Soft Tissue Sarcoma

Incidence and Survival

Tumours Diagnosed in England Between 1985 and 2009

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1. Introduction

1.0 INTRODUCTION

Soft tissue sarcomas are a group of rare heterogeneous forms of cancer, which collectively account for approximately 1% of all malignancies diagnosed annually in England. These sarcomas develop from soft tissue cells including smooth muscle cells (leiomyosarcomas), fat cells (liposarcomas), fibrous connective tissue (fibrosarcomas), skeletal muscles (rhabdomyosarcomas), synovium (synovial sarcomas), blood vessels (angiosarcomas) and breast ducts (phyllodes tumours), and nerves (nerve sheath tumours). Kaposi's sarcoma is a particular type of sarcoma linked to immune deficiency in patients with HIV infection and which is included in this report for completeness. Gastro-intestinal stromal tumours (GISTs) occur in the stomach or small intestine and were frequently coded as leiomyosarcomas in the past. Ewing's sarcomas and neuroectodermal tumours typically affect children rather than adults.

Soft tissue sarcomas represent a challenge to clinicians as they are rare and diagnosis is often delayed. Best practice guidelines advise that they should be treated within centres that specialise in the management of soft tissue sarcomas. There are over one hundred different morphological sub-types of sarcoma. This comprehensive report presents incidence and survival data for all patients diagnosed with malignant soft tissue sarcoma in England over a 25-year period. The 22 most common variants of soft tissue sarcoma have been grouped into 12 sub-types. Eleven of the sub-types are introduced and described in a separate section. The remaining very rare sarcoma variants (aggregated into a single "other category") are discussed briefly in Section 13. As there are problems with the coding of GISTs, incidence and survival data for these soft tissue sarcomas are not included in this report.

1.1 Methods and Data

The West Midlands Cancer Intelligence Unit (WMCIU) is the National Cancer Intelligence Network (NCIN) lead registry in England for bone and soft tissue sarcoma. As such, the WMCIU analyses national data on the incidence, mortality, survival and treatment of bone and soft tissue sarcomas in England. These analyses are usually conducted using the National Cancer Data Repository (NCDR), a compilation of data collected by the eight regional cancer registries, which covers all cases diagnosed in England.

Soft tissue sarcomas are classified by both the tenth revision of the International Classification of Diseases (ICD-10) site code and morphology. ICD-10 is the standard global system for reporting mortality and morbidity statistics[1]. Within that system, the prefix 'C' locates the code within the 'neoplasm', or cancer, sub-group, and the numbers that follow localise the tumour to a specific area of the body. A two number string denotes a general area of the body, while a three number string represents a more specific area; for example, 'C-03' denotes a malignant neoplasm of the gum, and 'C-031' represents a malignant neoplasm of the lower gum.

Over 100 different morphology codes relating to sarcoma are present within the ICD-O3 and World Health Organisation (WHO) classifications of sarcomas[2]. These can be grouped into 22 sub-types of related tumours. All malignant sarcomas (excluding bone sarcomas, ICD-10 codes C40 and C41) are included in the analyses in this report. The current version of the NCDR includes all malignancies diagnosed in England in the 25-year period 1985 to 2009. There are potential coding issues with regard to the soft tissue sarcomas recorded within the NCDR, particularly those registered in the 1980's and early 1990's which are discussed in the relevant sections of this report. However utilising the whole NCDR dataset allows observations of time trends in the incidence of each soft tissue sarcoma sub-type to be made.

1. Introduction

Confidence intervals around incidence rates were calculated using the gamma method[3]. Relative survival is defined as the observed survival in the patient group divided by the expected survival of the general population, matched by age, sex, and calendar year. Relative survival was calculated in Stata (v.11) using the strs programme which calculates relative survival estimates using the Ederer II method[4]. National life tables were obtained from the Cancer Research UK Cancer Survival Group at the London School of Hygiene and Tropical Medicine. Five-year relative survival was calculated using 5-year rolling averages.

For the purpose of reporting incidence and survival, soft tissue sarcomas in the 22 morphological groups were further combined according to the anatomical diagnostic site groups in Table 1.

Table 1: Anatomical cancer site groups for soft tissue sarcomas with ICD-10 codes and descriptions

Site	ICD-10 codes
Limb	C491 (connective and soft tissue of upper limb), C492 (connective and soft tissue of lower limb), C471 (peripheral nerves of upper limb), C472 (peripheral nerves of lower limb), C764 (other and ill defined sites: upper limb), C765 (other and ill defined sites: lower limb)
Head, face and neck	C00 (lip), C01 (base of tongue), C02 (other and unspecified parts of tongue), C03 (gum), C04 (floor of mouth), C05 (palate), C06 (other and unspecified parts of mouth), C07 (parotid gland), C08 (other and unspecified major salivary glands), C09 (tonsil), C10 (oropharynx), C11 (nasopharynx), C12 (pyriform sinus), C13 (hypopharynx), C14 (other and ill-defined sites in the lip oral cavity and pharynx), C30 (nasal cavity and middle ear), C31 (accessory sinuses), C32 (larynx), C69 (eye and adnexa), C490 (connective and soft tissue of head, face and neck), C760 (other and ill defined sites: head, face and neck), C761 (other and ill defined sites: thorax)
Retroperitoneum	C48 (retroperitoneum and peritoneum)
Connective tissue of trunk	C493 (connective and soft tissue of thorax), C494 (connective and soft tissue of abdomen), C495 (connective and soft tissue of pelvis), C496 (connective and soft tissue of trunk), C762 (other and ill defined sites: abdomen), C763 (other and ill defined sites: pelvis)
GI tract	C15 (oesophagus), C16 (stomach), C17 (small intestine), C18 (colon), C19 (rectosigmoid junction), C20 (rectum), C21 (anus and anal canal)
Organs within the trunk	C22 (liver and intrahepatic bile ducts), C23 (gallbladder), C24 (other and unspecified parts of biliary tract), C25 (pancreas), C26 (other and ill-defined digestive organs), C33 (trachea), C34 (bronchus and lung), C37 (thymus), C38 (heart, mediastinum and pleura), C39 (other and ill-defined sites in the respiratory system and intrathoracic organs), C64 (kidney, except renal pelvis), C65 (renal pelvis), C66 (ureter), C67 (bladder), C68 (other and unspecified urinary organs), C73 (thyroid gland), C74 (adrenal gland), C75 (other endocrine glands and related structures)
Skin	C44 (other malignant neoplasms of skin, not malignant melanoma)
Kaposi's sarcoma	C46 (Kaposi's sarcoma)
Peripheral nerves	C470 (peripheral nerves of head, face and neck), C473 (peripheral nerves of thorax), C474 (peripheral nerves of abdomen), C475 (peripheral nerves of pelvis), C476 (peripheral nerves of trunk, unspecified), C478 (overlapping lesion of peripheral nerves and autonomic nervous system), C479 (peripheral nerves and autonomic nervous system, unspecified)
Brain	C70 (meninges), C71 (brain), C72 (spinal cord, cranial nerves and other parts of the central nervous system)
Breast	C50 (breast)
Genital organs	C51 (vulva), C52 (vagina), C53 (cervix uteri), C54 (corpus uteri), C55 (uterus, part unspecified), C56 (ovary), C57 (other and unspecified female genital organs), C58 (placenta), C60 (penis), C61 (prostate), C62 (testis), C63 (other and unspecified male genital organs)
Gynaecological organs	C51 (vulva), C52 (vagina), C53 (cervix uteri), C54 (corpus uteri), C55 (uterus, part unspecified), C56 (ovary), C57 (other and unspecified female genital organs), C58 (placenta)
Male genitalia	C60 (penis), C61 (prostate), C62 (testis), C63 (other and unspecified male genital organs)
Other/Unknown	All others

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1.2 Data Quality

The WMCIU recently published a report outlining the completeness of soft tissue sarcoma data available in the latest iteration of the NCDR[5]. The completeness report profiles each of the core data items recorded by each English cancer registry. The most significant concerns are the incompleteness of detailed ICD-10 cancer site and ICD-O3 morphology codes, and the lack of staging data which are required in order to calculate case-mix adjusted survival rates. Only two of the cancer registries (the WMCIU and the Northern and Yorkshire Cancer Registration and Information Service [NYCRIS]), currently code all soft tissue sarcomas according to ICD-O3. This has a significant impact in particular on the coding of gastro-intestinal stromal tumours (GISTs). The WMCIU is currently working with the specialist sarcoma treatment centres to improve the quality of staging data.

1.3 Malignant Primary Soft Tissue Sarcomas

Over 100 different morphology codes relating to sarcoma are present within the ICD-O3 and WHO classification of sarcomas. This section shows how the overall sarcoma incidence rate varies with the age at diagnosis and sex of the patient, and how survival rates vary with time.

