



Global, regional, and national burden of soft tissue and extraosseous sarcomas from 1990 to 2021

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ABSTRACT

Objective: To conduct a comprehensive global epidemiological investigation of soft tissue and extraosseous sarcomas from 1990 to 2021 and uncover the demographic and geographical variations.

Methods: Incidence and death data of soft tissue and extraosseous sarcomas between 1990 and 2021 were derived from the Global Burden of Disease 2021. The estimated annual percentage change was calculated. The demographic patterns were analyzed in-depth based on age and gender.

Results: From 1990 to 2021, there was an increase in the number and crude rate of incidence and death of soft tissue and extraosseous sarcomas, while age-standardized rate declined. Males consistently exhibited a heavier burden compared to females. The incidence and death rates of soft tissue and extraosseous sarcomas generally increased with age, with a similar pattern in both males and females. Compared to 1990, the incidence rate among the elderly increased in 2021, while the incidence rate in children under 5 decreased, and there was little change in other age groups. The death rate among children and the elderly has decreased, while little change in other age groups has been observed.

Conclusions: The disease burden of soft tissue and extraosseous sarcomas remains a critical challenge. Data-driven analysis is crucial for guiding clinical practice, informing public health policies, and shaping future research agendas.

1. Introduction

Soft tissue and extraosseous sarcomas are a group of rare, aggressive malignancies that arise from mesenchymal tissues, often presenting diagnostic and therapeutic challenges. Soft tissue sarcoma (STS) accounts for no more than 1 % of all malignant tumors, yet it is one of the most common rare cancers in terms of incidence (Buscharino et al., 2023; Gatta et al., 2011; Group et al., 2016; Sandrucci et al., 2017; Stiller et al., 2013; Trama et al., 2019). STS can occur at any age, but they are most common in middle-aged and elderly individuals; however, as a pediatric malignancy, STS is relatively common, accounting for 7–10 % of all childhood cancers (Albritton et al., 2003; McTiernan, 2003). STS

originates from mesenchymal cells and can affect any anatomical part of the body, including various histological subtypes such as synovial sarcoma, undifferentiated sarcoma, dermatofibrosarcoma protuberans, liposarcoma, and leiomyosarcoma (Buscharino et al., 2023; Hsieh et al., 2013; Mulita et al., 2021; Sharma et al., 2024). The most commonly affected sites of STS are the limbs, superficial trunk, and head and neck regions (Group et al., 2016; Hsieh et al., 2013; Sharma et al., 2024). High mortality rates are associated with STS. The 5-year overall survival rate for STS remains only 55–65 %, and the 10-year survival rate for pediatric patients with STS is even less than 50 % (Bacon et al., 2023; Cosci et al., 2023; Kotilingam et al., 2006; Nakamura et al., 2024; Sant et al., 2009; Stiller, 1982; Stiller et al., 2018). Besides, patients with STS

Abbreviations: STS, soft tissue sarcoma; GBD, Global Burden of Disease; UI, uncertainty interval; EAPC, estimated annual percentage change; CI, confidence interval; ASIR, age-standardized incidence rate; ASDR, age-standardized death rate.

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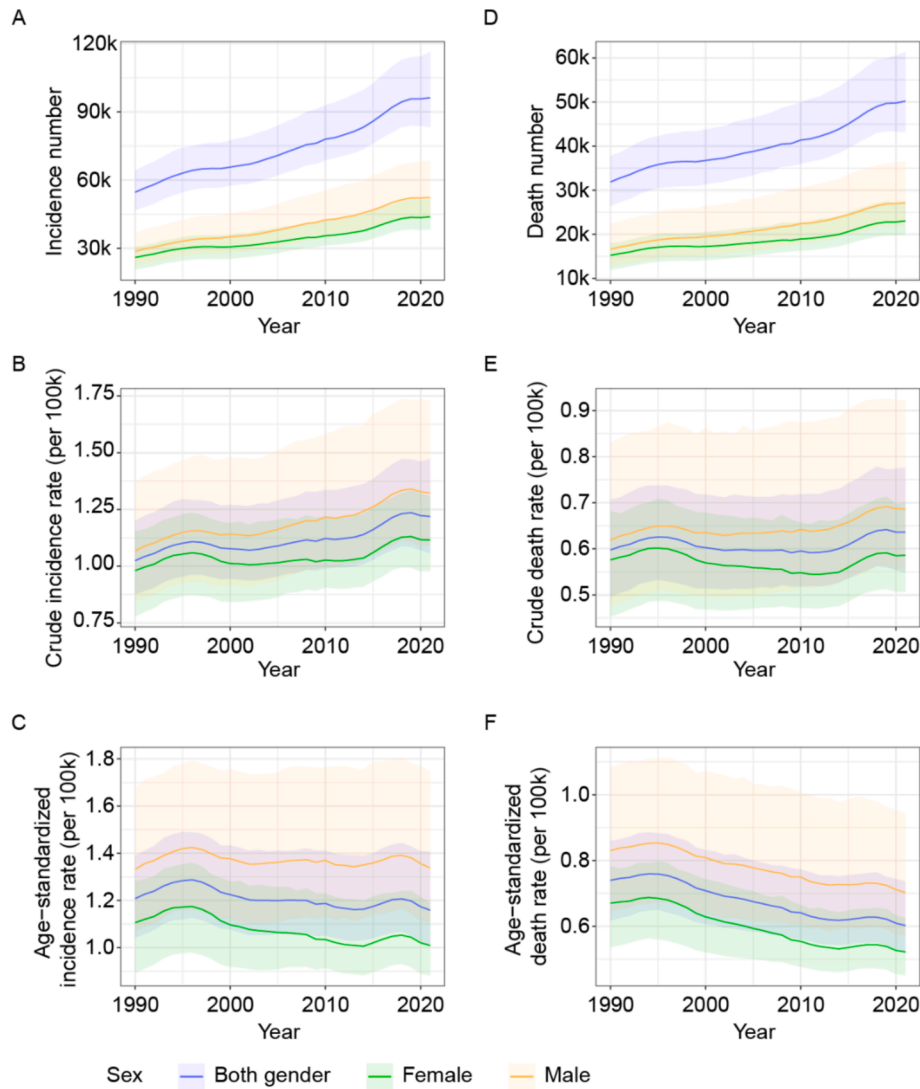


