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Steady survival improvements in soft tissue and bone sarcoma in the Nordic countries through 50 years

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ABSTRACT

Purpose: Sarcomas are rare cancers with many subtypes in soft tissues, bone and cartilage. International survival trends in these cancers are not well known. We present 50-year survival trends for soft tissue sarcoma (STS) and bone sarcoma (BS) in Denmark (DK), Finland (FI), Norway (NO) and Sweden (SE).

Methods: Relative 1-, 5/1 conditional- and 5-year survival data were obtained from the NORDCAN database for years 1971–20. We additionally estimated annual changes in survival rates and determined significant break points.

Results: In the last period, 2016–20, 5-year survival in STS was best for NO men (74.6%) and FI women (71.1%). For the rarer BS, survival rates for SE men (72.0%) and DK women (71.1%) were best. Survival in BS was lower than that in STS in 1971–75 and the difference remained in 2016–20 for men, but for women the rates were almost equal. Sex- and country-specific differences in survival in STS were small. The 50-year improvement in 5-year survival in STS was highest in NO men, 34.0 % units and FI women, 30.0 % units. The highest improvements in BS were in SE men 26.2 % units and in FI women 29.2 % units.

Conclusions: The steady development in survival over the half century suggests contribution by stepwise improvements in diagnostics, treatment and care. The 10–15% mortality in the first year probably indicates diagnostic delays which could be improved by organizing patient pathways for aggressive rare diseases. Early diagnosis would also reduce metastatic disease and breakthroughs in treatment are a current challenge.

1. Introduction

Connective tissue tumors or sarcomas are a heterogeneous group of neoplasms that arise from cells of mesenchymal origin and account for less than 1% of all malignancies [1]. The International Classification of Diseases (ICD) uses separate codes for soft tissue and bone tumors, of which soft tissue sarcomas (STSs) are more common than bone sarcomas (BSs) [2–4]. STSs may be diagnosed in any part of the body. The incidence in STS increases with age but BS has two age maxima, one before age 20 (common for osteosarcoma and Ewing sarcoma) and the other at around 75 years (chondrosarcoma and osteosarcoma) (https://nordcan.iarc.fr/en) [4]. Although the causes of these tumors are largely unknown, some environmental risk factors, such as ionizing radiation, immunosuppressive drugs, human immunodeficiency virus, and occupational exposures are known or suggested risk factors [5,6]. Family histories of STS and BS are other known risk factors [7,8]. A small fraction of STSs and BSs may be attributed to rare hereditary cancer syndromes, including Li-Fraumeni syndrome [9,10]. Soft tissue tumors are characterized by frequent somatic chromosomal rearrangements, including translocations (such as translocation between chromosomes 11 and 22 in Ewing sarcoma), which have diagnostic and clinical implications [11–14].

Symptoms for sarcomas include swollen tissue, pain and problems with movement [4]. Diagnostics may not be easy because of rarity of

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sarcomas, their possibly vague symptoms and the multiplicity of the tumor types; thus guidelines advise referral of patients to specialists without delays [4]. New imaging tools, including diffusion-weighted imaging and magnetic resonance imaging radiomics, allow assessment of tumor extension and help tumor grading but biopsy is required for histological confirmation [10,15]. Upfront diagnostics of fusion proteins are part of the current diagnostic routine [14,15]. Standard treatment for STS and for BS is based on complete surgical resection with or without adjuvant (or with neoadjuvant) radiotherapy and chemotherapy; for chemotherapy, multidrug regimens are often used [4, 10, 14, 15]. Novel chemotherapeutic regimens have become available with possible help to patients with metastatic disease, and improvements in radiotherapy have reduced local adverse effects with sustained good local control [4,15]. Whenever possible, the treatment should be done in specialist clinics by multidisciplinary teams [4]. Between 1999 and 2007, 5-year survival in Europe for STS was estimate at 60% and for BS at 50% [16]. Recent 5-survival for both of these cancers has reached close to 70% in the Nordic countries [17].

We will assess relative survival in STS and BS in Denmark (DK), Finland (FI), Norway (NO) and Sweden (SE) for a 50-year period from 1971 to 2020 with focus on changes in survival times between the countries and discuss the possible causes of observed survival changes. In addition to 1- and 5-year survival we report conditional survival from 1st to 5th (5/1) year and annual changes in survival. As background data to survival, we show incidence and mortality data on STS and BS from these countries.

2. Methods

The data were obtained from NORDCAN database 2.0 [18,19]. The data for NORDCAN were delivered by the cancer registries of each country, and these included both incidence and mortality data [20]. We accessed NORDCAN at the International Agency for Cancer (IARC) website (https://nordcan.iarc.fr/en) [20], and the available tools were used to extract data on incidence, mortality and 1-year and 5-year survival. ICD version 10 codes were used in NORDCAN to describe the tumor locations. For STS the code was C49 (including gastrointestinal stromal tumors, C49. A2) and for BS it was C40 and C41.

The follow-up was terminated at death, emigration or loss of follow-up or by the end of 2020. Incidence and mortality data were age-standardized for the world standard population. For incidence and mortality data, the starting date was 1961 (the earliest available for all countries). We considered that such early data were informative because such nation-wide data were not available elsewhere. Survival data for relative survival were available from 1971 onwards and the analysis was based on the cohort survival method for the first nine 5-year periods, and a hybrid analysis combining period and cohort survival in the last period 2016–2020, as detailed [21]. Age-standardized relative survival was estimated using the Pohar Perme estimator [22]. Age standardization was performed by weighting individual observations using external weights as defined on the IARC website. Age groups 0–89 were considered. The DK, FI, NO and SE life tables were used to calculate the expected survival.