1.3.1 Malignant Primary Soft Tissue Sarcoma Incidence

Between 1985 and 2009, 55,886 tumours were registered with a soft tissue sarcoma morphology code in England. On average, 2,626 soft tissue sarcomas were diagnosed annually between 2000 and 2009. There were 2,961 soft tissue sarcomas diagnosed in 2008 and 2,794 in 2009.

Figure 1.1: Soft tissue sarcoma age standardised incidence rates (3-year rolling average) (England: 1985–2009)

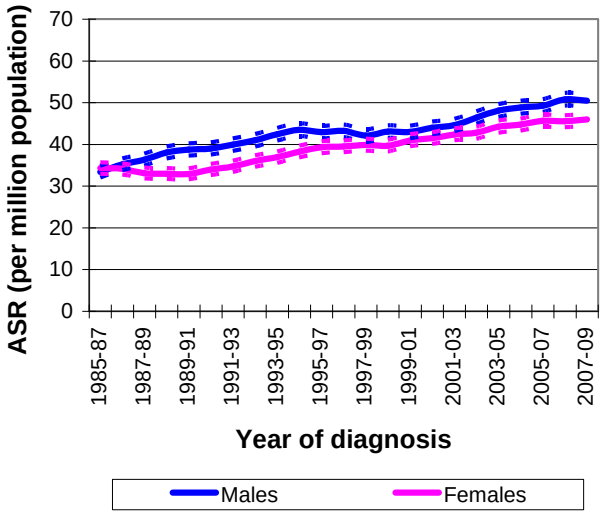

Figure 1.1 shows that age standardised soft tissue sarcoma incidence rates in England fluctuate around 41 cases per million, similar to the rates found in other registries outside the UK[6,7,8]. Incidence rates have increased significantly over the 25-year period examined; from 34 cases per million in 1985 to 48 cases per million in 2009. This increase may be due to improved diagnostic techniques and/or more accurate recording within the cancer registries.

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Unlike bone sarcomas, which have a very marked bi-modal age profile[9], after a small peak in children aged 0-4 years, the number of soft tissue sarcomas diagnosed increases gradually with age (Figure 1.2). A similar pattern is seen in males and females. Age specific incidence rates (ASR) are highest in males aged 85 years and over where they reach 200 per million (20 per 100,000) (Figure 1.3).

Figure 1.2: Number of soft tissue sarcomas diagnosed in each age group and sex (England: 1985–2009)

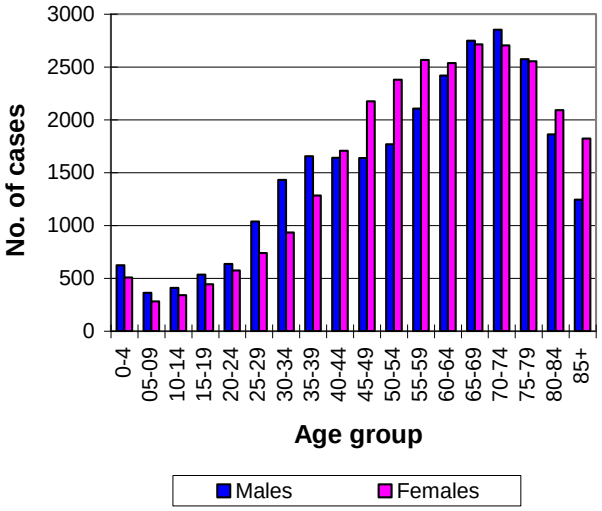


Figure 1.3: Soft tissue sarcoma age specific incidence rates (England: 1985–2009)

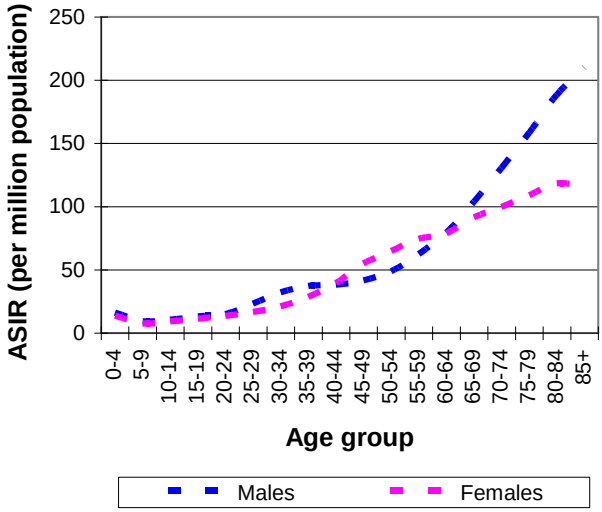
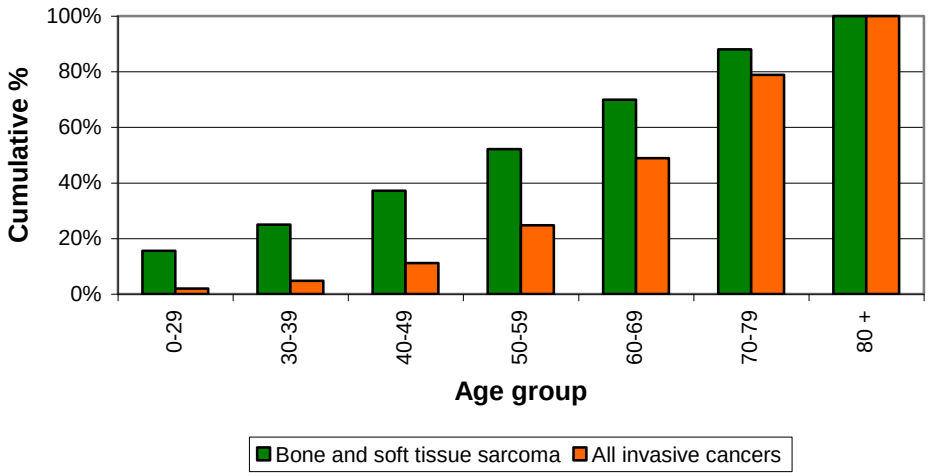


Figure 1.4: Age distribution of bone and soft tissue sarcoma and all invasive cancers (England: 1985–2009)



In general, patients with a bone or soft tissue sarcoma diagnosis tend to be younger than the majority of cancer patients (Figure 1.4, in which all invasive cancers include ICD-10 codes C00–C99 excluding C44: non-melanoma skin cancer). Sixteen percent of bone or soft tissue sarcomas are diagnosed in patients less than thirty years of age, compared to around 2% of all cancers, and 37% of bone or soft tissue sarcoma patients are aged less than 50 years compared with 11% of all cancer patients.

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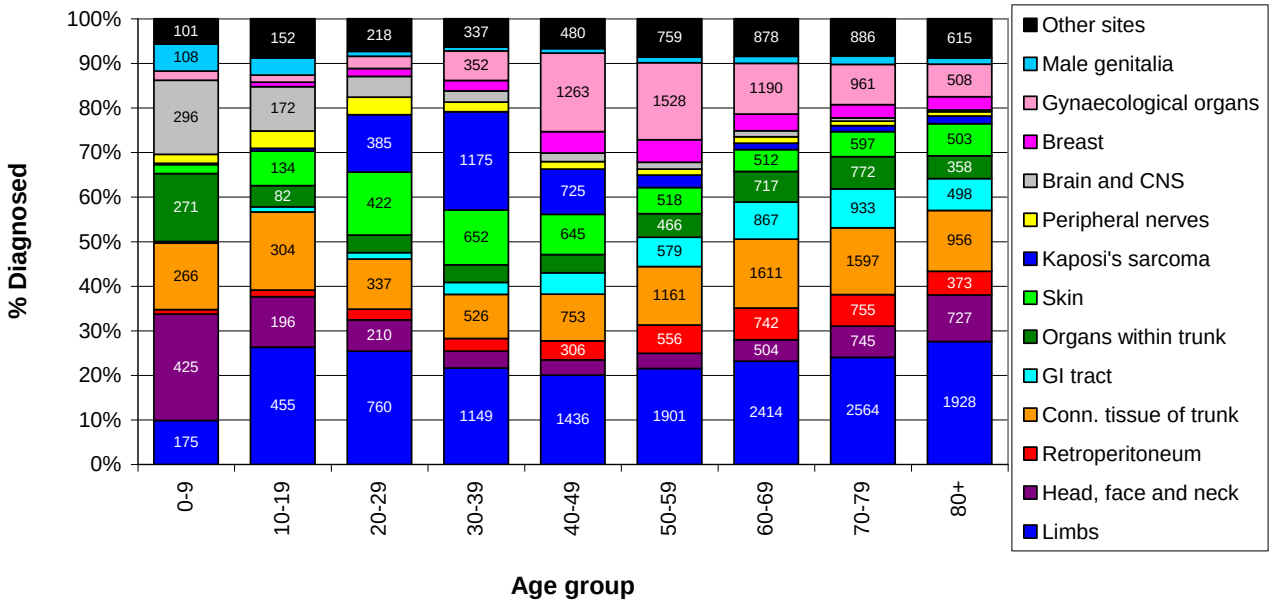
1.3.2 Variation in Malignant Primary Soft Tissue Sarcoma Incidence with Anatomical Site

Soft tissue sarcomas are most likely to arise in the limbs (23%) and the connective tissues of the trunk (13%), although they can occur at any site of the body. Incidence rates for each anatomical cancer site vary with age; with sarcomas arising in the brain and CNS being most common in patients under the age of 10 years, and sarcomas of the limbs being most common in patients aged between 10 and 29 and 80 years and over (Figure 1.5). Soft tissue sarcomas arising within the head, face and neck are also more prominent in patients aged under 20 years. Tumours of the retroperitoneum, on the other hand, are very rarely diagnosed in patients less than 40 years of age.

