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A population-based study of soft tissue sarcoma incidence and survival in Australia: An analysis of 26,970 cases

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ABSTRACT

Background: Soft tissue sarcomas (STS) are rare, often fatal tumors, but little is known of the epidemiology and survival in the Australian population. This study aims to provide the first epidemiological analysis of incidence and survival rates of STS in the Australian population.

Methods: A retrospective population-based observational study was conducted between 1982 and 2009 of all patients with a diagnosis of STS using the Australian Institute of Health and Welfare (AIHW) Australian Cancer Database. Incidence rates per 100,000; incidence rate ratios, age-standardized incidence rates, prevalence and incidence rates of subtypes of STS, median, one-year and 5-year survival rates were examined.

Results: A total of 26,970 patients were identified. Between 1982 and 2009 STS incidence rates significantly increased from 3.99 [95% CI 3.68–4.32] to 6.12 [95% CI 5.80–6.46] per 100,000 Australian population, with a peak incident rate ratio (IRR) of 1.59 [95% CI 1.51–1.69] ($p < 0.0001$) in 2001. Median age at diagnosis increased from 58 to 63 years. Incidence rates were stable across all 10-year age cohorts, except for people aged over 70 where it increased. Overall, age-standardized incidence rates increased from 4.70 [95% CI 4.42–5.00] in 1982 to 5.87 [95% CI 5.63–6.11] per 100 000 Australians in 2009. Leiomyosarcoma (20.43%), malignant fibrous histiocytoma (16.14%), and soft tissue tumors/sarcomas, not otherwise specified (10.18%) were the most common STS subtypes. Median survival from diagnosis increased from 5.80 years [95% CI 5.06–6.54] in 1985–1989 cohort to 8.18 years [95% CI 7.54–8.81] in the 2000–2004 cohort (log-rank test $p < 0.0001$).

Conclusion: The incidence of STS is increasing in Australia, most noticeably in those aged over 70 years, with a small but statistically significant increase in overall survival rates.

1. Introduction

Soft tissue sarcomas (STS) are a rare group of malignant tumors differentiating towards mesenchymal lineage, that can affect children and adults of all ages [1,2]. They may arise in the soft tissues, skin and the viscera [3]. Numerous specific histologic subtypes of STS have been delineated, each with unique appearance and biologic potential [4]. STS may exhibit differentiation towards a range of tissue types, including smooth muscle, myofibroblastic, lipomatous, osseous, endothelial, neural and rhabdomyocytes. Many appear primitive and may pursue an aggressive clinical course [5].

The rarity and heterogeneity of STS has presented a barrier to etiologic study and poses challenges in the understanding of incidence patterns, particularly at a population level [6]. The American Cancer Society estimates that 12,390 new STS will be diagnosed in the United States (US) in 2017 (including both adults and children); 56% will be in males; and 40% of all patients in the US are expected to die of their disease [7]. Little is known about the epidemiology of STS in Australia. The aim of this paper is to provide the first epidemiological analysis of STS in the Australian population between 1982 and 2009, specifically

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to describe trends in incidence over time, by gender, age, subtype of STS and to examine survival rates.

2. Methods

2.1. Data source and cohort selection

Patients diagnosed with STS between 1982 and 2009, were obtained from the Australian Institute of Health and Welfare (AIHW) Australian Cancer Database (ACD) 2010 [8]. The ACD is compiled at the AIHW from cancer data provided by State and Territorial registries through the ACD that requires mandatory reporting of every episode of malignancy that generates a histopathology report (excluding non-melanoma skin cancers). All data are de-identified, with approval from each State and Territory for release of combined data in line with AIHW policy. The dataset corresponds to 97.3% of all Australians with a diagnosis of STS in the study period (i.e., including residents of New South Wales, Queensland, South Australia, Tasmania, Victoria, Western Australia). The data used in this study are not available for sharing, but similar data may be obtained from the AIHW Australian Cancer Database upon request and appropriate approvals [8].

For the purpose of this study, STS was defined as all malignant sarcomas (apart from Kaposi sarcoma) that did not arise from or involve bone, identified in the ACD by morphology and topography coding according to the ICD-O-3 (2000) classification. Topographic codes C40-C41 (bones, joints, and articular cartilage of limbs/other and unspecified sites) and C70-C72 (meninges/brain/ spinal cord, cranial nerves and other parts of central nervous system) were excluded. Following exclusion by topography, remaining cases of Ewings sarcoma osteosarcoma and chondrosarcoma were deemed extra-skeletal. Histological codes included in the analysis are shown in Table 1.

Data were received from the ACD as a de-identified spreadsheet. All data have been managed in accordance with the Australian Code for the Responsible Conduct of Research. Variables supplied included vital status, multi-flag (for multiple primaries), histology, topography, gender, year of diagnosis and age at diagnosis. Age at diagnosis was calculated from complete dates of birth and diagnosis, rounded down to age at last birthday before diagnosis. Data on race, including indigenous ethnicity, were not available in this data set [9].