Statistical modelling and data visualizations were performed using R statistical software (https://www.r-project.org) in the R studio environment (https://posit.co/) (code available at https://github.com/filip-tichanek/nord_female). For a graphic presentation of incidence and mortality rates, lines were smoothed by the cubic smoothing spline using the R function 'smooth.spline' with a smoothing parameter ('spar') of 0.4 and with 12 knots.

Time trends of 1-year and 5-year relative survival (in %; obtained from NORDCAN for each of the 5-year periods) were modelled using the Gaussian generalized additive models (GAM) with thin plate splines (5 knots) and identity links. The GAM model included the effect of *country* and *country*-specific non-linear effect of *time* (timepoint = middle year of each 5-years period) as predictors, allowing estimation of the relative survival across a continuous time scale despite the discrete distribution of data points. As the input data (estimates of the 1-year and 5-year survival in each of the 5-year periods) were variably uncertain, standard errors for each data point (obtained from confidence intervals shown in the NORDCAN database) were included in the model. Models were run in the Bayesian framework using the 'brms' R package [23,24], which employs 'Stan' software for probabilistic sampling [25]. Separate models were used for different cancers and 1-year and 5-year survival.

The prior distribution for the effect of the *country* was explicitly defined to have Gaussian distribution with zero mean and sigma of 30. Default brms priors were used for other parameters. We used Hamiltonian Monte Carlo sampling (2 chains, each of 7000 samples including 2000 warm-ups). All models were checked in terms of convergence, effective sample sizes and posterior predictive check.

For the 5/1-year survival ratio estimation, we divided the posterior draws from the 5-year survival model by the posterior draws from the 1-year model to get the posterior distribution of the conditional survival and its estimated annual changes over time.

For all survival measures (relative 1-year and 5-year survival and 5/1-year ratio), we evaluated when the survival was changing over time with at least 95% plausibility (95% credible interval [Ci] of the 1st derivation of given survival measure did not cross zero for at least 5 years). We also aimed to identify 'breaking points', i.e. times when the annual change of survival changed with at least 95% plausibility. This was assessed by calculation of the 2nd derivation of the given survival measure and its 95% Ci; the 'breaking point' was defined as a peak value within at least a 3-year interval where 95% Ci for the 2nd derivation did not cross zero.

Comparisons with the US Surveillance, Epidemiology and End Results (SEER) data for years 2012–18 on Non-Hispanic white were done through (https://seer.cancer.gov/statistics-network/explorer/application.html?
site=1&data_type=1&graph_type=2&compareBy=sex&chk_sex_3=3&chk_sex_2
=2&rate_type=2&race=1&age_range=1&hdn_stage=101&advopt_precision=1&advopt_show_ci=on&hdn_view=0&advopt_display=2#graphArea).

3. Results

In Table 1 we show case numbers, incidence and mortality rates, cumulative risks and median ages for STS and BS in the Nordic countries for years 2011–2020. The incidence was over two times higher in STS compared to BS, and the male rates were somewhat higher than the female rates. Cumulative incidence up to age 74 was over 0.2% for male STS, below 0.2% for female STS, below 0.1% for male BS, and even lower for female BS. With a large adolescent patient share, the median diagnostic age in BS was lower than that in STS.

Incidence and mortality rates over 60 years are shown in Fig. 1. The incidence for STS and BS, both for men and women, was approximately equal in 1960, but thereafter incidence increased for STS and remained stable or decreased for BC, resulting in over 2-fold difference in 2020. Mortality for male STS declined in FI but remained fairly stable in the other countries. BC mortality, particularly for men, declined over time.

Fig. 2 shows relative 1-, 5/1- and 5-year survival for STS and BS in DK men (**a, b**) and women (**c,d**), The DK curves for both cancers were almost linear but the curves for BS started at a lower level and ended close to the level of STS, which can be witnessed as larger annual changes (bottom small panels). A breaking point was found for male 1-year survival at 1988 marking the trend change.

For FI in Fig. 3 and NO in Fig. 4 the curves show time dependent downward bending which indicated decreased rates of improvement.

The curves for SE (Fig. 5) were approximate linear except for female BS for which the development stopped after year 2000 for all survival parameters and particularly for 5-year survival.

Supplementary Table 1 lists 1- and 5-year survival rates in STS and

Table 1
Incidence (A) and mortality rates (B; both age-standardized (ASR) to the world population) in soft tissue and bone sarcomas from 2011–2020, separately for males (left part) and females (right part). Cumulative rate is shown in % and for age span 0–74 years. In the part (A), median age interval at diagnosis is also shown.

A) Case numbers, incidence (ASR - world), median age, and cumulative incidence (%, 0–74)							
Males	ASR	Cum. inc	Median age	Females	ASR	Cum. inc	Median age
Soft tissue							
Denmark, 1212	2.5	0.25	65–69	Denmark, 964	2.1	0.21	60–64
Finland, 1113	2.4	0.23	65–69	Finland, 868	1.6	0.16	65–69
Norway, 983	2.4	0.23	65–69	Norway, 725	1.8	0.17	65–69
Sweden, 1763	2.0	0.21	65–69	Sweden, 1312	1.5	0.15	65–69
Bone							
Denmark, 389	1.2	0.10	50–54	Denmark, 284	0.90	0.07	45–49
Finland, 299	0.88	0.08	50–54	Finland, 239	0.68	0.06	60–64
Norway, 324	1.0	0.09	50–54	Norway, 254	0.83	0.07	50
Sweden, 551	1.0	0.08	45–49	Sweden, 446	0.81	0.06	45–49
B) Death numbers, mortality (ASR - world) and cumulative mortality (%, 0–74)							
Soft tissue	**ASR**	**Cum. mort**		**Females**	**ASR**	**Cum. mort**	
Denmark, 362	0.74	0.08		Denmark, 322	0.64	0.07	
Finland, 408	0.78	0.07		Finland, 355	0.65	0.05	
Norway, 336	0.76	0.08		Norway, 306	0.66	0.07	
Sweden, 769	0.80	0.08		Sweden, 850	0.83	0.09	
Bone							
Denmark, 144	0.33	0.03		Denmark, 107	0.21	0.02	
Finland, 144	0.39	0.03		Finland, 79	0.16	0.01	
Norway, 140	0.38	0.04		Norway, 100	0.22	0.02	
Sweden, 239	0.35	0.03		Sweden, 169	0.23	0.02	