Figure 1.5: Proportion of soft tissue sarcomas diagnosed in each age group and anatomical site (England: 1985–2009)



1.3.3 Malignant Primary Soft Tissue Sarcoma Survival

Figure 1.6: Soft tissue sarcoma 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

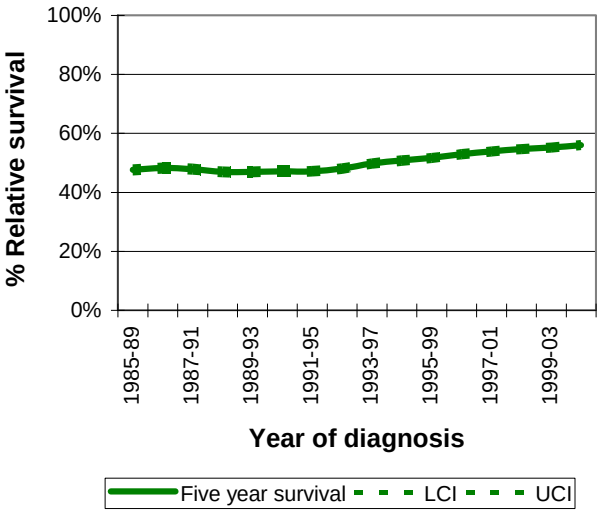
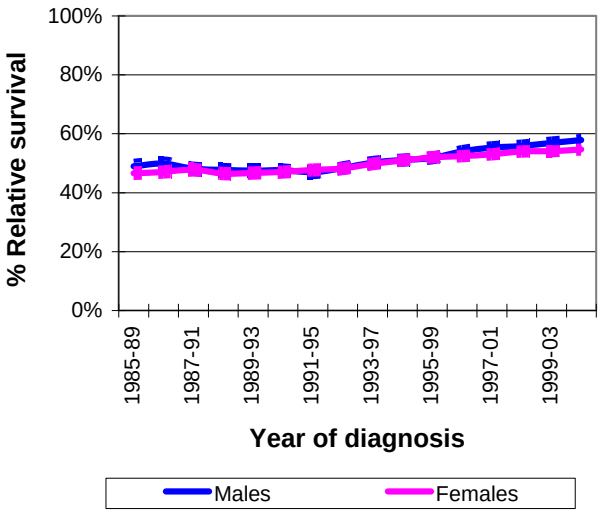


Figure 1.7: Soft tissue sarcoma 5-year relative survival rates in each sex (5-year rolling average) (England: 1985–2004)



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Soft tissue sarcoma 5-year relative survival rates have improved significantly during the 25-year period examined; from 48% in 1985-1989 to 56% in 2000-2004 (Figure 1.6). Five-year relative survival rates are similar in males and females (Figure 1.7). There are no comparative international studies with which to compare these overall relative survival rates. Survival rates for individual morphological sub-types are available for other countries, and these are included in the relevant sections of this report.

There are many factors which may have contributed to the improved overall 5-year relative survival of patients with soft tissue sarcoma. For example, the survival rates for Kaposi's sarcoma are now considerably better due to advancements in the treatment of these patients (the large majority of whom are HIV positive), and well-differentiated liposarcomas of the limbs are curable by resection with adequate margins.

1.4 References

1. World Health Organisation, 2012. *International Classification of Diseases (ICD).* Available at: http://www.who.int/classifications/icd/en/ [Accessed 24.07.2012].

2. World Health Organisation, 2012. *International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3).* Available at: http://www.who.int/classifications/icd/adaptations/oncology/en/ [Accessed 24.07.2012].

3. Fay, M. P. and Feuer, E. J., 1997. Confidence Intervals for directly standardised rates: a method based on the Gamma Distribution. *Statistics in Medicine*, 16 (7), 791-801.

4. Ederer, F. and Heise, H. 1959. Instructions to Ibm 650 programmers in processing survival computations. *Technical, End Results Evaluation Section, National Cancer Institute*.

5. West Midlands Cancer Intelligence Unit, 2012. The completeness of soft tissue sarcoma data in the National Cancer Data Repository. *National Cancer Intelligence Network.* Available at: http://www.ncin.org.uk/search/soft+tissue+sarcoma+datra+completeness.aspx.

6. Gutierrez, J. C., Perez, E. A., Franceschi, D., Moffat, F. L., Livingstone, A. S. and Koniaris, L. G., 2007. Outcomes for soft-tissue sarcoma in 8,249 cases from a large state cancer registry. *Journal of Surgical Research*, 141 (1), 105-114.

7. Nijhuis, P. H. A., Schaapveld, M., Otter, R., Molenaar, W. M., van der Graaf, W. T. A. and Hoekstra, H. J., 1999. Epidemiological aspects of soft tissue sarcomas (STS) - consequences for the design of clinical STS trials. *European Journal of Cancer*, 35 (12), 1705-1710.

8. Levi, F., La Vecchia, C., Randimbison, L. and Te, V.-C., 1999. Descriptive epidemiology of soft tissue sarcomas in Vaud, Switzerland. *European Journal of Cancer*, 35 (12), 1711-1716.

9. West Midlands Cancer Intelligence Unit, 2012. Bone sarcoma incidence and survival: Tumours diagnosed between 1985 and 2009. Available online: http://www.wmciu.nhs.uk/documents/ReportR1205_BoneSarcomaIncidenceAndSurvival.pdf [Accessed 12.10.2012]

2. Leiomyosarcoma

Key Facts

- **Most common anatomical sites of diagnosis: limbs, retroperitoneum, gastro-intestinal tract, female genital tract**
- **12,199 leiomyosarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 9 per million in 2007-2009**
- **Number diagnosed in 2008 and 2009: 554 and 470**
- **Sub-types:**
  - **Leiomyosarcoma NOS: 11,764 diagnosed 1985-2009**
  - **Epithelioid leiomyosarcoma: 279 diagnosed 1985-2009**
  - **Myxoid leiomyosarcoma: 128 diagnosed 1985-2009**
  - **Smooth muscle tumour: 28 diagnosed 1985-2009**

2.0 LEIOMYOSARCOMA

2.1 Leiomyosarcoma Incidence

Leiomyosarcomas develop from the smooth muscle cells found all over the body. For the purpose of this report, four distinct morphological sub-types of leiomyosarcoma (leiomyosarcoma NOS, epithelioid leiomyosarcoma, myxoid leiomyosarcoma and smooth muscle tumour), all of which affect patients of similar age profiles, have been aggregated in the leiomyosarcoma sub-group. Leiomyosarcoma NOS is by far the most commonly recorded sub-type, accounting for 96% of cases.

The overall age standardised leiomyosarcoma incidence rate fluctuates around 9 cases per million. This is somewhat lower than the 12.3 per million incidence rate reported by Toro et al (2006)[1], based on the SEER database (1978-2001). There is some variation in overall leiomyosarcoma incidence rates in the 25-year period examined: between 1992 and 2004 the overall age standardised incidence rate rose significantly above the incidence rate observed in 1985. Prior to obtaining their own ICD-O3 morphology code in 2003, gastro-intestinal stromal tumours (GISTs) were registered as leiomyosarcoma. This partly explains why incidence rates have decreased from the year 2000 onwards.

