordingly in order to specify the relevant characteristics of the study. Within our Patient Cohort section of Table 2 we had already specified the number of participants for a given study, further distinguished by the type of malignancy and which patients had infections. We did add additional columns to specify location/setting as well as study design for each individual study included.	Table 2 was updated to provide additional pertinent details from each article included for the systematic review.

16. PRISMA for abstracts checklist item 9 Please provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Thank you, we reviewed both our protocol for conducting the systematic review as well as the contents of each of the articles included in the review and noted particular limitations due to risk of bias due to confounding, inconsistency amongst the outcomes compared in terms of type of survival and length of survival measured, as well as slight differences in patient populations between studies including patients selected for inclusion within the study group.	Within the Abstract, a brief summary of the systematic review was added to the Results in lines 55 - 56: “Limitations of findings from the systematic review included study risk of bias due to confounding, inconsistency comparing outcomes, and differences in patient populations.”
17. PRISMA for abstracts checklist item 12 If available, authors are encouraged to provide the registration name and number	This review was not formally registered and as such a registration name and number was not provided.	No changes were made.
18. PRISMA checklist item 5 The author is advised to provide a more precise definition for the inclusion criteria - “an experimental cohort of subjects had associated infection”. How will the presence of an associated infection be determined?	Thank you for the feedback. The purpose of this inclusion criteria was to ensure that the included studies had a cohort of subjects with infection. The presence of this associated infection was determined by the study authors on review of how patients were screened in each individual study, and included perioperative as well as postoperative infections based on author discretion. In essence, this was an inclusion criteria for the sole purpose of excluding publications which did not compare groups with or without an infection.	The first inclusion criteria in the Methods section was updated in lines 154-156: “(1) Participants included in the study had a proven diagnosis of a bone sarcoma and an experimental cohort of subjects had associated infection, including either perioperative or postoperative infection”

19. PRISMA checklist item 8 The process of records screening and assessment should be described in the Methods section, instead of Results	Thank you, we updated the sections accordingly so that the Methods detailed the screening and assessment protocol.	The following section was removed from Results and added to Methods in lines 161-166: “Within the systematic review performed, our initial literature search retrieved 426 publications. 331 articles using “Postoperative Infection + Osteosarcoma” as the terms of the search query and 95 articles using “Postoperative Infection + Chondrosarcoma” as the terms of the search query (Figure 3). Two investigators (M.F.G., A.J.F.) performed the literature review independently. After consolidation of review, any disagreements on inclusion or exclusion of articles were discussed with manuscript contents reviewed collaboratively.” Additional lines were added in lines 169-170 and as detailed in subsequent responses below: “Ultimately, six studies were determined to meet inclusion criteria for the study.”
20. PRISMA checklist item 9 Please specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Thank you, the protocol for data collection was expanded on in the Methods section, namely the independent collection process and comparison after collection was complete between the collecting investigators.	In Methods section in lines 170-173: “Both investigators then collected data independently from each included study, including the year of publication, authors, location, study design, patient cohort, infection rate, type of infection, 5-year survival rate, and 10-year survival rate. All data points were collected based on availability within each publication. After data collection, data was compared and confirmed between the two study investigators.”