BS in 5-year periods to allow comparison of the country-specific rates. In 2016–20, 5-year survival in STS was best for NO men (74.6%) and FI women (71.1%). Overall the country-specific differences were small. For BS, SE men (72.0%) and DK women (71.1%) were on top. Comparing sex differences for 5-year survival in 2016–20 in STS, male rates were higher than female rates in all countries but FI; for BS, female rates were higher in all countries but SE.

Data from Supplementary Table 1 enable estimation of the magnitude of survival improvements over the 50-year period. Improvement in 5-year survival in STS was highest in NO men, 34.0 % units, and FI women, 30.0 % units. The highest improvement in BS were also in SE men 26.2 % units and in FI women 29.2 % units.

In Supplementary Table 2, 5/1-year survival is reported in 5-year periods. These figures allow comparison with 1-year survival figures (cf. Supplementary Table 1) and estimation of death rates in year 1 and in the 4 subsequent years. While 1-year survival in STS was around 90% in the last period, 5/1-year survival was about 10% units lower, indicating about a doubling of mortality in these four years compared to year 1. Similarly, higher 5/1-year mortality compared to 1-year mortality was also observed for BS.

4. Discussion

Sarcomas constitute numerous tumor types each of which are rare, hampering survival studies, particularly between countries. The Nordic cancer registries have a long history of collaboration and it is assumed that the data are in general comparable [19]. In the field of rare cancer oncology, Nordic sarcoma specialists have a history of collaborative studies and trials [26]. Country-specific differences in survival in STS were small. In the last period, 2016–20, 5-year survival in STS was best for NO men (74.6%) and FI women (71.1%). For the rarer BS, survival rates for SE men (72.0%) and DK women (71.1%) were best. Survival in BS was lower than that in STS in 1971–75 and the difference remained in 2016–20 for men, but for women the rates were almost equal. Sex differences were in general small. A curious 'anomaly' was noted for survival in BS for SE women; at around year 2000 their survival improvements stalled and 5-year survival was lower in 2016–20 (64.87%) than it was in 1996–00 (74.3%). For SE men, survival kept on improving. The 50-year improvement in 5-year survival in STS was highest in NO men, 34.0 % units and FI women, 30.0 % units. The highest improvements in BS were also in SE men 26.2 % units and in FI women 29.2 % units.

In STS 1-year survival in 2016–20 was close to 90% but survival in BS was more than 5 % units lower (FI men 10 % units lower). However, in SE 1-year survival in both cancers was equally high indicating that early mortality could be effectively prevented also in BS. How this was achieved in SE is not known but expert clinical recommendations emphasize early referral of sarcoma patients from primary care to specialist centers for diagnostic precision and appropriate treatment based on the findings [4, 10, 27, 28].

Sarcomas are a complex entity and they are rarely considered in international comparisons because of possible diagnostic differences resulting in variable incidence estimates, as discussed by the Scandinavian Sarcoma Group [26]. The first comprehensive European sarcoma study applied strict validation procedures to guarantee high quality for all included sarcoma subtypes [29]. High-quality data were also included into a later European study for which 5-year relative survival for STS was 61% and for BS it was 59% in 2005–7 [30]. A recent UK study on STS from years 2013–17 reported 1-year survival for malignant STS at 84% for men and 82% for women; 5-year survival was 68% for men and 62% for women [31]. These data were below the present Nordic ones for 5-year survival in STS (male range 69.6–74.6% and female range 68.1–71.1%). In US SEER database 5-year survival for non-Hispanic whites in period 2012–18 was for 'soft tissues and heart' 65.2% for men and 65.7% for women. For cancers of 'bones and joints' the rates were 65.8% and 69.5%. How comparable the data are with the NORDCAN data is not known but the reported US data for STS were below the Nordic data. For BS the US data were within the Nordic range (men 57.2–72.0%, women 64.8–71.1%) and give support to our data on female survival advantage in BS.