Figure 2.1: Leiomyosarcoma age standardised incidence rates (3-year rolling average) (England: 1985–2009) All sites

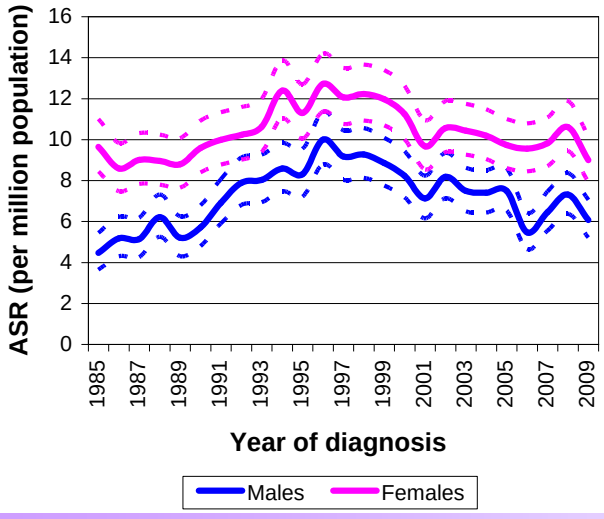
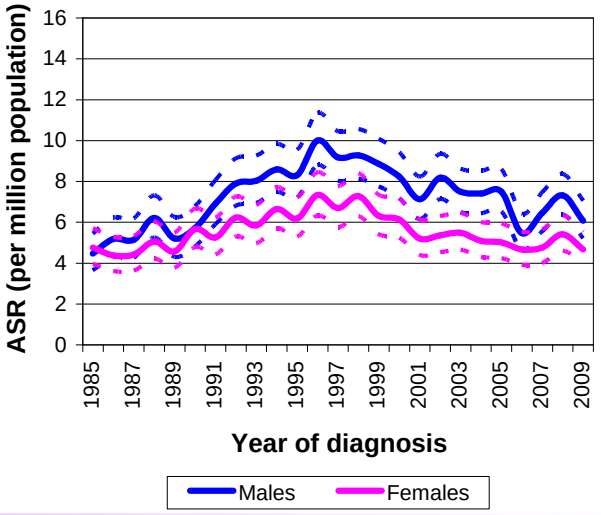


Figure 2.2: Leiomyosarcoma age standardised incidence rates (3-year rolling average) (England: 1985–2009) Excluding gynaecological sites



2. Leiomyosarcoma

Leiomyosarcoma incidence rates are significantly higher in females than males, with age standardised rates of approximately 6.6 per million in males and 9.8 per million in females between 2007 and 2009 (Figure 2.1). However, when gynaecological tumours are excluded, the age standardised rates for males and females are no longer significantly different (Figure 2.2).

Figure 2.3: Number of leiomyosarcomas diagnosed in each age group and sex (England: 1985–2009)

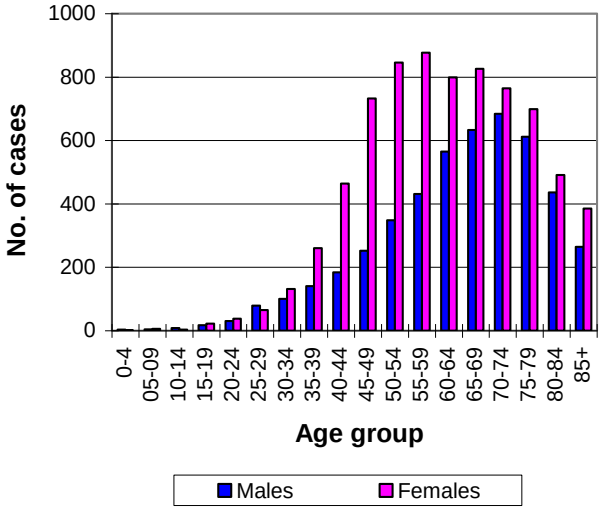
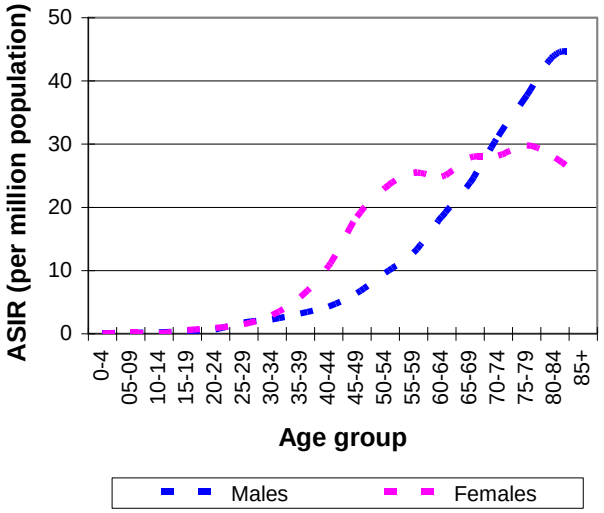


Figure 2.4: Leiomyosarcoma age specific incidence rates (England: 1985–2009)



Leiomyosarcoma is exceptionally rare in patients under 20 years of age. The total number of leiomyosarcomas diagnosed in females is higher than in males for all age groups (Figure 2.3). Overall leiomyosarcoma age specific incidence rates in females increase rapidly from the age of 35 years, and then plateau in patients aged 50 years and above (Figure 2.4). The age specific incidence rates of leiomyosarcoma are higher in females than in males under the age of 65 years, while this trend reverses in more elderly patients. This is primarily due to females having a higher life expectancy, with the comparatively smaller number of males inflating the male age specific rate in the older age groups.

Figure 2.5: Number of leiomyosarcomas diagnosed in each age group and sex excluding gynaecological cancer sites (England 1985–2009)

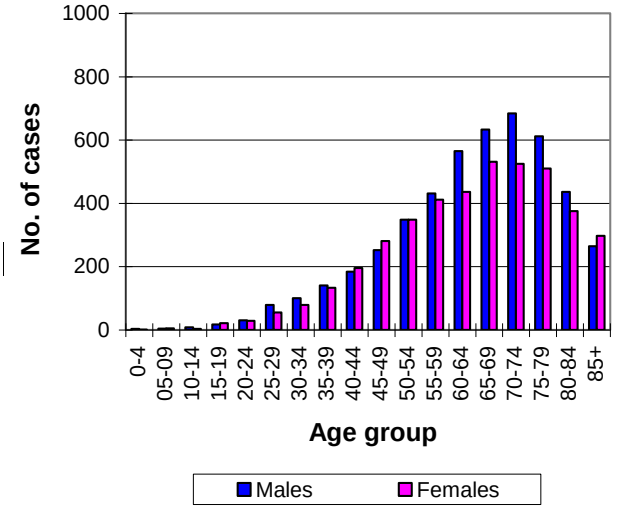
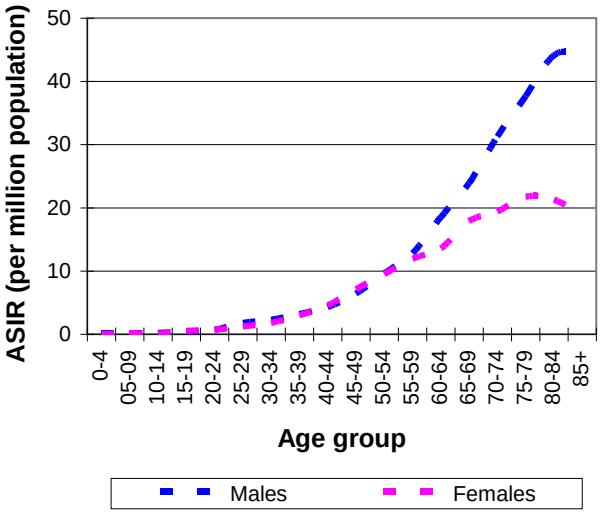


Figure 2.6: Leiomyosarcoma age specific incidence rates excluding gynaecological cancer sites (England: 1985–2009)



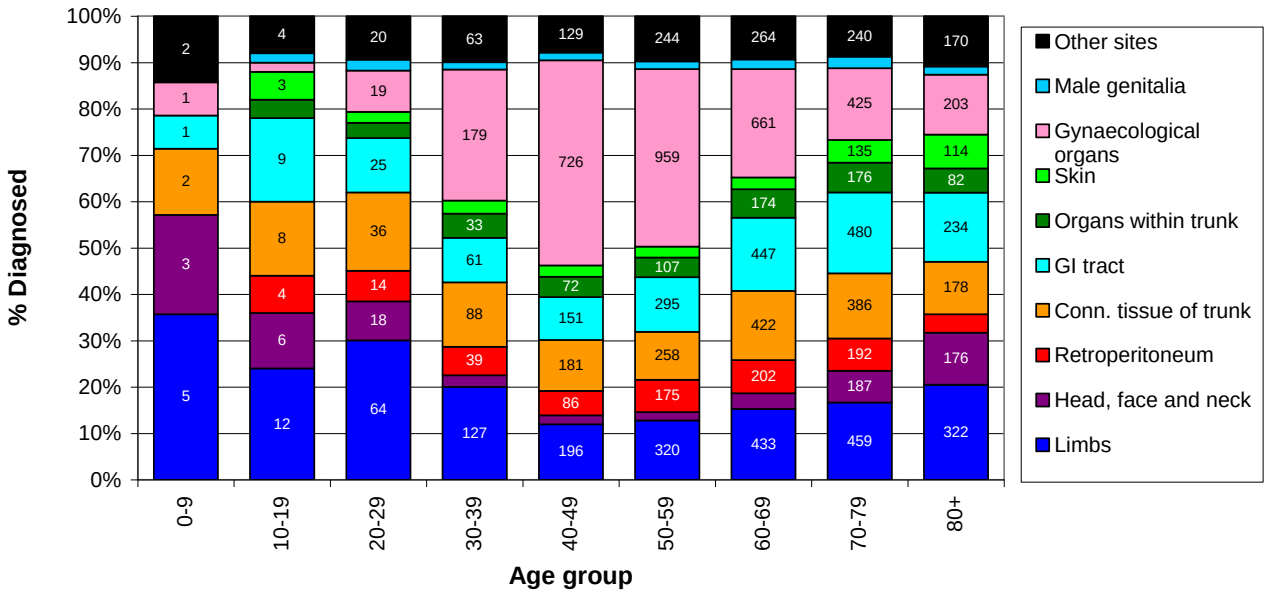
2. Leiomyosarcoma

Leiomyosarcomas account for 54% of sarcomas arising within the female genital tract. When gynaecological sarcomas are excluded (Figure 2.5), the number of leiomyosarcomas diagnosed in males in each age group is generally higher. When age specific incidence rates are calculated excluding sarcomas in the gynaecological organs, male age specific rates increase more steeply than female rates, finally becoming 2.5 times higher in patients aged 85 years or older (Figure 2.6). Figures 2.3 to 2.6 therefore demonstrate the significance of the inclusion of gynaecological leiomyosarcomas on sex specific incidence rates.