2.2. Incidence and proportions of STS subtypes analysis

Incidence of STS in Australia by year of diagnosis was calculated between 1982–2009. Number of cases per year, median age at diagnosis (IQR), gender (% male), incidence rate (per 100,000) and incidence rate ratio (with 95% CI) were calculated. The proportions of STS diagnoses were presented by morphological groupings so as to broadly match those used in a similar size US population study from 1978 to 2001, with morphological subtypes identified by unique ICD-O-3 codes [3]. Proportions of each morphological subtype were presented as a percentage of all STS diagnoses between 1982–2009. Incidence rate per 100,000 population were calculated using the estimated resident mid-year Australian population from each year, from the Australian Bureau of Statistics [10].

Incidence rates were presented separately by gender (males and females) and by age at diagnosis, grouped into 10-year age cohorts from 0 to 9 years to ≥80 years (to give a total of 9 age cohorts). Age-standardized incidence rates of STS (with 95% CI) were calculated adjusting for the age distribution of the total Australian population in 2001 [11]. Incidence rates per 100,000 population were also calculated per year between 1982–2009 for the three most common STS subtypes.

Table 1
Included Histology Codes of Soft Tissue Sarcoma for Study Cohort (n = 26,970).

ICD-O-3 Histology Codes Included
8710-11, 8800-06, 8810-15, 8830, 8832-33, 8840, 8850-55, 8857-58, 8890-91, 8894-96,
8900-02, 8910, 8912, 8920-21, 8930-31, 8933, 8935-36, 8940, 8950-8951, 8963, 8982, 8990-
91, 9020, 9040-44, 9120, 9124, 9130, 9133, 9150, 9170, 9180-87, 9192-9195, 9220-21, 9230-
31, 9240, 9242-43, 9250-52, 9260-61, 9310, 9364-65, 9473, 9540, 9560-61, 9571, 9580-81

2.3. Survival analysis

Survival outcomes (from all-cause mortality) of patients with STS in Australia were calculated in 5-year cohorts from year of diagnosis: 1985–1989, 1990–1994, 1995–1999 and 2000–2004 (n = 18,872). At the time of the original study data request from AIHW, complete mortality data was only available up to 2005. Kaplan Meier survival analyses were conducted to examine overall median (95% CI) survival (years) and the log rank test was used to identify significant differences. One-year and 5-year cumulative survival rates and SE were also calculated for each of the four cohorts.

All analyses were conducted using Statistical Package for the Social Sciences (SPSS) version 25 (Chicago, IL).

3. Results

A total of 26,970 patients were identified with STS in the Australian population from 1982–2009. The incidence rate of sarcoma between 1982 and 2009 significantly increased from 3.99 [95% CI 3.68–4.32] to 6.12 [95% CI 5.80–6.46] / 100,000 Australian population (Table 2). Using the 1982 cohort as the reference, the incident rate ratio (IRR) increased over time, peaking at IRR 1.59 in 2001 [95% CI 1.51–1.69] ($p < 0.001$), after which it plateaued to IRR 1.53 [IQR 1.45–1.62] by 2009. The median age at diagnosis increased from 58 (IQR 41–70) in the 1982 cohort to 63 (IQR 47–75) years old in the 2009 cohort. Males were less commonly diagnosed with STS than females over the study period, ranging from 44.8% to 49.7.4% with the proportion over time remaining stable (Table 2).

Incidence rates of STS by gender and age at diagnosis are shown in Fig. 1a–c. The incidence rate of STS increased in both males and females (Fig. 1a and b) between 1982–2009. Over the study period the incidence rate of STS was stable for all age groups under 60 years of age. Among older individuals there was an increase in the incidence rate. For those 60–69 years at diagnosis the incidence increased from 11.11 per 100,000 in 1982 to 13.54 per 100,000 in 2009. The largest increase in incidence rate was in patients aged > 70 years, for whom the rate increased from 15.94 to 21.50 per 100,000 between 1982 and 2009 for patients aged 70–79 years at diagnosis, and from 18.42 to 27.23 per 100,000 for patients ≥80 years (Fig. 1c). Age-standardized incidence rates increased from 4.70 [95% CI 4.42–4.98] in 1982 to 6.40 [95% CI 6.13–6.66] in 2001 per 100, 000 Australian population (Fig. 2), with a slight decrease between 2002 and 2009 from 6.26 [95% CI 6.00–6.51] to 5.87 [95% CI 5.63–6.11] per 100,000.