Fig. 1. Global epidemiological trends of soft tissue and extraosseous sarcomas across gender from 1990 to 2021. A The global incidence number of soft tissue and extraosseous sarcomas across gender from 1990 to 2021; B The global crude incidence rate of soft tissue and extraosseous sarcomas across gender from 1990 to 2021; C The global age-standardized incidence rate of soft tissue and extraosseous sarcomas across gender from 1990 to 2021; D The global death number of soft tissue and extraosseous sarcomas across gender from 1990 to 2021; E The global crude death rate of soft tissue and extraosseous sarcomas across gender from 1990 to 2021; F The global age-standardized death rate of soft tissue and extraosseous sarcomas across gender from 1990 to 2021.

typically require surgical treatment, which often leads to functional impairment, severely affecting the quality of life of the patients.

Despite advancements in medical science, their incidence and mortality remain poorly understood due to limited epidemiological data. The existing literature on soft tissue and extraosseous sarcomas is characterized by fragmentation, often due to its reliance on small sample sizes, regional biases, and inconsistent data collection methods. Many studies lack a long-term perspective, making it difficult to discern temporal trends. The current gap in comprehensive epidemiological research necessitates a thorough analysis to inform targeted prevention and intervention measures.

The updated Global Burden of Disease (GBD) data highlights the urgent need for targeted interventions and policy changes to address the escalating disease burden and promote universal health coverage. It also underscores the importance of increased investment in research, particularly in low- and middle-income countries, to better comprehend and address the complex determinants of health inequalities.

This study seeks to supplement the shortness of previous literature by conducting a comprehensive epidemiological investigation of soft tissue and extraosseous sarcomas from 1990 to 2021 using the GBD 2021. By

examining this extensive time frame, we aim to uncover the demographic and geographical variations, thereby advancing global public health and informing the development of future research and clinical management strategies.

2. Methods

The GBD, initiated by the Institute for Health Metrics and Evaluation, is a global health project that quantifies the health-related consequences of various diseases, injuries, and risk factors worldwide. The GBD serves as a critical resource for policymakers, researchers, and global health stakeholders, providing a comprehensive understanding of the global health landscape and informing evidence-based decision-making. The latest edition, GBD 2021, incorporates the most up-to-date data and methodologies, reflecting the dynamic nature of global health trends (GBD 2021 Risk Factors Collaborators, 2024; GBD 2021 Causes of Death Collaborators, 2024; GBD 2021 Diseases and Injuries Collaborators, 2024). This latest iteration offers a wealth of new insights to guide public health strategies, research, and international development initiatives.