2.2 Variation in Leiomyosarcoma Incidence with Anatomical Site

Leiomyosarcomas most commonly arise in the female gynaecological organs (26%) and in the limbs (16%). However, leiomyosarcomas can be diagnosed anywhere in the body, including in the connective tissues of the GI tract (14%), the trunk (13%) and the retroperitoneum (6%). Incidence rates in each anatomical site vary according to age; with leiomyosarcomas of the gynaecological organs being most common in females aged 40 to 49 years, and limb and head, face and neck leiomyosarcomas being most common in children aged 9 years and under (Figure 2.7). Leiomyosarcomas are, however, rarely diagnosed in patients under 20 years of age, with only 64 tumours diagnosed between 1985 and 2009.

Figure 2.7: Proportion of leiomyosarcomas diagnosed in each age group and anatomical site (England: 1985–2009)



2.3 Leiomyosarcoma Survival

Five-year leiomyosarcoma relative survival in England has improved significantly over the last 25 years, from 35% to 48% (Figure 2.8). This is somewhat lower than the cumulative 5-year survival rate of 64% reported by Gustafson and colleagues (1992)[2], whose study followed 48 patients, all of whom were treated with surgery. However, it is higher than the rate reported by Hare and Cerny in their classic study of 200 soft tissue sarcoma patients (1963)[3], which reported a survival rate of only 23%. However, it is recognised that these small series are not directly comparable.

2. Leiomyosarcoma

Figure 2.8: Leiomyosarcoma 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

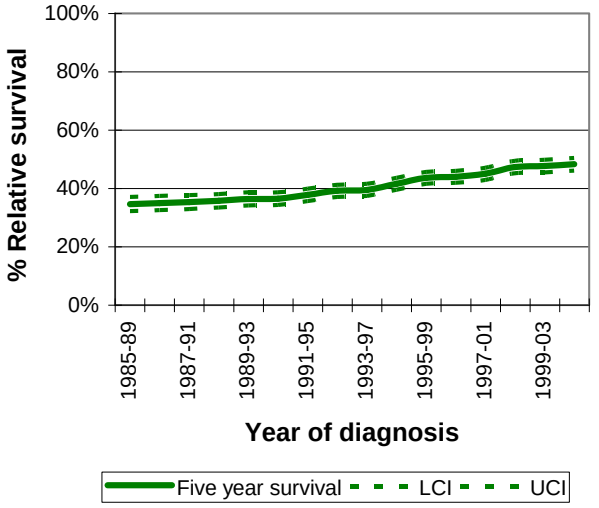


Figure 2.9: Leiomyosarcoma 5-year relative survival rates– variation with age (5-year rolling average) (England: 1985–2004)

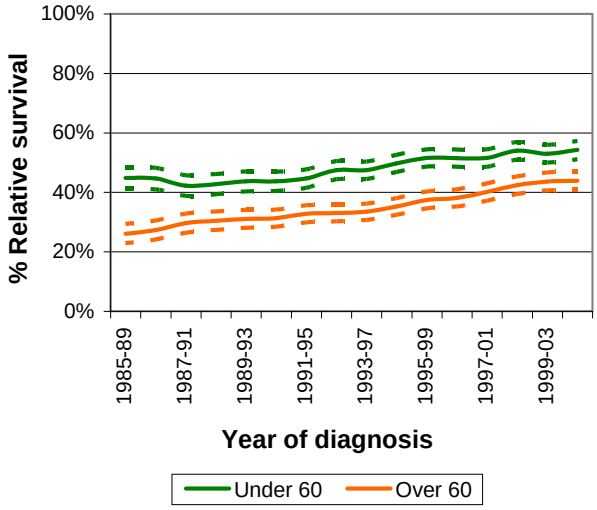
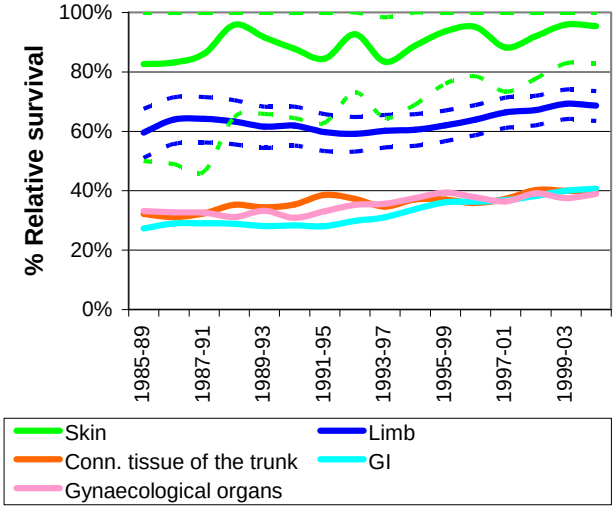


Figure 2.10: Leiomyosarcoma 5-year relative survival rates in the most common anatomical sites (5-year rolling average) (England: 1985–2004)



Leiomyosarcoma 5-year relative survival rates are significantly higher in patients under the age of 60 years (Figure 2.9). Survival has improved significantly over the past 25 years, from 45% to 54% in those aged under 60 years and from 26% to 44% in those aged 60 years and over. The difference in survival rates between the two age groups narrowed between 1985-1989 and 2000-2004, from a 19 percentage point difference at the start of the period to a 10 percentage point difference at its end.

2. Leiomyosarcoma

Patients diagnosed with leiomyosarcoma of the skin have the highest 5-year relative survival rates (95%) (Figure 2.10). Patients diagnosed with leiomyosarcoma of the limb have a significantly higher 5-year relative survival rate (69%) than patients with leiomyosarcomas of the connective tissue of the trunk (40%), the GI tract (41%) or the gynaecological organs (39%). This is the case over the entire 25-year period studied. There are no significant differences between the relative survival rates for leiomyosarcomas of the latter three sites. These 5-year relative survival rates are broadly comparable with those previously reported; 43% for digestive tract leiomyosarcomas[4] and approximately 40% for uterine leiomyosarcomas[5,6,7].

The anatomical location of a leiomyosarcoma is clearly an important factor which has a direct impact on survival. Leiomyosarcomas arising within the connective tissue of the trunk have a poor prognosis as they are often difficult to excise with clear margins, and hence, are prone to both local recurrence and distant metastasis[8]. Gynaecological sarcomas behave differently to carcinomas arising within this cancer site: sarcomas tend to be more aggressive[9]. The highest survival rates are associated with sarcomas of the skin, as these are more likely to be superficial tumours which are curable through resection with adequate margins. Access to staging data, particularly the size of the tumour at diagnosis, would provide a greater insight into the factors which lead to different survival rates across anatomical sites.

2.4 References

1 Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

2 Gustafson, P., Rydholm, A., Willen, H., Akerman, M., Baldetorp, B. and Ferno, M., 1992. Soft tissue leiomyosarcoma: A population-based epidemiologic and prognostic study of 48 patients, including cellular DNA content, *Cancer*, 70 (1), 114-119.

3 Hare, H. F. and Cerny, M. J. Jr., 1963. Soft tissue sarcoma: A review of 200 cases, *Cancer*, 16 (10), 1332-1337.

4 He, L.-J., Wang, B.-S. and Chen, C.-C., 1988. Smooth muscle tumours of the digestive tract: Report of 160 cases, *British Journal of Surgery*, 75 (2), 184-186.

5 Echt, G., Jepson, J., Steel, J., Langholz, B., Luxton, G., Hernandez, W., Astrahan, M. and Petrovich, Z., 1990. Treatment of uterine sarcomas, *Cancer*, 66 (1), 35-39.