Presented in Table 3 are the proportions of specific types of STS diagnosed between 1982 and 2009. The most common STS in Australia was leiomyosarcoma which accounted for 20.43% of all STS, followed by malignant fibrous histiocytoma (MFH), and complex mixed and stromal neoplasms (15.60%) (Table 3). The incidence rates peaked at 1.48 per 100,000 population for Leiomyosarcoma in 2000 and 1.03 per 100,000 for MFH in 1992, before declining. The incidence rate of complex mixed and stromal neoplasms rose steadily over time from to 0.40 per 100,000 in 1992 to 1.31 per 100,000 in 2003 (Fig. 3a–c).

Median survival from diagnosis increased from 5.80 years [95% CI 5.06–6.54] in 1985–1989 cohort to 8.18 years [95% CI 7.54–8.81] in the 2000–2004 cohort (log-rank test $p < 0.0001$). Over this time period no significant differences in the proportion of males were

Table 2
Incidence of Soft Tissue Sarcoma in Australia 1982–2009 by Diagnosis Year (n = 26,970).

Diagnosis Year	Cases N	Age Median (IQR)	Gender % Male [95% CI]	Incidence Rate per 100,000 [95% CI]	Incidence Rate Ratio [95% CI], p-value
1982	610	58 (41-70)	44.8 [40.8-48.7]	3.99 [3.68-4.32]	Reference
1983	593	56 (40-69)	46.4 [42.4-50.4]	3.83 [3.53-4.15]	0.96 [0.89-1.04] 0.32
1984	579	58 (41-70)	49.2 [45.2-53.3]	3.69 [3.40-4.00]	0.93 [0.85-1.01] 0.06
1985	607	58 (43-70)	44.0 [40.0-48.0]	3.82 [3.52-4.13]	0.96 [0.88-1.04] 0.28
1986	685	57 (39-69)	45.7 [42.0-49.4]	4.24 [3.94-4.57]	1.06 [0.99-1.15] 0.53
1987	638	59 (42-70)	46.9 [43.0-50.7]	3.89 [3.60-4.20]	0.98 [0.90-1.05] 0.53
1988	721	60 (43-72)	46.2 [42.6-49.8]	4.32 [4.01-4.65]	1.08 [1.01-1.17] 0.032
1989	758	60 (41-72)	45.6 [42.1-49.2]	4.48 [4.17-4.80]	1.22 [1.04-1.20] 0.001
1990	779	62 (41-72)	48.1 [44.6-51.7]	4.54 [4.23-4.86]	1.14 [1.06-1.22] 0.0003
1991	804	61 (44-72)	47.5 [44.1-51.0]	4.63 [4.32-5.00]	1.16 [1.08-1.24] 0.0002
1992	882	59 (44-72)	45.1 [41.8-48.4]	5.02 [4.70-5.36]	1.26 [1.18-1.34] < 0.0001
1993	858	60.5 (43-73)	44.0 [40.6-47.3]	4.84 [4.53-5.17]	1.21 [1.14-1.30] < 0.0001
1994	904	60 (44-72)	49.7 [46.4-52.9]	5.05 [4.74-5.39]	1.27 [1.19-1.35] < 0.0001
1995	927	61 (44-73)	47.1 [43.9-50.4]	5.12 [4.80-5.45]	1.28 [1.20-1.37] < 0.0001
1996	1025	61 (44-73)	48.2 [45.1-51.3]	5.59 [5.26-5.94]	1.40 [1.32-1.49] < 0.0001
1997	1020	61 (44-74)	46.4 [43.3-49.3]	5.51 [5.18-5.86]	1.38 [1.30-1.47] < 0.0001
1998	1095	62 (46-74)	48.8 [45.8-51.7]	5.85 [5.52-6.21]	1.47 [1.38-1.58] < 0.0001
1999	1089	63 (45-75)	49.3 [46.3-52.3]	5.76 [5.42-6.11]	1.44 [1.36-1.53] < 0.0001
2000	1180	60 (46-74)	43.8 [41.0-46.6]	6.16 [5.83-6.52]	1.55 [1.46-1.64] < 0.0001
2001	1233	60 (46-74)	47.3[44.5-50.1]	6.36 [6.01-6.73]	1.59 [1.51-1.69] < 0.0001
2002	1231	59 (44-73)	47.6[44.8-50.4]	6.28 [5.94-6.64]	1.57 [1.49-1.66] < 0.0001
2003	1214	61 (46-75)	47.0 [44.1-50.0]	6.12 [5.77-6.48]	1.53 [1.45-1.62] < 0.0001
2004	1222	61 (46-75)	48.0 [45.2-50.8]	6.10 [5.76-6.45]	1.53 [1.44-1.62] < 0.0001
2005	1255	61 (46-74)	45.7 [43.0-48.5]	6.18 [5.84-6.53]	1.55 [1.47-1.64] < 0.0001
2006	1224	61 (47-74)	48.3 [45.5-51.1]	5.93 [5.61-6.27]	1.49 [1.41-1.57] < 0.0001
2007	1242	62 (47-75)	47.6 [44.8-50.4]	5.91 [5.59-6.25]	1.48 [1.40-1.57] < 0.0001
2008	1256	62 (47-75)	48.4 [45.6-51.2]	5.85 [5.53-6.18]	1.47 [1.39-1.55] < 0.0001
2009	1339	63 (47-75)	46.0 [43.4-48.6]	6.12 [5.80-6.46]	1.53 [1.45-1.62] < 0.0001