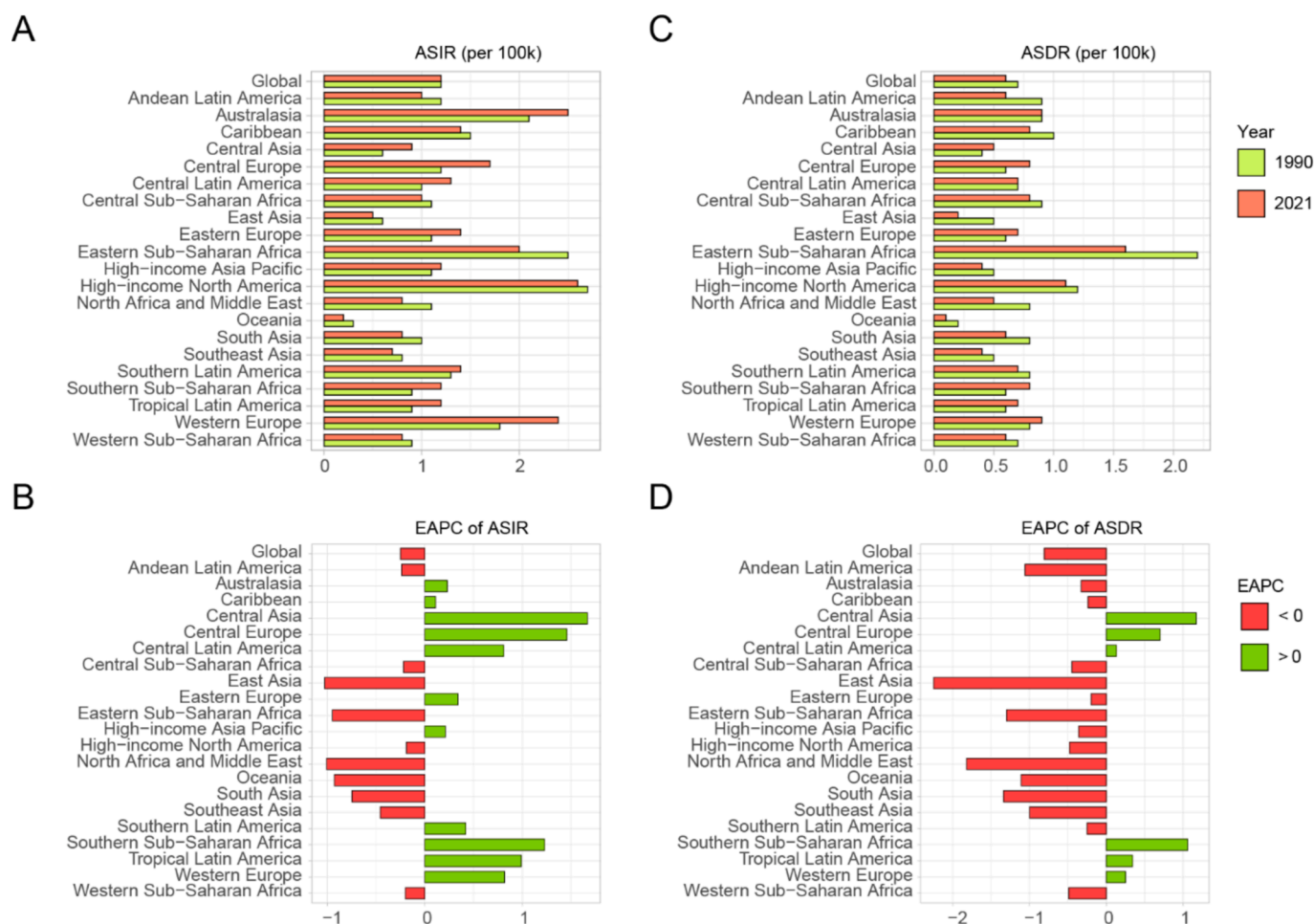


Fig. 2. The age-standardized incidence rate (ASIR) and age-standardized death rate (ASDR) of soft tissue and extraosseous sarcomas in Global Burden of Disease regions in 1990 and 2021, as well as their estimated annual percentage change (EAPC) from 1990 to 2021. A The age-standardized incidence rate of soft tissue and extraosseous sarcomas in Global Burden of Disease regions in 1990 and 2021; B The estimated annual percentage change of age-standardized incidence rate of soft tissue and extraosseous sarcomas in Global Burden of Disease regions from 1990 to 2021; C The age-standardized death rate of soft tissue and extraosseous sarcomas in Global Burden of Disease regions in 1990 and 2021; D The estimated annual percentage change of age-standardized death rate of soft tissue and extraosseous sarcomas in Global Burden of Disease regions from 1990 to 2021.

The GBD 2021 classified 204 countries into 21 GBD regions, which share similar health profiles, development indicators, and epidemiological trends (<https://ghdx.healthdata.org/countries>). The GBD 2021 data are publicly available and can be accessed through its website (<https://vizhub.healthdata.org/gbd-results/>). In this study, incidence and death data, as well as their 95 % uncertainty interval (UI), of soft tissue and extraosseous sarcomas from 1990 to 2021 were extracted.

2.1. Statistical analysis

A systematic assessment of the global burden of soft tissue and extraosseous sarcomas was conducted using the GBD 2021 dataset. Incidence and death data were derived from the GBD results tool, accessible at <https://vizhub.healthdata.org/gbd-results>. We calculated the estimated annual percentage change (EAPC) with 95 % confidence intervals (CI), where positive values represent an upward trend and negative ones represent a downward trend. Subsequently, the demographic patterns of soft tissue and extraosseous sarcomas were analyzed in-depth based on age and gender. R software (version 4.2.2) was used for data analysis and visualization.