6 Dinh, T. A., Oliva, E. A., Fuller, A. F. Jr., Lee, H. and Goodman, A., 2004. The treatment of uterine leiomyosarcoma: Results from a 10-year experience (1990-1999) at the Massachusetts General Hospital. *Gynecologic Oncology*, 92 (2), 648-652.

7 Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone, p 35-46. Geneva: WHO Press.

8 Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone, p 134. Geneva: WHO Press.

9 Kelly, K.-L. J. and Craighead, P. S. (2005). Characteristics and management of uterine sarcoma patients treated at the Tom Baker Cancer Centre, International. *International Journal of Gynaecological Cancer*, 15 (1), 132-139.

3. Liposarcoma

Key Facts

- **Most common anatomical sites of diagnosis: soft and connective tissue of the trunk, limbs, retroperitoneum**
- **6,370 liposarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 6 per million in 2007-2009**
- **Number diagnosed in 2008 and 2009: 398 and 361**
- **Sub-types:**
  - **Liposarcoma NOS: 3,153 diagnosed 1985-2009**
  - **Well-differentiated liposarcoma: 877 diagnosed 1985-2009**
  - **Pleomorphic liposarcoma: 843 diagnosed 1985-2009**
  - **Myxoid and round cell liposarcoma: 1,498 diagnosed 1985-2009**

3.0 LIPOSARCOMA

Liposarcomas are a group of sarcomas that arise from fat cells (adipocytes) within the body and can occur at any anatomical site. Collectively, liposarcomas represent the third most commonly diagnosed type of soft tissue sarcoma and account for approximately 11-12% of all soft tissue sarcomas diagnosed in England between 1985 and 2009. Liposarcomas are rarely diagnosed in children and are more common in elderly patients. Seven different variants of liposarcoma exist within the WHO classification of bone and soft tissue sarcomas[1]. Incidence and survival rates are presented for the four most common sub-groups: liposarcoma NOS, well-differentiated liposarcoma, pleomorphic liposarcoma, and myxoid and round cell liposarcoma.

Table 3.1: Summary of liposarcoma morphologies, anatomical sites, numbers and incidence rates

Name	ICD-O3 morphology code	Common anatomical sites of diagnosis	Number of tumours 1985-2009	Number of tumours 2008, 2009	Age-standardised incidence rate 2009 (per million)
Liposarcoma NOS	8850 (Liposarcoma, NOS) 8855 (Mixed liposarcoma) 8857 (Fibroblastic liposarcoma) 8860 (Angiomyolipoma)	Soft tissue of limbs: 35% Connective tissue of trunk: 22% Retroperitoneum: 18%	3,153	156, 129	2.1 (1.7, 2.5)
Well differentiated liposarcoma	8851 (Liposarcoma, well differentiated)	Soft tissue of limbs: 36% Connective tissue of trunk: 21% Retroperitoneum: 18%	877	104, 106	1.8 (1.5, 2.2)
Pleomorphic liposarcoma	8854 (Pleomorphic liposarcoma) 8858 (Dedifferentiated liposarcoma)	Soft tissue of limbs: 40% Connective tissue of trunk: 23% Retroperitoneum: 17%	843	70, 70	1.1 (0.9, 1.4)
Myxoid liposarcoma	8852 (Myxoid liposarcoma) 8853 (Round cell liposarcoma)	Soft tissue of limbs: 57% Connective tissue of trunk: 18% Retroperitoneum: 7%	1,498	68, 56	1.1 (0.8, 1.4)

3.1 Liposarcoma Incidence

Between 1985 and 2009, 6,370 liposarcomas were diagnosed in England, with an age standardised incidence rate of 6 per million in 2009. Liposarcoma age standardised rates are significantly higher in males (8 per million) than in females (4 per million). Incidence rates in

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males increased significantly between 1985 and 2009 from 4.5 to 8.0 per million and in females from 3.2 to 4.4 per million. Liposarcoma NOS is the most common sub-type of liposarcoma (Table 3.1), accounting for 50% of liposarcomas, with an age standardised incidence rate of 2.5 per million in 2009.

3.2 Liposarcoma Sub-groups

For the purpose of reporting incidence and survival rates, the seven sub-types of liposarcoma were aggregated into four sub-groups (Table 3.1).

3.2.1 Liposarcoma NOS Incidence

Liposarcoma NOS (3,058), mixed liposarcomas (84), fibroblastic liposarcomas (2) and angiomyoliposarcomas (9) have been aggregated into a single sub-group, due to the rarity of the latter types. Liposarcoma NOS accounts for 97% of the diagnoses in this sub-group.

The age standardised incidence rate for the liposarcoma NOS sub-group fluctuates around 2.3 per million, which is somewhat higher than the rate of 1.5 per million within the SEER database, reported by Toro et al (2006)[2]. Age standardised rates are significantly higher in males than females (Figure 3.2a), with rates of 3.3 per million and 1.8 per million in males and females respectively in 2007-2009. The decreases in the age standardised incidence rates in males and females for the liposarcoma NOS sub-group between 2005 and 2009 (Figure 3.2a) correlate inversely with the increases seen in the age standardised incidence rates for the well differentiated and pleomorphic liposarcoma sub-groups (Figure 3.3a and Figure 3.4a). This probably reflects changes in reporting practice within pathology laboratories.

Liposarcoma NOS is rarely diagnosed in patients under the age of 50 years, and never in children. Between 1985 and 2009 only 27 cases were reported in people aged 25 years and under (Figure 3.2b),. Age specific rates increase steeply after the age of 50 years, especially in males, and are as high as 13 per million in males aged 80 years and over (Figure 3.2c). This is more than twice the rate seen in females of the same age.

3.2.2 Well Differentiated Liposarcoma Incidence

Well differentiated liposarcomas are the second most common variant of liposarcoma, accounting for approximately 30% percent of diagnoses in 2008 and 2009 (Table 3.1). They can recur locally but have no potential for metastasis[3] unless the tumour dedifferentiates.

The incidence rates of well differentiated liposarcomas increased significantly between 1985 and 2009, from 0.3 to 2.0 per million in males, and 0.2 to 1.1 per million in females (Figure 3.3a). These observed increases in incidence probably reflect changes in reporting practice within pathology laboratories which allows more specific coding by cancer registries. However, as well-differentiated liposarcomas are now classified as being synonymous with tumours previously deemed as non-registerable such as atypical lipomatous tumour[3], incidence rates based on cancer registration data may underestimate the occurrence of these tumours. Well differentiated liposarcomas arising within deep anatomical locations, such as the

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Figure 3.2a: Liposarcoma NOS age standardised incidence rates (3-year rolling average)

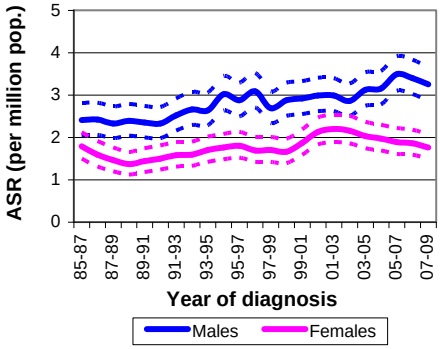


Figure 3.2b: Number of liposarcoma NOS tumours diagnosed in each age group and sex

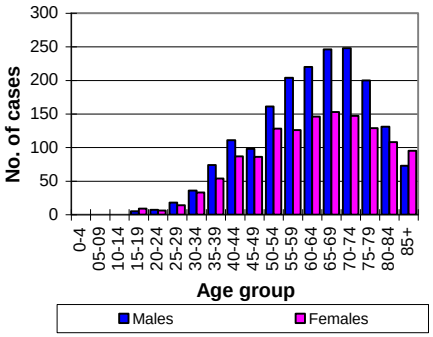


Figure 3.2c: Liposarcoma NOS age specific rates (England: 1985–2009)

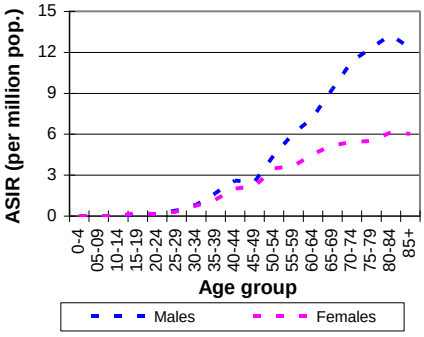


Figure 3.3a: Well differentiated liposarcoma age standardised incidence rates (3-year rolling average)

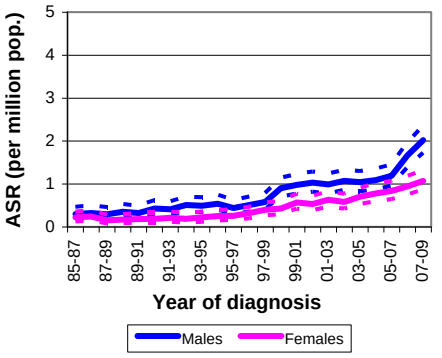


Figure 3.3b: Number of well differentiated liposarcomas diagnosed in each age group and sex