For most part the improvements in survival in STS and BS took place throughout the 50-year period, with the few exceptions which were pointed out above. This would be in line with gradual improvements in diagnostics, treatment and patient care in line with expert assessments [4,15]. However, 30% or more of the patients died within 5 years which is most likely due to recurrent and/or metastatic disease. The means of fighting metastasis are early detection and therapeutic improvements. Early detection involves the time between diagnosis and appearance of symptoms; novel molecular markers and imaging tools facilitate the process when in expert hands [4, 14, 15]. While surgery, chemotherapy and radiation are still the main treatments, some tumor types have shown success to more novel treatments – imatinib has been very

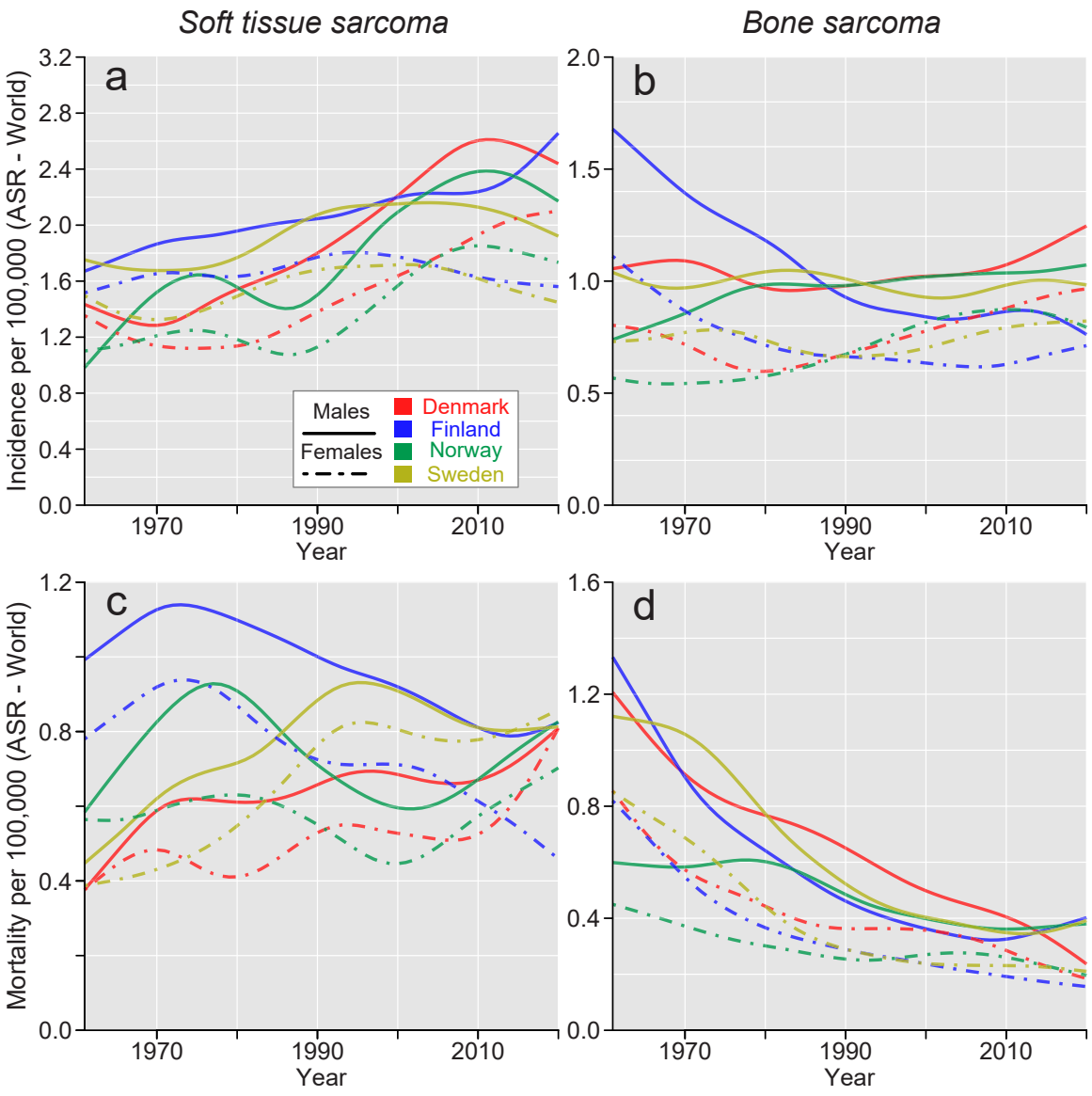

Fig. 1. Incidence (a,b) and mortality (c,d) in soft tissue (a,c) and bone (b,d) sarcomas from 1961 to 2020 in Denmark, Finland, Norway and Sweden, separately for males and females. Lines were smoothed via cubic smoothing spline.

successfully applied in gastrointestinal stromal tumors [4,32] and immunotherapy has gained popularity. While the role of immunotherapy is still being defined in sarcomas, there is rising interest in combinations of PD-1 inhibitors with standard-of-care treatments, especially chemotherapy [33]. Application of immunotherapy modalities for sarcoma requires yet to identify and overcome the barriers posed by the sarcoma microenvironment to immunotherapy [34].

The limitations in the present study are lacking of information of the defined types of STS and BS which vary in their clinical presentation. Age distribution of sarcomas is variable and unfortunately the NORDCAN data do not allow age-specific survival analyses. However, the NORDCAN data are uniquely long in follow-time and allow estimation of the most recent survival figures up to year 2020. Sarcomas are a complex collection of tumors which require high diagnostic precision; this is a characteristic of the Nordic cancer registries as certified by the quality criteria of IARC [35].

In conclusion, we could document a steady 50-year improvement in survival in STS and BS in the Nordic countries. In STS 1-year survival in 2016–20 was close to 90% and in BS it was a few % points lower. The overall improvement in 5-year survival in BS was somewhat better than survival in STS, and the final survival in women was equal in STS and BS reaching 70%. Male 5-year survival in STS also reached that level but male survival in BS remained at about 65%. The steady development in survival over the half century suggests contribution by stepwise improvements in diagnostics, treatment and care. The 10–15% mortality in the first year probably indicates diagnostic delays which could be improved by organizing patient pathways to aggressive rare diseases. Early diagnosis would also reduce metastatic disease but breakthroughs in treatment are yet to be hoped for most types of sarcoma, and treatment of gastrointestinal stromal tumors provides a welcome exception.