IQR, Inter-quartile range.

observed but the mean age at time of diagnosis significantly increased from 55.0 years (SD 20.3) (1985-89) to 58.4 years (SD 19.9) (2000-04) (Table 3). The 1-year survival rate increased between 1985-89 and 2000–2004 cohorts from 76% (SE 0.007) to 81% (SE 0.005) and the 5-year survival increased from 52% (SE 0.009) in 1985-89 to 58% (SE 0.006) in 2000–2004 (Table 4).

4. Discussion

This is the first study to determine the incidence and survival STS in the Australian population. The incidence of STS is increasing, with age-standardised incidence rates increasing from 4.70 to 5.87 per 100,000 Australian population over the study period, with the greatest increase in incidence in patients aged over 70. A statistically significant increase in median survival was observed for patients with STS from 5.80 to 8.18 years over the study period.

Population-based studies investigating the incidence of STS have been performed in the US (SEER program) and the European Union (RARECARE project), with reported annual age-standardized incidence rates, similar to those observed in our Australian study [2,3]. The SEER analysis included 26,758 STS from 1978 to 2001, with an incidence rate of 5.03 per 100,000 person years, age-adjusted to the 2000 US (19 age groups) standard. In that study, incidence rates for all STS combined rose with age, following a peak in early childhood from rhabdomyosarcoma [3]. Similar to our study, the most common types of STS included leiomyosarcomas (23.9%) and MFH (17.1%). The European RARECARE project analyzed 38,127 STS from 1995 to 2002. Total crude incidence was 5.6 per 100,000 per year, with age-standardized incidence rate of 4.2 per 100,000 (SE < 0.1) [2]. The most frequent subtype in the RARECARE study was leiomyosarcoma (20%), followed by unspecified sarcomas (18%) and liposarcoma (10%), with MFH accounting for only 8% of all sarcomas [2]. As in our study, the US and European data demonstrated an increase in incidence of STS with age, and leiomyosarcoma as one of the most prevalent tumors [2,3].

The increasing incidence of STS in the older Australian population is of particular interest. The proportion of people aged 65 years and older in Australia increased from 11% in 1987 to 15% in 2017, with the greatest increases in those aged 80 years and older [12]. The increasing size of the population at risk who are older than 70 years of age is not sufficient to explain the largest increases in age-specific incidence rates of STS arising in this cohort. Increasing knowledge of sarcomas, demographic change and the increasing susceptibility of the older population to a range of neoplasms, including sarcomas, are all plausible reasons for the observations concerning increased incidence of sarcomas in the aged. Over the long period of time under consideration in this study, significant advances in knowledge have been achieved, leading to increasing awareness and enhanced diagnostic capabilities for evaluating sarcomas [13]. Our widening therapeutic and diagnostic abilities, as well as changing community expectations have likely led to more thorough investigation of mass lesions in the older population and to the documentation of sarcoma diagnoses, rather than presumptive diagnoses of cancer NOS.

Sarcomas, like other classes of neoplasms, increase in incidence with age. This is partly due to the accumulated somatic genetic damage over a lifetime. The reduced effectiveness of the immune defences in the older population contributes to the establishment of neoplasia. Specifically relating to the pathogenesis of sarcomas, there are two major classes of somatic genetic abnormalities observed in mesenchymal neoplasms [13]. The most common genetic anomalies in sarcomas, seen in two thirds of cases and particularly in the subtypes common in the older population, are complex arrays of numerous chromosomal imbalances, affecting multiple chromosomes, producing highly complex, apparently unpredictable patterns and leading to neoplasms of high mutational load. These are the most common, undifferentiated, pleomorphic high-grade sarcomas. The less common pattern of genetic anomalies in sarcomas, seen in approximately a third of cases and including many of the sarcomas of the young, involve simple mutations in specific genes that produce recurrent structural abnormalities, often translocations, so characteristic of the histologic subtype of the sarcoma as to be diagnostic [13]. One way to account for the observation of increased incidence of sarcoma with age is that over time, somatic cells develop various unchecked genetic changes,