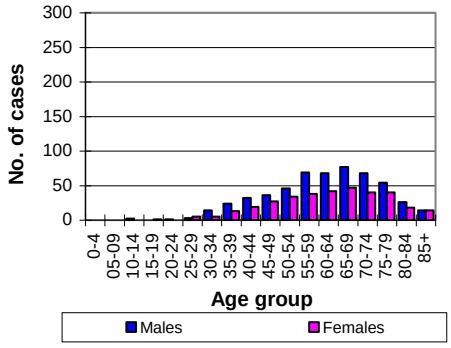


Figure 3.3c: Well differentiated liposarcoma age specific rates (England: 1985–2009)

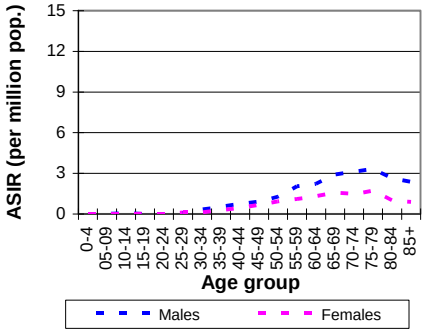


Figure 3.4a: Pleomorphic liposarcoma age standardised incidence rates (3-year rolling average)

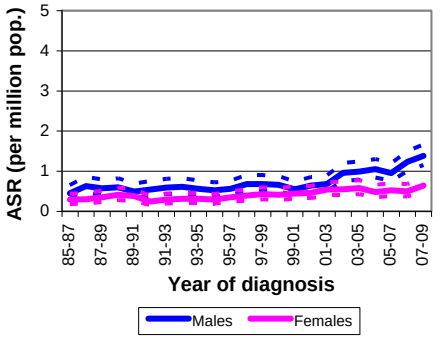


Figure 3.4b: Number of pleomorphic liposarcomas diagnosed in each age group and sex

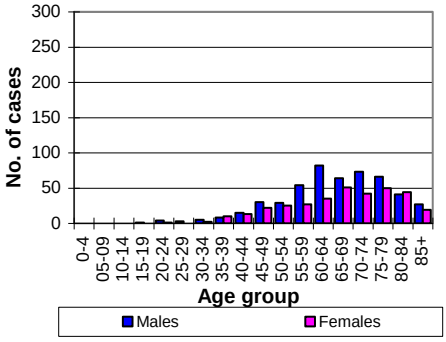


Figure 3.4c: Pleomorphic liposarcoma age specific rates (England: 1985–2009)

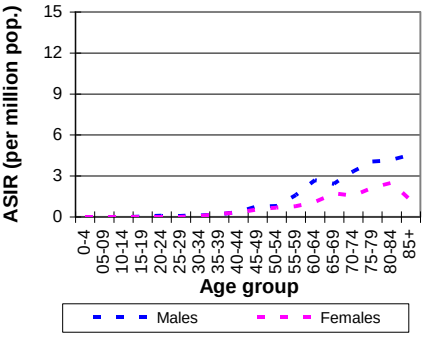


Figure 3.5a: Myxoid liposarcoma age standardised incidence rates (3-year rolling average)

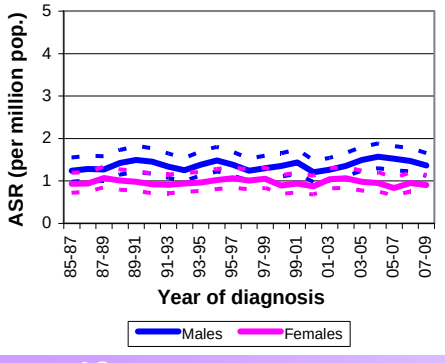


Figure 3.5b: Number of myxoid liposarcomas diagnosed in each age group and sex

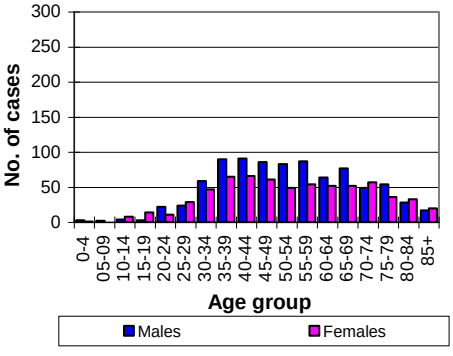
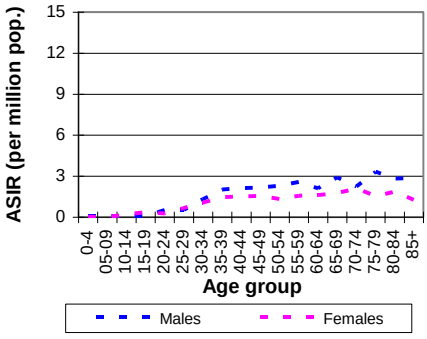


Figure 3.5c: Myxoid liposarcoma age specific rates (England: 1985–2009)



3. Liposarcoma

the retroperitoneum, have the potential to dedifferentiate in more than 20% of cases, and cancer registries probably receive information on all retroperitoneal liposarcomas. In contrast, superficial tumours in the extremities are classified as atypical lipomatous tumours rather than well-differentiated liposarcomas and as such may not have been counted by cancer registries.

Although well differentiated liposarcoma incidence rates are higher in males than females throughout the 25-year period examined, the difference only reaches statistical significance in 2007-2009 because of a large increase in the incidence rates in males (Figure 3.3a). Well differentiated liposarcomas are exceptionally rare in patients aged under the age of 30 years, with only 12 cases reported between 1985 and 2009 (Figure 3.3b). The number of tumours diagnosed in all age groups is higher in males. Age specific well differentiated liposarcoma incidence rates increase sharply between the 25-29 and 75-79 year age groups, before dropping slightly in older patients (Figure 3.3.c). The age specific incidence rate in males aged 75 years and over is double the rate in females of the same age.

3.2.3 Pleomorphic Liposarcoma Incidence

Pleomorphic liposarcomas are high grade tumours with a metastatic rate of between 30% and 50%[4]. The term ”pleomorphic” is applied to describe a concept whereby cells take on multiple structural forms visible through variability in the size and shape of cells or their nuclei. For the purpose of analysis, this sub-group includes two distinct sub-types of liposarcoma (Table 3.1): pleomorphic liposarcoma and dedifferentiated liposarcoma. These tumours have very similar survival curves, age profiles and anatomical sites of diagnosis.

There appears to be a void in existing research providing population based incidence and survival statistics of patients with pleomorphic liposarcoma, with the only comparable statistics provided by the surveillance, epidemiology and end results (SEER) program from the USA.

Pleomorphic and dedifferentiated liposarcomas collectively account for around 17% of all liposarcomas diagnosed annually in England. Between 1985 and 2009 the age standardised incidence rate increased significantly for both males and females, from 0.5 to 1.4 per million and 0.3 to 0.6 per million respectively (Figure 3.4a). These rates are very similar to those reported by Toro et al (2006)[2] based on the SEER database. The significant increases seen probably reflect changes in reporting practice within pathology laboratories and more specific coding by cancer registries.

Pleomorphic liposarcomas are exceptionally rare in patients aged under 35 years, with only 16 cases reported between 1985 and 2009, and are never diagnosed in children (Figure 3.4b). Pleomorphic liposarcoma age specific incidence rates increase with age, and peak in the 80-84 age group in females (Figure 3.4c). In the 85 and over age group, the rates observed in males are almost five times as high as those in females, but the overall numbers are small.

3.2.4 Myxoid Liposarcoma Incidence

The term myxoid is used to describe tumours which have mucus like appearance. Between 1985 and 2009, myxoid liposarcoma was one of the more common variants of liposarcoma diagnosed, accounting for around 24% of lipomatous malignancies. Myxoid liposarcomas typically occur in the extremities. For the purpose of analysis, this sub-group aggregates two distinct sub-types of liposarcoma: myxoid liposarcoma and round cell liposarcoma (Table 3.1), as by definition, these are the same tumour[5].