Ethics

Anonymous data from a publically available database were used posing no ethical issues.

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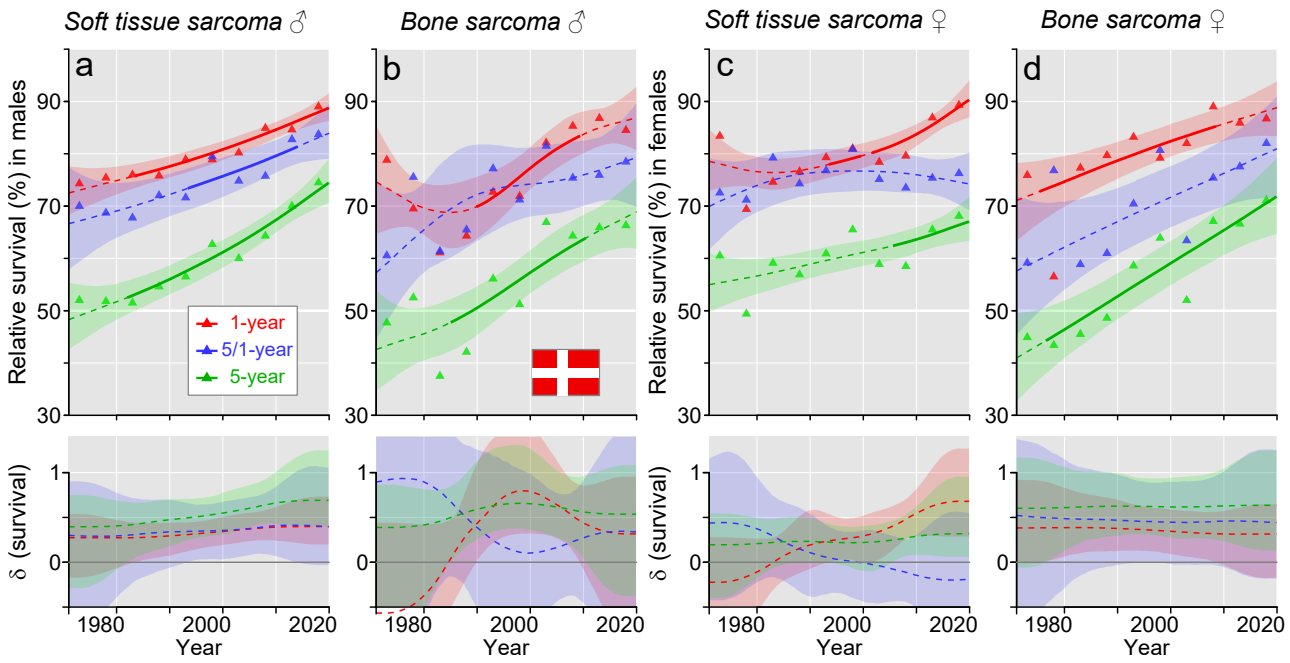

Fig. 2. Relative 1-, 5/1- and 5-year survival in Danish men (a,b) and women (c,d) in soft tissue (a,c) and bone (b,d) sarcomas. The vertical lines mark a detectable change in the survival trends ('breaking points') and the bottom curves show estimated annual changes in survival. The curves are solid if there is > 95% plausibility that the curve grows or declines. Shadow areas indicate 95% credible interval. All curves are color coded (see the insert).