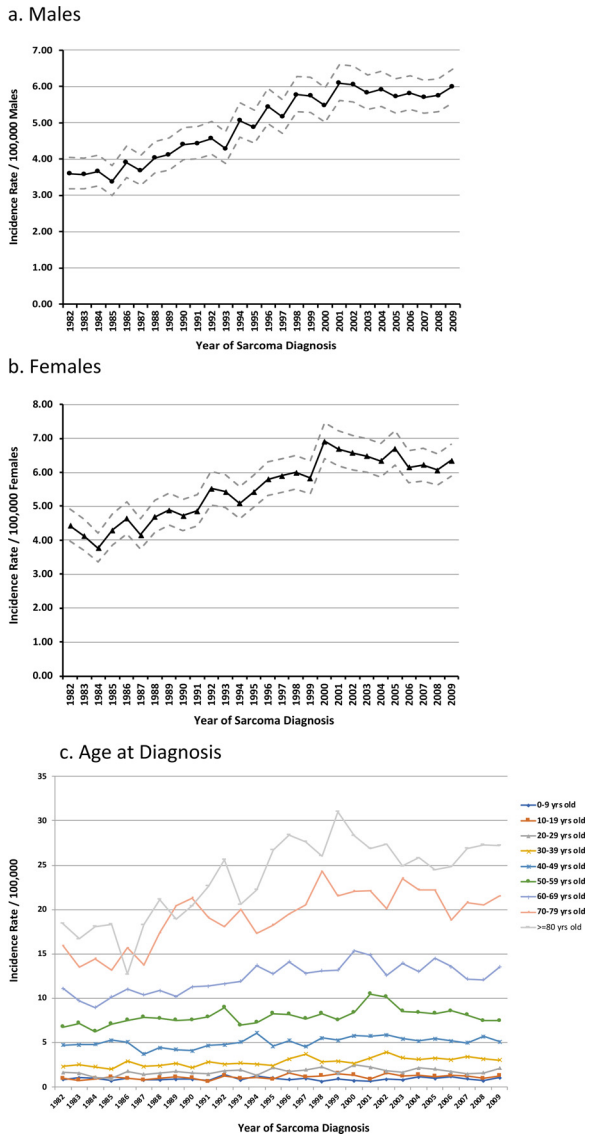

Fig. 1. Incidence Rates of Soft Tissue Sarcoma by Gender and 10-year age groups, 1982–2009.

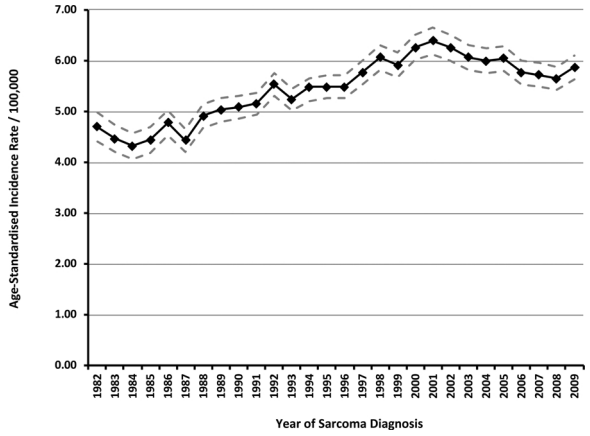

Fig. 2. Age-Standardised* Incidence Rate [95% CI] of Soft Tissue Sarcoma, 1982–2009.
*Age-standardised to the age distribution of the 2001 Australian population.

Table 3
Proportions of Types of Soft Tissue Sarcoma Diagnoses 1982–2009 (n = 26,970).