3. Results

3.1. The burden of soft tissue and extraosseous sarcomas at the global level

From 1990 to 2021, there was an increase in the number and crude rate of incidence and death of soft tissue and extraosseous sarcomas, while the age-standardized rate declined. Notably, males consistently exhibited a heavier burden compared to females, as illustrated in Fig. 1.

The global incidence number of soft tissue and extraosseous sarcomas escalated from 54631 (95 % UI: 46757 to 64000) in 1990 to 96201 (95 % UI: 83424 to 116185) in 2021. The crude incidence rate increased from 1.02 (95 % UI: 0.88 to 1.2) in 1990 to 1.22 (95 % UI: 1.06 to 1.47) in 2021, with an EAPC of 0.46 (95 % CI: 0.38 to 0.55). However, the age-standardized incidence rate (ASIR) exhibited a different trend, decreasing from 1.21 (95 % UI: 1.04 to 1.39) in 1990 to 1.16 (95 % UI: 1 to 1.41) in 2021, with an EAPC of -0.25 (95 % CI: -0.32 to -0.18).

During the same period, the death number of soft tissue and extraosseous sarcomas rose from 31878 (95 % UI: 26446 to 37708) in 1990 to 50203 (95 % UI: 43232 to 61280) in 2021. The crude death rate increased from 0.6 (95 % UI: 0.5 to 0.71) in 1990 to 0.64 (95 % UI: 0.55 to 0.78) in 2021, with an EAPC of 0.07 (95 % CI: -0.03 to 0.16). By contrast, the age-standardized death rate (ASDR) decreased from 0.74 (95 % UI: 0.62 to 0.86) in 1990 to 0.6 (95 % UI: 0.52 to 0.74) in 2021,

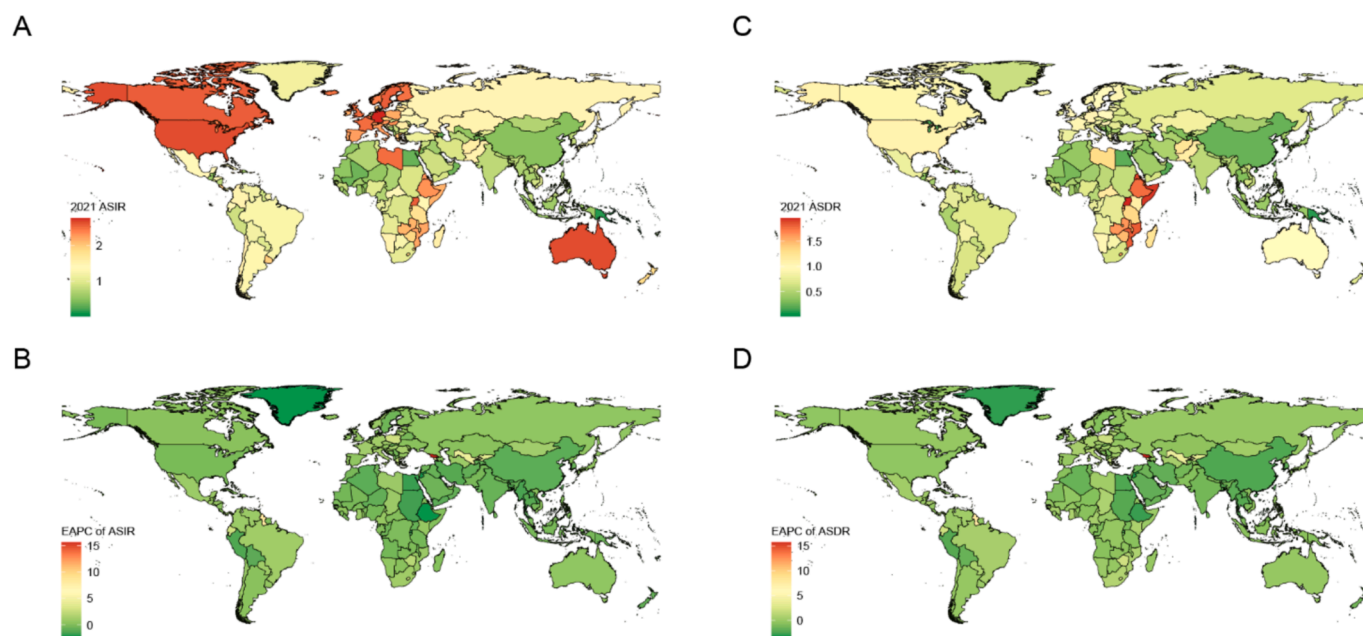


Fig. 3. The age-standardized incidence rate (ASIR) and age-standardized death rate (ASDR) maps of soft tissue and extrasosseous sarcomas by countries and territories in 2021, as well as their estimated annual percentage change (EAPC) maps from 1990 to 2021. A The age-standardized incidence rate maps of soft tissue and extrasosseous sarcomas by countries and territories in 2021; B The estimated annual percentage change maps of age-standardized incidence rate of soft tissue and extrasosseous sarcomas by countries and territories from 1990 to 2021; C The age-standardized death rate maps of soft tissue and extrasosseous sarcomas by countries and territories in 2021; D The estimated annual percentage change maps of age-standardized death rate of soft tissue and extrasosseous sarcomas by countries and territories from 1990 to 2021.

with an EAPC of -0.81 (95 % CI: -0.88 to -0.74).