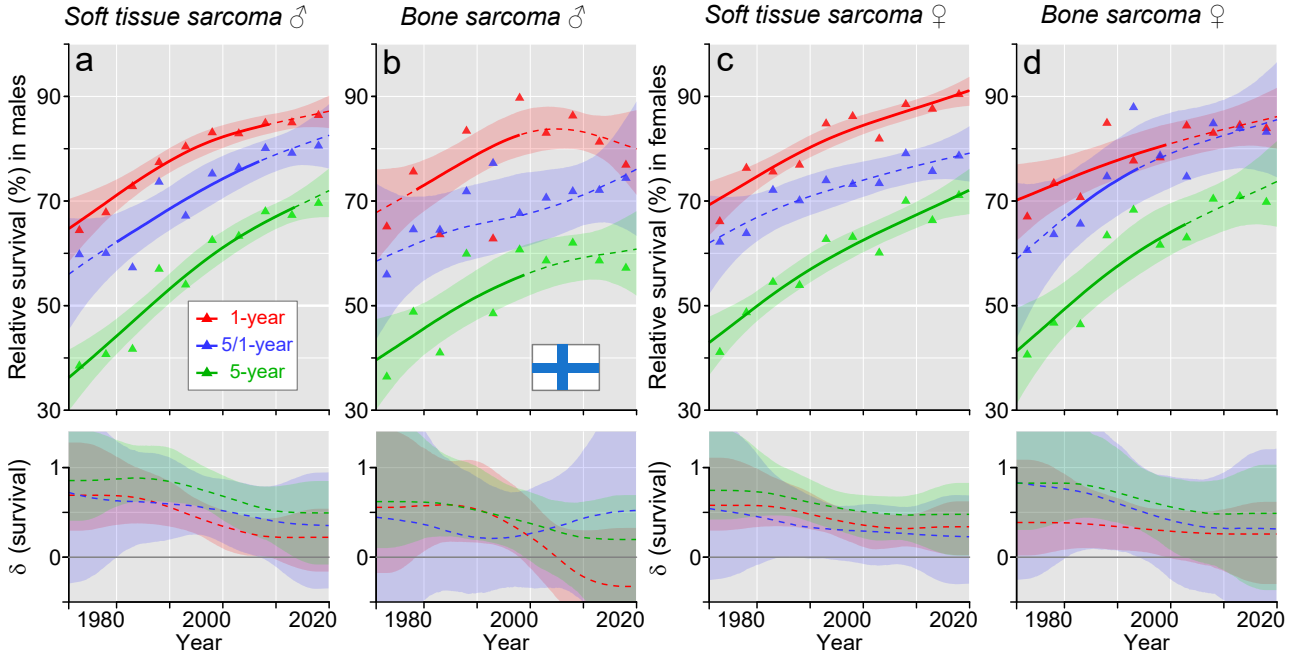

Fig. 3. Relative 1-, 5/1- and 5-year survival in Finnish men (a,b) and women (c,d) in soft tissue (a,c) and bone (b,d) sarcomas. No 'breaking points' were found but the bottom curves show estimated annual changes in survival. The curves are solid if there is > 95% plausibility that the curve grows or declines. Shadow areas indicate 95% credible interval. All curves are color coded (see the insert).

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CRediT authorship contribution statement

Design: KH, Acquisition of data: FT, KH, Statistical analysis and interpretation: KH, FT, AF, AH, Manuscript writing: KH, FT and all other authors. Approval of the final text: All authors.

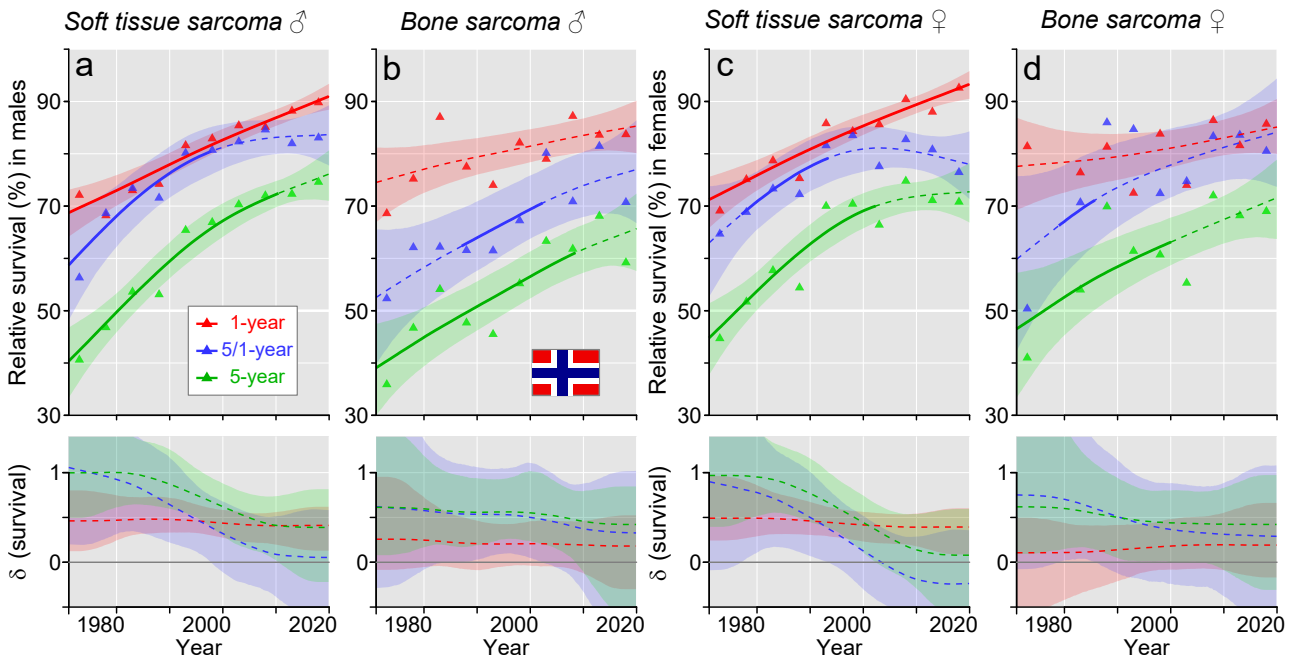

Fig. 4. Relative 1-, 5/1- and 5-year survival in Norwish men (a,b) and women (c,d) in soft tissue (a,c) and bone (b,d) sarcomas. No 'breaking points' were found but the bottom curves show estimated annual changes in survival. The curves are solid if there is > 95% plausibility that the curve grows or declines. Shadow areas indicate 95% credible interval. All curves are color coded (see the insert).