Type of Soft Tissue Sarcoma	ICD10-O-3 Code	Count, N	%
All Sarcoma		**26,970**	
GLOMANGIOSARCOMA		7	0.03
Glomangiosarcoma	8710	4	0.02
Glomus tumor, malignant	8711	3	0.01
SOFT TISSUE TUMORS / SARCOMAS, NOS		**2746**	10.18
Sarcoma, NOS	8800	1715	6.36
Spindle cell sarcoma	8801	393	1.46
Giant cell sarcoma (except of bone)	8802	267	0.99
Small cell sarcoma	8803	19	0.07
Epithelioid sarcoma	8804	216	0.80
Undifferentiated sarcoma	8805	89	0.33
Desmoplastic small round cell tumor	8806	47	0.17
FIBROSARCOMA		**774**	2.87
Fibrosarcoma, NOS	8810	358	1.33
Fibromyosarcoma	8811	325	1.21
Periosteal fibrosarcoma	8812	1	0.004
Infantile fibrosarcoma	8814	30	0.11
Solitary fibrous tumor, malignant	8815	60	0.22
MALIGNANT FIBROUS HISTIOCYTOMA	8830	**4354**	16.14
DERMATOFIBROSARCOMA		**1813**	6.72
Dermatofibrosarcoma, NOS	8832	1804	6.69
Pigmented dermatofibrosarcoma protuberans	8833	9	0.03
MYXOSARCOMA	8840	46	0.17
LIPOSARCOMA		**2693**	9.99
Liposarcoma, NOS	8850	758	2.81
Liposarcoma, well differentiated	8851	865	3.21
Myxoid liposarcoma	8852	572	2.12
Round cell liposarcoma	8853	48	0.18
Pleomorphic liposarcoma	8854	185	0.69
Mixed liposarcoma	8855	53	0.20
Dedifferentiated liposarcoma	8858	212	0.79
LEIOMYOSARCOMA		**5510**	20.43
Leiomyosarcoma, NOS	8890	5225	19.37
Epithelioid leiomyosarcoma	8891	222	0.82
Angiomyosarcoma	8894	8	0.03
Myosarcoma	8895	13	0.05
Myxoid leiomyosarcoma	8896	42	0.16
RHABDOMYOSARCOMA		**996**	3.69
Rhabdomyosarcoma, NOS	8900	329	1.22
Pleomorphic rhabdomyosarcoma, adult type	8901	77	0.29
Mixed type rhabdomyosarcoma	8902	12	0.04
Embryonal rhabdomyosarcoma, NOS	8910	395	1.46
Spindle cell rhabdomyosarcoma	8912	13	0.05
Alveolar rhabdomyosarcoma	8920	168	0.62
Rhabdomyosarcoma, ganglionic differentiation	8921	2	0.01
COMPLEX MIXED and STROMAL NEOPLASMS		**4208**	15.60
Endometrial stromal sarcoma, NOS	8930	518	1.92
Endometrial stromal sarcoma, low grade	8931	127	0.47
Adenosarcoma	8933	196	0.73
Stromal sarcoma, NOS	8935	71	0.26
Gastrointestinal stromal sarcoma	8936	1018	3.77
Mixed tumor, malignant, NOS	8940	205	0.76
Mullerian mixed tumor	8950	1602	5.94
Mesodermal mixed tumor	8951	308	1.14
Malignant rhabdoid tumor	8963	38	0.14
Malignant myoepithelioma	8982	68	0.25
Mesenchymoma	8990	37	0.14
Embryonal sarcoma	8991	20	0.07
PHYLLODES TUMOR, MALIGNANT	9020	**488**	1.81
SYNOVIAL NEOPLASMS		**782**	2.90
Synovial sarcoma, NOS	9040	371	1.38
Synovial sarcoma, spindle cell	9041	179	0.66
Synovial sarcoma, epithelioid cell	9042	9	0.03
Synovial sarcoma, biphasic	9043	129	0.48
Clear cell sarcoma, NOS	9044	94	0.35
ANGIOSARCOMA		**1139**	4.22
Hemangiosarcoma	9120	845	3.13
Hemangioendothelioma, malignant	9130	72	0.27
Epithelioid hemangioendothelioma, malignant	9133	50	0.19
Hemangiopericytoma, malignant	9150	157	0.58
Lymphangiosarcoma	9170	15	0.06

(*continued on next page*)

Table 3 (*continued*)

Type of Soft Tissue Sarcoma	ICD10-O-3 Code	Count, N	%
OSTEOSARCOMA & CHONDROSARCOMA, EXTRASKELETAL		**275**	1.2
Osteosarcoma	9180	57	0.21
Chondroblastic osteosarcoma	9181	4	0.015
Telangiectatic osteosarcoma	9183	1	0.004
Small cell osteosarcoma	9185	1	0.004
Chondroma, NOS	9220	105	0.39
Myxoid chondrosarcoma	9231	70	0.26
Mesenchymal chondrosarcoma	9240	36	0.13
Clear cell chondrosarcoma	9242	1	0.004
MALIGNANT GIANT CELL TUMOR		**46**	0.17
Giant cell tumor, malignant	9250	1	0.004
Malignant giant cell tumor of soft parts	9251	36	0.13
Malignant tenosynovial giant cell tumor	9252	9	0.03
EWING SARCOMA/AMEOLOBLASTOMA/ PNET		**367**	1.36
Ewing sarcoma	9260	147	0.55
Ameloblastoma	9310	7	0.03
Peripheral neuroectodermal tumor	9364	157	0.58
Askin tumor	9365	2	0.01
Primitive neuroectodermal tumor, NOS	9473	54	0.20
NERVE SHEATH TUMOR		**651**	2.41
Malignant peripheral nerve sheath tumor	9540	364	1.35
Neurilemoma, malignant	9560	267	0.99
Malignant peripheral nerve sheath tumor, rhabdomyoblastic differentiation	9561	17	0.06
Perineurioma, malignant	9571	3	0.01
GRANULAR CELL AND ALVEOLAR SARCOMA		**75**	0.28
Malignant granular cell tumor	9580	36	0.13
Alveolar soft part sarcoma	9581	39	0.14

Eligible codes without identified cases are not included in the table, e.g. 8813, 8857, 9124 etc.

although individually not pathogenic, in the older population, this accumulated damage, accrued over a lifetime, finally leads to oncogenesis. Unrepaired genetic damage leads to the genome becoming increasingly error prone with age, leading to disproportionate increases in cancer incidence.