21. PRISMA checklist item 10a Please list and define all outcomes (e.g., for all measures, time points, analyses) for which data were sought in included studies. And if there are results of studies were incompatible with outcome domain, please describe the methods used to decide which results to collect.	We expanded upon the data we sought to collect in our Methods section to better clarify this. Furthermore, we elaborated that due to variability in data presented or reported, we made the decision to report both key outcomes of survival at 5 years or at 10 years, which was not uniform amongst the six included publications.	Variables collected are noted in the responses from the row immediately above, and were detailed in Methods section for lines 170-173. Additional clarification was added to Methods in lines 174 – 178 regarding outcomes which were collected and ultimately included in the review: "Upon comparison of data collected, the six studies reviewed had some variability in terms of type of infection reports and time points for survival rates. The decision was made to report type of infection if available, and report survival rates at both 5-years and 10-years due to the differences in reporting between publications. All p-values reported were obtained from log-rank analyses results reported within each individual publication."
22. PRISMA checklist item 10b Please list and define all other variables for which data were sought. Variables of interest might include characteristics of the study (such as countries, settings, number of centers, funding sources, registration status), characteristics of the study design (such as randomized or nonrandomized), characteristics of participants (such as age, sex, socioeconomic status), number of participants enrolled and included in analyses, the results (such as summary statistics, estimates of effect and measures of precision, factors adjusted for in analyses), and competing interests of study authors, etc.	Based on this feedback we further expanded our Methods section noting our protocol for collecting data variables, namely which were specifically included from each of the included studies.	Within the Methods section, lines 170-172 detail variables collected: "Both investigators then collected data independently from each included study, including the year of publication, authors, location, study design, patient cohort, type of infection, 5-year survival rate, and 10-year survival rate." In terms of summary results, significance of the findings were obtained from each study as detailed in lines 177-178: "All p-values reported regarding significance were obtained from log-rank analyses reported within each individual publication."

23. PRISMA checklist item 11 One essential component of a systematic review is the study risk of bias assessment, without which it cannot be considered a systematic review. Thus, please specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Study risk of bias was performed by a single author utilizing the Cochrane ROBINS-I (Risk of Bias in Non-randomized Studies – of Interventions) assessment tool. This was updated accordingly in the Methods section, and the findings from this assessment were detailed in the Results section.	Methods section was updated in lines 180-182: "A study risk of bias assessment was performed utilizing the Cochrane ROBINS-I (Risk of Bias in Non-randomized Studies – of Interventions) assessment tool by a single investigator (M.F.G.)."
24. PRISMA checklist item 16a The flow diagram representing the study selection process (Fig. 3) does not need to completely replicate the template. Any sections of the template that are not applicable to this study, such as "Registers" and "Records marked as ineligible by automation tools" can be omitted. Additionally, please provide detailed reasons for exclusion during the full-text sscreening step, rather than using vague phrases such as "for abstract" or "for manuscript". Figure 1 in this example (https://www.annalscts.com/article/view/16587/16907) is for your reference.	Thank you for this feedback, we updated this accordingly for a more concise flow diagram detailing how studies were selected. We also provided further clarity on reasons for exclusion of full-texts, namely either because of an inappropriate patient population that did not capture bone sarcomas as the majority of tumors, did not have an appropriate experimental design comparing patients with and without infection, or did not have an appropriate outcome of interest (namely patient survival).	Figure 3 detailing the flow diagram utilized for the study was updated. Furthermore, clarification for the main reasons why full texts which were reviewed were excluded was provided in the Methods section in lines 166-169: "Articles which were excluded on full-text review were primarily due to an inappropriate patient population without primarily bone sarcoma patients (n = 5), an experimental design which did not compare patient groups with and without infection (n = 5), or did not report the desired outcome of interest of patient survival (n = 9)."