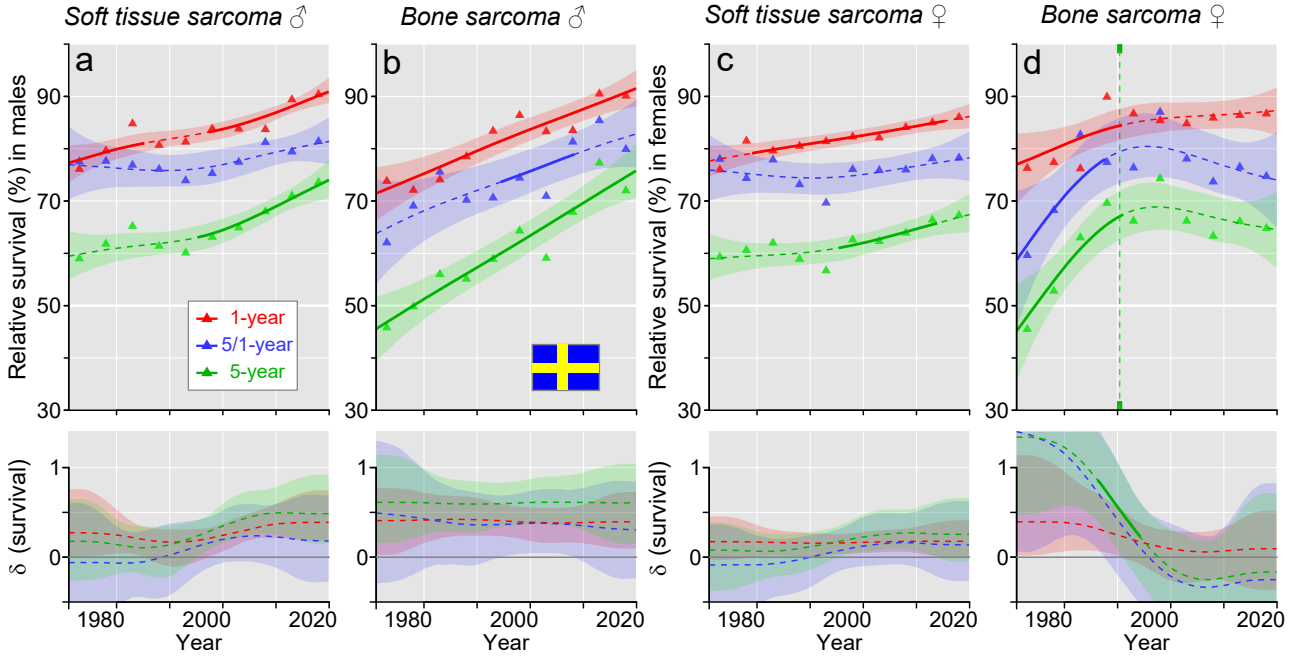

Fig. 5. Relative 1-, 5/1- and 5-year survival in Swedish men (a,b) and women (c,d) in soft tissue (a,c) and bone (b,d) sarcomas. The vertical lines mark a detectable change in the survival trends ('breaking points') and the bottom curves show estimated annual changes in survival. The curves are solid if there is > 95% plausibility that the curve grows or declines. Shadow areas indicate 95% credible interval. All curves are color coded (see the insert).

Declaration of Competing Interest

A.H. is shareholder in Targovax ASA. A.H. is employee and shareholder in TILT Biotherapeutics Ltd. Other authors declared no conflict of interest.

Data Availability

Aggregated data from a publically accessible database were used, posing no ethical issues. Full statistical R code is available at https://github.com/filip-tichanek/nord_melanoma.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2023.102449.