3.2. The burden of soft tissue and extrasosseous sarcomas at the GBD regional level

At the regional level, significant disparities were revealed. Fig. 2 presents a comparison across different GBD regions, with detailed data provided in Tables S1 and S2.

In 2021, High-income North America (2.63 (95 % UI: 2.48 to 2.77)), Australasia (2.52 (95 % UI: 2.18 to 2.88)), and Western Europe (2.41 (95 % UI: 2.21 to 2.59)) had the highest ASIR. The highest EAPC of ASIR were found in Central Asia (1.67 (95 % CI: 1.3 to 2.04)), Central Europe (1.46 (95 % CI: 1.25 to 1.68)), and Southern Sub-Saharan Africa (1.23 (95 % CI: 0.9 to 1.56)).

With regards to ASDR, Eastern Sub-Saharan Africa (1.58 (95 % UI: 1.18 to 2.45)), High-income North America (1.07 (95 % UI: 1 to 1.11)), and Australasia (0.94 (95 % UI: 0.82 to 1.08)) had the highest ASDR in 2021. Among the regions with high EAPC of ASDR, Central Asia (1.17 (95 % CI: 0.86 to 1.47)), Southern Sub-Saharan Africa (1.06 (95 % CI: 0.68 to 1.44)), and Central Europe (0.7 (95 % CI: 0.46 to 0.94)) ranked the highest.

3.3. The burden of soft tissue and extrasosseous sarcomas at the national and territory level

At the national and territories level, ASIR in 2021 was highest in Germany (2.77 (95 % UI: 2.45 to 3.05)), Malta (2.74 (95 % UI: 2.22 to 3.38)), and Bermuda (2.7 (95 % UI: 2.14 to 3.49)). The highest EAPC of ASIR were found in Georgia (15.63 (95 % CI: 14.03 to 17.26)), Guyana (7.87 (95 % CI: 5.04 to 10.79)), and Armenia (4.49 (95 % CI: 3.71 to 5.27)).

For ASDR, Uganda (1.96 (95 % UI: 1.3 to 3.28)), Somalia (1.92 (95 % UI: 1.23 to 3.17)), and Eritrea (1.89 (95 % UI: 1.19 to 3.02)) had the highest ASDR in 2021. Georgia (15.75 (95 % CI: 14.13 to 17.4)), Guyana (7.38 (95 % CI: 4.59 to 10.25)), and Armenia (3.94 (95 % CI: 3.17 to

4.73)) had the highest EAPC of ASDR.

The geographical distribution of these findings is visualized in Fig. 3. Tables S3 and S4 provide a comprehensive analysis of the burden of soft tissue and extrasosseous sarcomas across different nations and territories.

3.4. Age and gender patterns of soft tissue and extrasosseous sarcomas

Fig. 4 displays the age and gender patterns of the disease burden for soft tissue and extrasosseous sarcomas. The incidence and death rates of soft tissue and extrasosseous sarcomas generally increased with age (after the age of 5), with a similar pattern in both males and females. It is worth noting that children under the age of 5 bear a heavier burden of incidence and mortality compared to other younger populations. Fig. 5 presents the disease burden across different age groups in 1990 and 2021, with similar patterns observed across genders. Compared to 1990, the incidence rate among the elderly increased in 2021, while the incidence rate in children under 5 decreased, and there was little change in other age groups. Encouragingly, the death rate among children and the elderly has decreased, while little change in other age groups has been observed.

4. Discussion

This study provides a unique opportunity to understand the impact of soft tissue and extrasosseous sarcomas on public health globally. By analyzing the data from 1990 to 2021, trends in incidence and mortality can be identified, and high-risk populations or geographic areas can be determined. This study can also inform policies aimed at addressing health disparities and improving global health outcomes by revealing inequalities between different geographical areas. Such epidemiological insights are crucial for allocating medical resources effectively.