25. PRISMA checklist item 17 The categories of study characteristics presented in Table 1 are too limited. Reporting the details of the included studies allows readers to understand the characteristics of studies that have addressed the review questions. For example, additional categories such as study design type, study duration, sample characteristics (age, sex), disease characteristics (tumor grade, metastasis status), etc. could be added to Table 1.	We updated Table 1 to expand on study characteristics in order to provide a more detailed overview of the different studies included. *Of note, we had difficulty formatting our table to be completely included in the submitted manuscript, as a result the table is an attached image. We can provide the complete table in its original format on request.	Table 1 (now Table 2) was updated with an expanded set of study characteristics obtained from each study including study location, study design type, and demographic data when available including age, gender, and tumor stage.
26. PRISMA checklist item 18 Present assessments of risk of bias for each included study.	Individual risk of bias assessments utilizing the Cochrane ROBINS-I assessment tool were updated and provided for each included study in the Results section. The consolidated figure was added to the article and the results were summarized in the manuscript text itself.	Results section was updated to include risk of bias assessments summary utilizing the ROBINS-I assessment, while providing a figure with more detailed results which was referenced in lines 230-232): “The ROBINS-I risk of bias assessment found that all six articles were susceptible to a moderate risk of bias overall, primarily from bias due to confounding and patient selection (Figure 4).” Figure 4 attached after the references provides the risk of bias assessment results in a visual diagram for all six articles included in the systematic review, as well as a summary diagram consolidating the risk of bias in all six articles across the seven bias domains reviewed through the ROBINS-I assessment tool.
27. PRISMA checklist item 24a Provide registration information for the review, including register name and registration number, or state that the review was not registered	The review was not registered and this was updated accordingly.	In Methods section in line 178-179, the following was added: “This review was not formally registered and a protocol was not prepared.”

28. PRISMA checklist item 24b If available, please indicate where the review protocol can be accessed, or state that a protocol was not prepared.	The protocol was not prepared and this was updated accordingly.	In Methods section in line 178-179: “This review was not formally registered and a protocol was not prepared.”
Other concerns: 29. The authors should ensure the accuracy of the cited information, as we could not find the information “... and metastatic disease conferring a five-year survival rate of 23%.” (Introduction, para 1) from references 4 and 10. Please verify this information.	Thank you for this comment. The statistic we quoted in this section can be found from reference 10 located in table 2 within the manuscript, which specifies that the study’s Distant Metastasis Overall Survival at 5 years is reported as 23%.	No changes were made as the statistic cited was verified in the reference provided.
30. We suggest combining Figures 1 and 2 under a common title, and providing separate descriptions of the contents of each figure.	We appreciate this feedback and have made the recommended change.	The previous Figures 1 and 2 were combined into a single figure (now Figure 3A and 3B), and accompanying descriptions for each individual survival curve were provided.
31. Osteosarcoma, Ewing sarcoma, and chondrosarcoma are rare diseases but the most common primary tumors of bone. We suggest the authors add the classification of bone sarcoma and explain why excluded Ewing sarcoma in the Introduction.	We appreciate this feedback and have revised our Introduction to provide a better scope of the types of bone sarcomas which exist. We also provided a rationale for excluding Ewing sarcoma, namely based on prior literature which has primarily studied osteosarcoma, and the intent to expand to chondrosarcoma as a primary bone tumor with a known cell of origin. Furthermore, chondrosarcoma and osteosarcoma are the most common primary bone sarcomas overall.	We provided additional background on Ewing sarcoma in lines 79-83: “Comparatively, Ewing sarcoma is another common bone sarcoma which is primarily seen in younger patient populations. OS and CS both have known cells of origin arising from bone, whereas Ewing sarcoma’s cell of origin still remains unknown. For the purposes of evaluating primary bone sarcomas known to arise from bone or cartilage cell lines of origin, our subsequent investigation primarily focused on OS and CS.”

32. Please note that “*, **, ***” should be reserved for P-values. If other symbols are needed, †, ‡, §, ¶ (in this order) can be used. Therefore, please replace the * in “45 Primary Bone Tumor*” and “*7 Osteosarcoma” in Table 1 with appropriate symbols, and indicate the meaning of each symbol in the footnote.	Thank you, we made changes accordingly in order to use appropriate symbols in our figures and tables.	In our revised table (now Table 2), we removed any symbols reserved for P-values and replaced them with appropriate symbols.
33. Is the follow-up time shown in Figures 1 and 2 273 months (2000.1 - 2022.9)? Please explain in the legends.	Clarification was provided in the legend for follow-up time. Although this was not depicted clearly the follow-up time was performed through 5/2021 (May 2021).	The caption to the figure (now Figure 3 was addended to specify the follow-up time for the study in Line 503: “The end time-point for both figures was from 1/2000 through 5/2021.”