The variance in MFH between the UK, US and the current study may be attributed to changing histologic diagnostic criteria that have led to a decline in the use of the term MFH, in favor of more specific subtypes in recent times [14,15]. Gastrointestinal stromal tumors were only recognized as a separate entity in the late 1990s and are included within the category complex mixed and stromal neoplasms in our study (third most common observed subtype of STS), but because of the earlier data capture of the US and UK population studies gastrointestinal stromal tumors are likely to be under-registered in these studies [16]. It is unclear why there was a slight decrease in the age-standardized incident rates of STS in our study between 2001 and 2009; this may be attributable to fewer children (< 18 years) and adults aged 50–59 years with a diagnosis of sarcoma, however the reasons for this are unknown. It is not likely to be a matter of incomplete data capture as increases were observed between the time period for other age groups.

Survival rates for STS are reported to range from 83% for sarcomas diagnosed at the primary site (localized) to 16% for STS diagnosed with distant spread [17]. There are limited data for overall survival following STS diagnosis at the population level in Australia. In the current study, an increase in survival was observed over the study period with median survival of 5.80 years in the 1985-89 cohort and 8.18 years in the 2000-04 cohort, despite changes in treatment regimens over the study period. Effective treatment of STS is increasingly focussing on chemotherapy regimens tailored to specific sarcoma types (e.g. trabectedin for leiomyosarcomas and liposarcomas). A lack of clinical trials for Australian STS patients, together with poor participation, especially in the older population, is postulated in part, to contribute to the relatively small increase in survival [18]. Our findings are

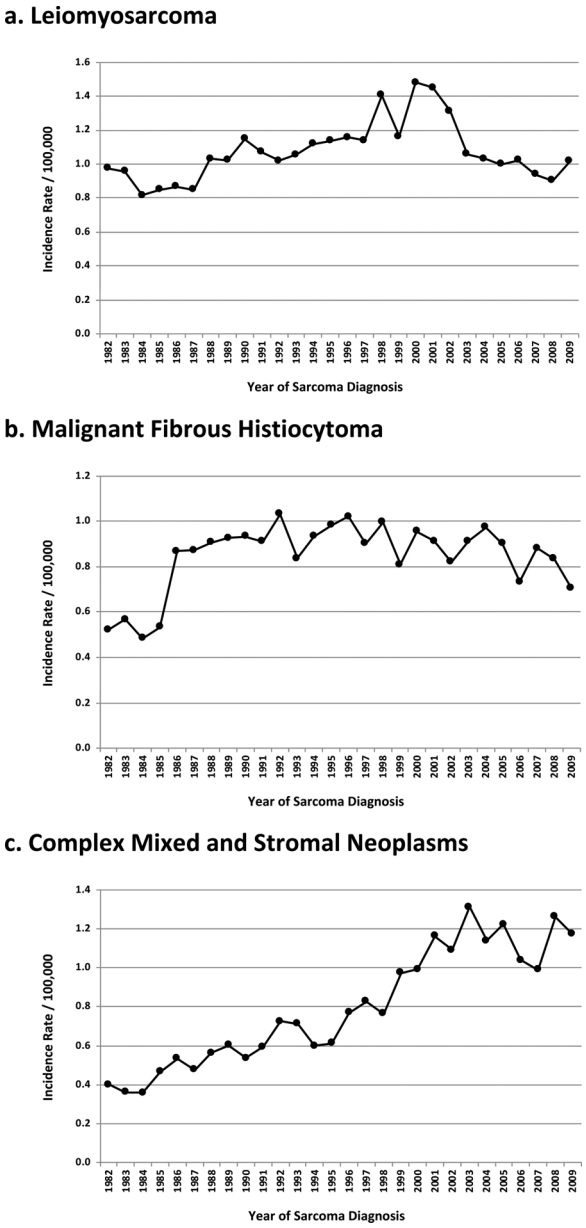

Fig. 3. Incidence of the Three Most Common STS Types between 1982–2009.

concordant with international studies that have also reported little or modest changes in overall survival in the past 30 years [2]. The 5-year overall survival for STS during the study period ranged from 52% in 1985-89 to 58% in 2000–2004 and is similar to that reported from Europe with an estimated 5-year overall survival of approximately 50% for patients with STS of any stage [2]. Furthermore, the most recent EUROCARE-5 study reported a 5-year relative survival between 2000 and 2009 for adults in Europe with STS to be 60%, with an increase in survival after 2005 attributed to the new therapeutic developments such as immunotherapies and targeted therapies [19]. We were unable to examine survival by type of treatment received or staging of STS at diagnosis, which potentially limits our findings. For example, an Australian study of 253 patients with advanced STS reported a median survival of only 18 months [20].

Population-level mapping of STS incidence requires accurate and consistent diagnosis. This is challenged where STS may be misclassified by topographic cancer group e.g. breast angiosarcoma and therefore omitted or overlooked [21]. The classification of STS has continued to evolve and be refined, integrating new insights gained from cellular and

Table 4
Median, 1-year and 5-year survival after sarcoma diagnosis (n = 18,872).