In recent years, the incidence of STS has steadily increased globally, with significant disparities in incidence rates among different regions (Amadeo et al., 2020; Gage et al., 2019). The cancer registry systems of eight university hospitals in Japan recorded a crude incidence rate of 3.4

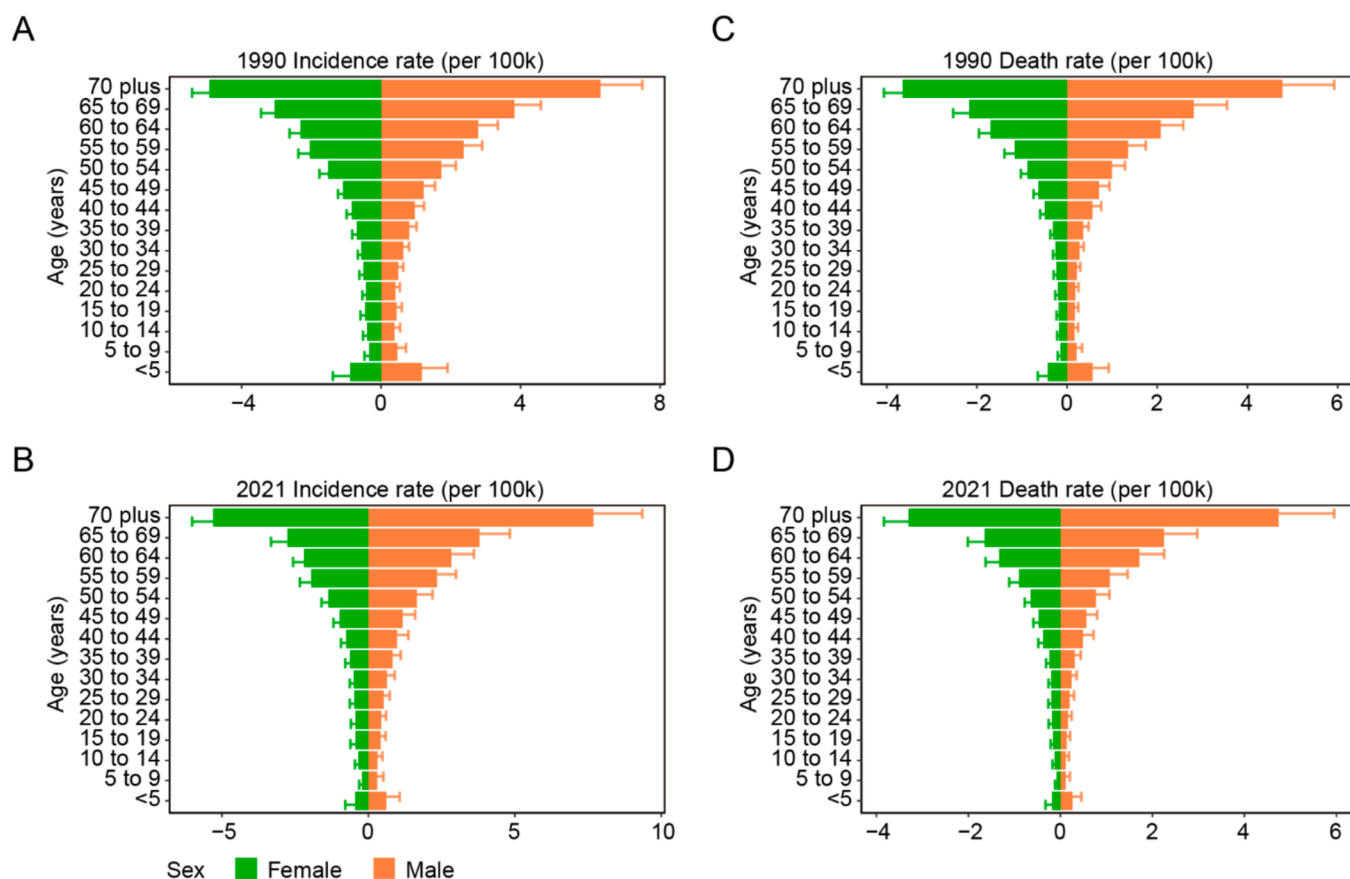


Fig. 4. The gender disparities in the global incidence and death rates of soft tissue and extraosseous sarcomas across age in 1990 and 2021. A The gender disparities in the global incidence rates of soft tissue and extraosseous sarcomas across age in 1990; B The gender disparities in the global incidence rates of soft tissue and extraosseous sarcomas across age in 2021; C The gender disparities in the global death rates of soft tissue and extraosseous sarcomas across age in 1990; D The gender disparities in the global death rates of soft tissue and extraosseous sarcomas across age in 2021.

per 100,000 from 2016 to 2019 (Nakamura et al., 2024). According to two European epidemiological studies, the total crude incidence rate of adult STS was 4.2 to 4.7 per 100,000 per year between 1995 and 2007 (Gatta et al., 2017; Stiller et al., 2013). Social factors may affect the prognosis of patients with STS (Nakamura et al., 2024).