References

[1] C. Fletcher, K. Unni, F. Mertens, Pathology and genetics of tumors of soft tissue and bone, IARC Press, Lyon, 2002.
[2] J. Ji, K. Hemminki, Incidence of multiple primary malignancies among patients with bone cancers in Sweden, J. Cancer Res Clin. Oncol. 132 (8) (2006) 529–535.
[3] J. Ji, K. Hemminki, Second primary malignancies among patients with soft tissue tumors in Sweden, Int J. Cancer 119 (4) (2006) 909–914.
[4] E. Andritsch, M. Beishon, S. Bielack, S. Bonvalot, P. Casali, M. Crul, et al., ECCO essential requirements for quality cancer care: soft tissue sarcoma in adults and bone sarcoma. a critical review, Crit. Rev. Oncol. Hematol. 110 (2017) 94–105.
[5] T. Brown, C. Young, L. Rushton, Occupational cancer in Britain. Remaining cancer sites: brain, bone, soft tissue sarcoma and thyroid, Br. J. Cancer 107 (Suppl 1) (2012) S85–S91. Suppl 1.
[6] J.Y. Hui, Epidemiology and etiology of sarcomas, Surg. Clin. North Am. 96 (5) (2016) 901–914.
[7] J. Ji, C. Eng, K. Hemminki, Familial risk for soft tissue tumors: a nation-wide epidemiological study from Sweden, J. Cancer Res Clin. Oncol. 134 (5) (2008) 617–624.
[8] J. Ji, K. Hemminki, Familial risk for histology-specific bone cancers: an updated study in Sweden, Eur. J. Cancer 42 (14) (2006) 2343–2349.
[9] B. Vogelstein, K. Kinzler. The Genetic Basis of Human Cancer, 2nd ed., McGraw-Hill, New York, 2002.
[10] H.C. Beird, S.S. Bielack, A.M. Flanagan, J. Gill, D. Heymann, K.A. Janeway, et al., Osteosarcoma, Nat. Rev. Dis. Prim. 8 (1) (2022) 77.
[11] B. Johansson, F. Mertens, T. Schyman, J. Björk, N. Mandahl, F. Mitelman, Most gene fusions in cancer are stochastic events, Genes Chromosomes Cancer 58 (9) (2019) 607–611.
[12] M.A. Black, G.W. Charville, Diagnosis of soft tissue tumors using immunohistochemistry as a surrogate for recurrent fusion oncoproteins, Semin Diagn. Pathol. 39 (1) (2022) 38–47.
[13] U. Flucke, M.M. van Noesel, V. Siozopoulou, D. Creytens, B.B.J. Tops, J.M. van Gorp, et al., EWSR1-the most common rearranged gene in soft tissue lesions, which also occurs in different bone lesions: an updated review, Diagn. (Basel) 11 (6) (2021).
[14] D.S. Shulman, S.B. Whittle, D. Surdez, K.M. Bailey, E. de Álava, J.T. Yustein, et al., An international working group consensus report for the prioritization of molecular biomarkers for Ewing sarcoma, NPJ Precis Oncol. 6 (1) (2022) 65.
[15] J. Gómez, P. Tsagozis, Multidisciplinary treatment of soft tissue sarcomas: an update, World J. Clin. Oncol. 11 (4) (2020) 180–189.
[16] P. Baili, F. Di Salvo, R. Marcos-Gragera, S. Siesling, S. Mallone, M. Santaquilani, et al., Age and case mix-standardised survival for all cancer patients in Europe 1999-2007: Results of EUROCARE-5, a population-based study, Eur. J. Cancer 51 (15) (2015) 2120–2129.
[17] J. Hemminki, A. Försti, A. Hemminki, K. Hemminki, Survival trends in solid cancers in the Nordic countries through 50 years, Eur. J. Cancer 175 (2022) 77–85.
[18] G. Engholm, J. Ferlay, N. Christensen, F. Bray, M.L. Gjerstorff, A. Klint, et al., NORDCAN–a Nordic tool for cancer information, planning, quality control and research, Acta Oncol. 49 (5) (2010) 725–736.
[19] E. Pukkala, G. Engholm, L.K. Hojsgaard Schmidt, H. Storm, S. Khan, M. Lambe, et al., Nordic cancer registries - an overview of their procedures and data comparability, Acta Oncol. 57 (2018) 440–455.
[20] Larønningen S., Ferlay J., Beydogan H., Bray F., Engholm G., Ervik M., et al. NORDCAN: Cancer Incidence, Mortality, Prevalence and Survival in the Nordic Countries. Association of the Nordic Cancer Registries. Cancer Registry of Norway.; 2022.
[21] G. Engholm, M. Gislum, F. Bray, T. Hakulinen, Trends in the survival of patients diagnosed with cancer in the Nordic countries 1964-2003 followed up to the end of 2006, Mater Methods Acta Oncol. 49 (5) (2010) 545–560.
[22] F.E. Lundberg, T.M. Andersson, M. Lambe, G. Engholm, L.S. Mørch, T. B. Johannesen, et al., Trends in cancer survival in the Nordic countries 1990-2016: the NORDCAN survival studies, Acta Oncol. 59 (11) (2020) 1266–1274.
[23] P. Bürkner, An R package for Bayesian multilevel models using Stan, J. Stat. Softw. 80 (1) (2017) 28.
[24] P. Bürkner, Advanced Bayesian multilevel modeling with the R package (brms), R. J. 10 (2018) 395–411.
[25] B. Carpenter, A. Gelman, M. Hoffman, D. Lee, B. Goodrich, al e. Stan: a probabilistic programming language, J. Stat. Softw. (2017) 76.
[26] C. Trovik, H.C.F. Bauer, E. Styring, K. Sundby Hall, F. Vult Von Steyern, S. Eriksson, et al., The Scandinavian Sarcoma Group Central Register: 6,000 patients after 25 years of monitoring of referral and treatment of extremity and trunk wall soft-tissue sarcoma, Acta Orthop. 88 (3) (2017) 341–347.
[27] A. Gronchi, A.B. Miah, A.P. Dei Tos, N. Abecassis, J. Bajpai, S. Bauer, et al., Soft tissue and visceral sarcomas: ESMO-EURACAN-GENTURIS clinical practice guidelines for diagnosis, treatment and follow-up(☆), Ann. Oncol. 32 (11) (2021) 1348–1365.
[28] S.J. Strauss, A.M. Frezza, N. Abecassis, J. Bajpai, S. Bauer, R. Biagini, et al., Bone sarcomas: ESMO-EURACAN-GENTURIS-ERN PaedCan clinical practice guideline for diagnosis, treatment and follow-up, Ann. Oncol. 32 (12) (2021) 1520–1536.
[29] C.A. Stiller, A. Trama, D. Serraino, S. Rossi, C. Navarro, M.D. Chirlaque, et al., Descriptive epidemiology of sarcomas in Europe: report from the RARECARE project, Eur. J. Cancer 49 (3) (2013) 684–695.
[30] C.A. Stiller, L. Botta, D.H. Brewster, V.K.Y. Ho, A.M. Frezza, J. Whelan, et al., Survival of adults with cancers of bone or soft tissue in Europe-Report from the EUROCARE-5 study, Cancer Epidemiol. 56 (2018) 146–153.
[31] A. Bacon, K. Wong, M.S. Fernando, B. Rous, R.J.W. Hill, S.D. Collins, et al., Incidence and survival of soft tissue sarcoma in England between 2013 and 2017, an analysis from the National Cancer Registration and Analysis Service, Int J. Cancer (2022).
[32] ESMO Pg, Gastrointestinal stromal tumours: ESMO clinical practice guidelines for diagnosis, treatment and follow-up, Ann. Oncol. 25 (Suppl 3) (2014) iii21-6.
[33] M.M. Lynch, B.A. Alexiev, B.A. Schroeder, S.M. Pollack, Combinations of chemotherapy and PD-1/PD-L1 inhibitors in sarcoma, Curr. Treat. Options Oncol. 23 (12) (2022) 1861–1876.
[34] M. Panagi, P. Pilavaki, A. Constantinidou, T. Stylianopoulos, Immunotherapy in soft tissue and bone sarcoma: unraveling the barriers to effectiveness, Theranostics 12 (14) (2022) 6106–6129.
[35] IARC, in: M. Curado, B. Edwards, H. Shin, H. Storm, J. Ferlay, M. Heanue, et al. (Eds.), Cancer Incidence in Five Continents, Vol. IX, IARC, Lyon, 2007.