Dx Year	Mean age (SD)[a]	Gender[b] N (% Male)	Median Survival (years) [95% CI][c]	1 year Survival % (SE) N Events / N Alive	5 year Survival % (SE) N Events / N Alive
1985-89 N = 3409	55.0 (20.3)	1558 (45.7)	5.80 [5.06-6.54]	0.76 (0.007) 813/2596	0.52 (0.009) 1632/1777
1990-94 N = 4427	56.5 (20.5)	1981 (46.9)	6.56 [5.85-7.27]	0.78 (0.006) 943/3284	0.54 (0.008) 1939/2288
1995-99 N = 5156	57.8 (20.4)	2475 (48.0)	7.67 [6.95-8.39]	0.79 (0.006) 1065/4091	0.56 (0.007) 2266/2890
2000-04 N = 6080	58.4 (19.9)	2842(46.7)	8.18 [7.54-8.81]	0.81 (0.005) 1135/4945	0.58 (0.006) 2652/33518

[a] $p < 0.0001$ one-way anova with Bonferroni post-hoc test for multiple comparisons.
[b] $p = 0.98$ Chi-squared test.
[c] Log-Rank Median Survival $p < 0.0001$.

molecular genetics [15]. Most relevant to our dataset, is that MFH has been deleted in the 2013 World Health Organization (WHO) classification of STS. Pleomorphic sarcomas that may have been classified previously as MFH are now either reclassified to other, more specific subtypes highlighted through the use of ancillary analysis, or if they still remain undifferentiated, classified as "undifferentiated sarcoma" [15]. Whilst this does not impact on the analysis of the current dataset, as our study period predates the change in classification, it does hamper direct comparison with future datasets where MFH is unlikely to be diagnosed. STS coding, despite national AIHW standardization, provides particular challenges to registry staff, due to a combination of the histological heterogeneity of STS, changes in WHO classifications over time and lack of universal use of ICD-10 codes. This is compounded by the not infrequent changes in histopathologic diagnosis following second opinion [21]. Analysis by state/territory or postcode was not permissible due to small patient numbers potentially making individuals identifiable. The ACD has an agreed minimum dataset of person-level and tumor-level attributes, and agreements between the AIHW and jurisdictional cancer registries specify conditions of data supply, analysis and publication. Our study reports on the years 1982–2009, for six states of Australia. This current analysis was based on the most recently available complete data available from AIHW at the time of data request. Data were unavailable from Australian Capital Territory and Northern Territory, but this represents only 2.7% of the Australian population [10]. The ACD records only the first occurrence of a cancer with no data currently collected for recurrence and metastases, and due to the lack of a national person identifier there could be people in this dataset with two primary sarcomas where one is registered in one state and one in another state. Additionally, Aboriginal and Torres Strait Islander status is not easily available in Australia therefore limiting the current analysis to age and gender.

The broad range of histological subtypes identified in international studies are also present in the Australian population [2,3]. The clinical diversity of STS poses challenges not only to understanding disease incidence at a population level, but also in providing timely, effective and equitable services to patients; and for planning future health care research. For example, patients treated for Hodgkin's lymphoma (HL) have an increased incidence of adult-onset sarcoma [5], and carriers with germline TP53 mutations are more likely to have multiple cancers (including sarcoma) and earlier cancer onset than non-carriers [22]. This has implications for provision of screening in at risk subgroups (e.g. survivors of childhood cancer, genetic predisposition syndromes) [23]. An understanding of regional differences in STS incidence is necessary to ensure equitable access and treatment outcomes for patients in both Australian metropolitan and rural communities and the wider Asia-Pacific region. Future health services research is needed to identify current gaps in service provision and to plan cost-effective diagnosis, treatment and follow-up for patients with STS, particularly in the older population.

5. Conclusion

This is the first study to determine the incidence of STS in an Australian population; 5.87 per 100,000 Australians in the 2009 cohort. While still relatively rare, the incidence of STS has increased, particularly in the older population aged over 70, and is comparable to population-based studies in the US and Europe. The increasing incidence in the most rapidly expanding segment of our population and little advances in survival suggest the healthcare needs of patients with STS will require greater focus in the coming years. The logistics of such care provision and the health economic implications of this reality require advance planning and should be an area of future research.

Authorship contributions

A Population-Based Study of Soft Tissue Sarcoma Incidence and Survival in Australia: An Analysis of 26,061 Cases

All named authors have participated in the study to a sufficient extent to be named as authors.

TB and SN conceived the study. TB and JAP acquired the data. All authors were involved in the study design and analysis plan. TB, GC and SS analysed the data and wrote drafts of the paper. All authors critically reviewed the study results, commented on the drafts, and approved the final manuscript.

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Declaration of Competing Interest

None

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