Despite the recent rise in the incidence of STS, patient survival rates have slightly improved. In Europe, the 5-year relative survival rate for adult STS was 60 % from 2000 to 2007, with an insignificant change in the 5-year relative survival rate from 2002 to 2004, but an increase of 3–4 % from 2005 to 2007 (Stiller et al., 2018). A retrospective registry study from the National Institute for Cancer Epidemiology and Registration in Switzerland for the years 1996 to 2015 revealed that the 5-year relative survival rate for STS significantly improved from 56.4 % in 1996–2001 to 61.6 % in 2011–2015 due to advances in STS management (Kollar et al., 2019). It is worth noting that while the overall population increased, the number of deaths from STS rose significantly.

The epidemiology of STS shows variations between genders. A study based on surveillance, epidemiology and end results program, covering 26,758 STS cases in the United States from 1978 to 2001, reported a higher incidence in males compared to females (Toro et al., 2006). A study on the North American Association of Central Cancer Registries examined STS incidence in adolescents and young adults aged 15–29 years from 1995 to 2008 and found a 34 % higher incidence in males compared to females (Hsieh et al., 2013). There was a male-to-female gender ratio of 1.73:1 in North India (Sharma et al., 2024). In the Italian Veneto region between 1990 and 2018, there were higher incidence rates of STS in males across all age groups, with a mild increasing trend over the past three decades in males, while female STS incidence remained stable (Buja et al., 2023). These findings may be associated

with environmental toxic substances and occupational exposures, predominantly involving males. Additionally, the sites and subtypes of STS differ between genders. In women, retroperitoneal STS is more prevalent, whereas men are more susceptible to developing STS in the limb, head, and neck (Buja et al., 2023). Undifferentiated sarcomas and liposarcomas are more frequent in men, while leiomyosarcomas, especially uterine leiomyosarcomas, are most common in women (Bacon et al., 2023).

Age is a critical factor in the epidemiology of STS. A positive correlation between age and incidence of STS was found in a study based on surveillance, epidemiology and end results program in the United States (Toro et al., 2006). In Europe, there was an increasing incidence rate with age in STS, except for cardiac and parorbital STS (Stiller et al., 2013). A study in Switzerland found a steady increase in the incidence and mortality of STS up to the age of 89 (Kollar et al., 2019). The survival rate for those aged 65 and above is lower than that of younger individuals (Ferrari et al., 2022; Nakamura et al., 2024; Stiller et al., 2013).

It is noteworthy that the incidence of STS in children has been increasing in recent years (Stiller, 1982). STS account for about 15 % of all cancers in children, with a 10-year survival rate of no more than 50 % (Cosci et al., 2023; Stiller, 1982). There are significant gender differences in sarcomas in young children, with a stronger association in males, especially for STS (Cosci et al., 2023).

With the aging world population, the incidence of STS in the elderly is also rising, and older STS patients generally have a poorer prognosis (Lv et al., 2024; Tsuchie et al., 2018). The Italian Cancer Registries' research reported a high crude incidence rate among the elderly: 9.23/100,000 for ages 55–64, and 13.97/100,000 for ages 65 and above,

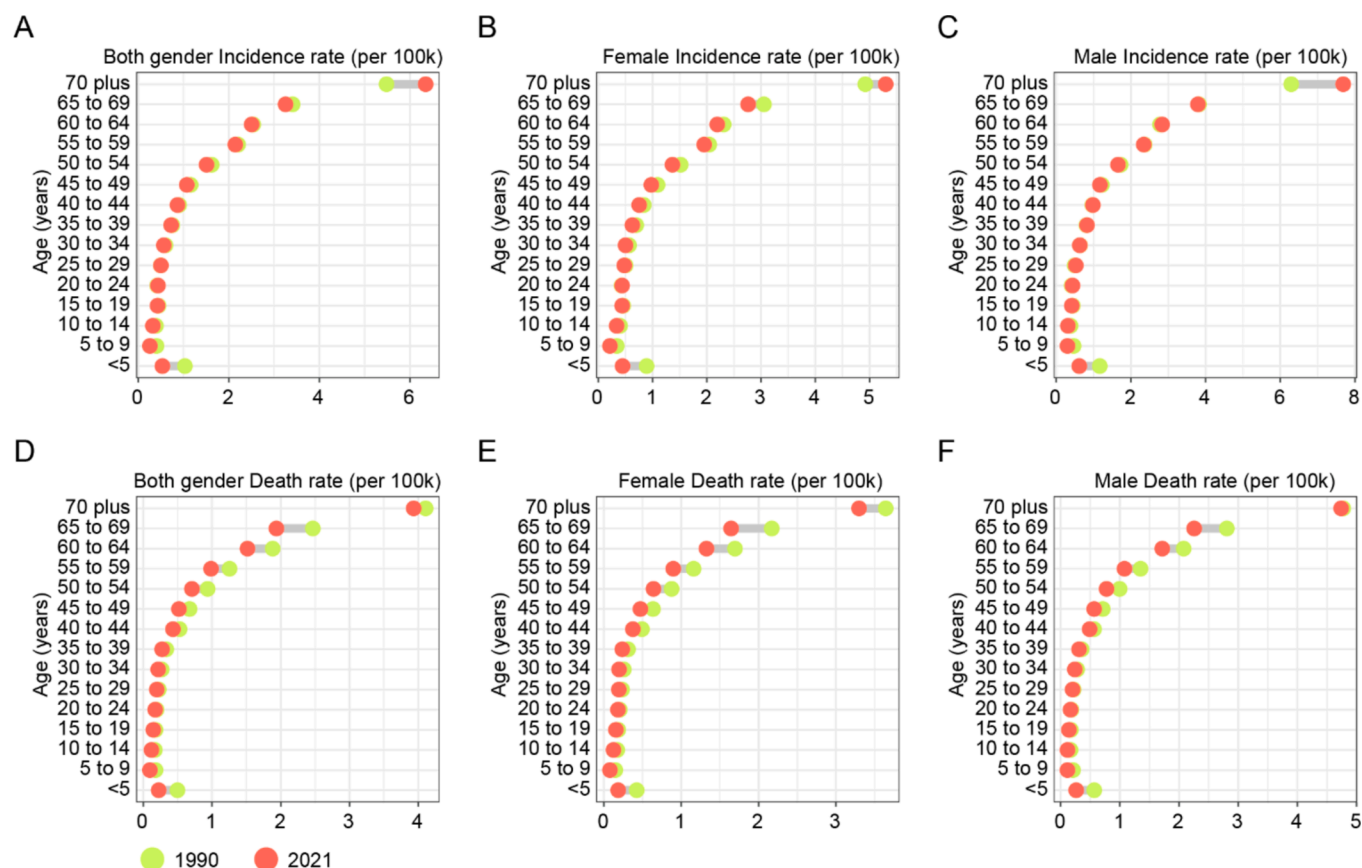


Fig. 5. The change of global incidence and death rates of soft tissue and extraosseous sarcomas across age and gender from 1990 to 2021. A The change of global incidence rates of soft tissue and extraosseous sarcomas across age for both genders from 1990 to 2021; B The change of global female incidence rates of soft tissue and extraosseous sarcomas across age from 1990 to 2021; C The change of global male incidence rates of soft tissue and extraosseous sarcomas across age from 1990 to 2021; D The change of global death rates of soft tissue and extraosseous sarcomas across age for both genders from 1990 to 2021; E The change of global female death rates of soft tissue and extraosseous sarcomas across age from 1990 to 2021; F The change of global male death rates of soft tissue and extraosseous sarcomas across age from 1990 to 2021.

compared with 3.49/100,000 for ages 0–54. Recent studies indicated that nearly half of STS patients were over the age of 65, and the incidence of sarcomas increased with age (Verras et al., 2022; Younger et al., 2018). Age is also significantly associated with survival rates in STS patients. A study on the Netherlands Cancer Registry system for adult extremity STS patients between 1989 and 2008 showed a 5-year survival rate of 43.8 % for those over 85 years old, compared to 72.7 % for young STS patients (Hoven-Gondrie et al., 2016). In recent years, with the exploration of personalized multidisciplinary comprehensive treatment methods to control disease progression, the life expectancy of elderly STS patients is expected to increase (Bleckman et al., 2022).

4.1. Limitations of this study

This study possesses certain limitations. Firstly, it lacks an analysis of soft tissue and extraosseous sarcoma subtypes and locations. Secondly, the availability of health data constrains the GBD 2021. The accuracy of the data may vary due to the quality and completeness of the information collected, especially in low-income and underdeveloped regions. This variability could result in underestimation or misrepresentation of health burdens in these areas. Thirdly, the model used for GBD 2021 has limitations that can introduce errors or uncertainties in estimating disease burden. This means it might not fully capture the complexity of the situation. Despite these limitations, GBD 2021 has made significant efforts to address them, including updating methods and data sources based on GBD 2019 to ensure the reliability and robustness of its results. Future versions of the GBD will likely continue to improve data

collection methods and incorporate the latest scientific evidence.

5. Conclusion

The disease burden of soft tissue and extraosseous sarcomas remains a critical challenge. Data-driven analysis is crucial for guiding clinical practice, informing public health policies, and shaping future research agendas.

6. Ethics approval and consent to participate

This study was a secondary analysis of GBD 2021, using public data. Ethical compliance is exempted for this study.

CRediT authorship contribution statement

Cheng Chen: Writing – original draft, Investigation. **Cheng Wang:** Writing – original draft, Investigation. **ShiJie Li:** Writing – review & editing, Investigation. **Xu Zheng:** Visualization, Methodology, Formal analysis, Data curation. **YunFeng Yang:** Writing – review & editing, Project administration, Funding acquisition.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pmedr.2024.102903>.

Data availability

Data will be made available on request.

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