The age standardised incidence rate for the myxoid liposarcoma sub-group fluctuates

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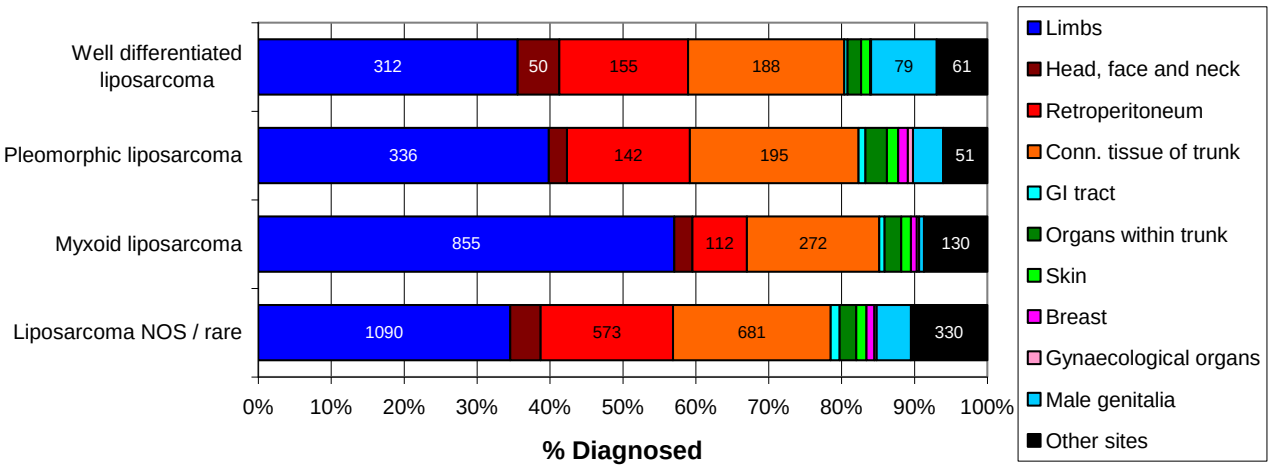
around 1.2 per million and does not change significantly over the 25-year time period studied. Although myxoid liposarcoma age standardised incidence rates in males are generally higher than those in females (1.4 per million and 0.9 per million respectively in 2007-2009) the rates in males and females are not significantly different (Figure 3.5a). These rates are considerably lower than the 3.8 per million observed in the SEER database (1998-2001) reported by Toro et al (2006)[2].

Unlike other variants of liposarcoma, myxoid liposarcomas have a relatively high incidence from the age of 30 years upwards. These tumours are rarely diagnosed in patients aged 15 years and under, with only 18 cases reported between 1985 and 2009 (Figure 3.5b). The number of myxoid liposarcomas diagnosed in most age groups is higher in males. Myxoid liposarcoma age specific incidence rates increase sharply in both males and females between the ages of 15 and 39 years. They then generally increase slowly across the age groups into old age (Figure 3.5c).

3.3 Variation in Liposarcoma Incidence with Anatomical Site

Liposarcomas can occur within any anatomical site in the body, but most commonly arise within the connective and soft tissue of the limbs or trunk, or within the retroperitoneal cavity (Figure 3.6). Liposarcoma NOS, pleomorphic liposarcoma and well-differentiated liposarcoma variants all share similar anatomical site profiles, with around 35% of tumours arising in the limbs, 20% in the connective tissue of the trunk and 20% in the retroperitoneal cavity.

Figure 3.6: Liposarcoma variants diagnosed in the most common anatomical sites (England: 1985–2009)



The majority of myxoid liposarcomas, arise in the limbs (55%) and connective tissue of the trunk (20%). Myxoid liposarcomas rarely arise within the retroperitoneum; only 112 of these tumours were reported in England between 1985 and 2009. It is thought that myxoid liposarcomas of the retroperitoneum never occur, and the identification of a myxoid liposarcoma in this area should prompt an investigation for a primary tumour within the limbs[6]. Also, myxoid liposarcomas are different from other sarcomas in that they have the unique ability to metastasise to fat-containing areas of the body, including extraperitoneal fat[7]. It is therefore possible that the myxoid liposarcomas reported as arising in the retroperitoneum represent metastatic disease from cancers originating in other anatomical sites. However, an audit of the pathology reports of 15 tumours coded as "myxoid liposarcoma of the retroperitoneum" confirmed that the correct coding had been used, and the possibility of metastasis from another primary was ruled out.

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3.4 Liposarcoma Survival

Figures 3.7 to 3.10 show how 5-year relative survival rates for the four sub-groups of liposarcoma vary for the most common anatomical sites. Survival curves based on fewer than 10 sarcoma diagnoses are depicted by a fuzzy line (applicable to Figure 3.10 only). Figure 3.7 shows 5-year relative survival rates for the four liposarcoma sub-groups across all anatomical sites, with the well differentiated liposarcoma sub-group showing the highest 5-year relative survival rate and the pleomorphic liposarcoma sub-group the lowest. This is consistent with studies by Spittle, Newton and MacKenzie (1970)[8] who reported a myxoid liposarcoma 5-year survival rate of approximately 85% and a pleomorphic liposarcoma 5-year survival rate of approximately 50%, although these analyses are based on 60 patients treated within a single centre.

Only the liposarcoma NOS sub-group 5-year relative survival rates showed any significant improvements over the 25-year period studied, increasing significantly from 62% to 77% between 1985 and 2004. The 5-year relative survival rates for the well differentiated liposarcoma sub-group have remained steady over the 25-year period at approximately 85%. This is comparable to the rate found by Lahat et al (2008)[9] in their study of 58 well differentiated liposarcomas.

The 5-year relative survival rate for the myxoid liposarcoma sub-group did not vary significantly across the 25-year period examined; increasing, slightly but not significantly, from 71% in 1985 to 82% in 2004. This is also comparable to previously reported rates[10]. There is no significant variation in the 5-year relative survival rate of the pleomorphic liposarcoma sub-group, which fluctuates around 50% across the 25-year period examined. This is somewhat lower than the 63% rate reported by Hornick et al (2004), based on 57 patients[11] and the 57% rate based on 63 patients reported by Gebhard et al (2002)[12]. The survival rates for the myxoid liposarcoma and liposarcoma NOS sub-groups follow very similar patterns.

Liposarcoma survival rates vary according to both morphological sub-group and anatomical site (Figures 3.8 to 3.10). Liposarcomas arising within the connective and soft tissue of the limbs (extremities) generally have better survival rates than those arising in the retroperitoneum; with survival rates for tumours arising in the connective tissue of the trunk lying in between. This pattern is consistent with the results previously reported by Moore Dalal et al (2006)[13].

In the case of liposarcomas arising in the limbs, 5-year relative survival rates for the well differentiated liposarcoma sub-group generally approach 100% and fluctuate around 60% for the pleomorphic liposarcoma sub-group (Figure 3.8). Pleomorphic liposarcomas are usually associated with a poor prognosis due to their high potential to metastasise to distant sites, and survival rates of patients with a diagnosis of pleomorphic liposarcoma are significantly lower than for all other liposarcoma sub-types across all cancer sites. The myxoid liposarcoma and liposarcoma NOS sub-groups have 5-year relative survival rates between those of the well differentiated and pleomorphic sub-groups[14], at around 83%. Eilber et al (2004) reported a disease free 5-year survival of 64% for patients with extremity liposarcoma[15], a rate close to that found in the current analysis.

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Figure 3.7 Liposarcoma 5-year relative survival rates for all cancer sites (5-year rolling average)

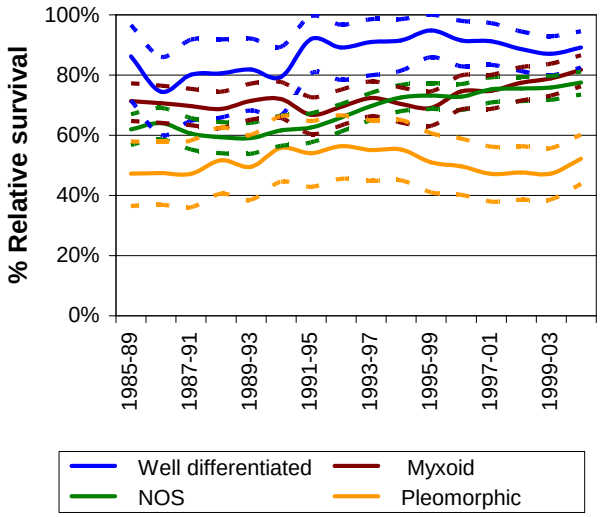


Figure 3.8 Liposarcoma 5-year relative survival rates for extremities (limbs) (5-year rolling average)

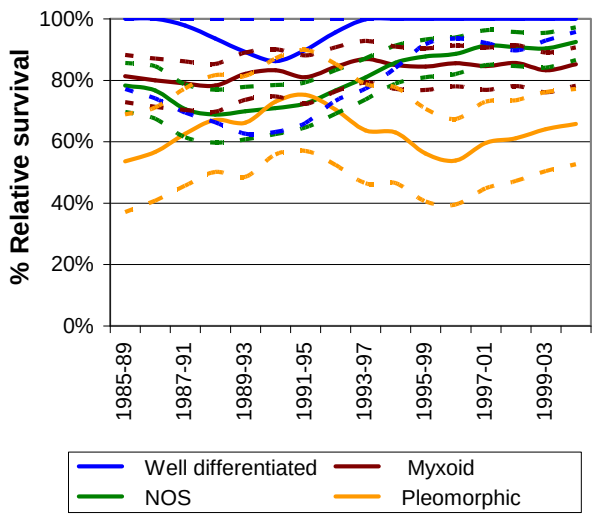


Figure 3.9 Liposarcoma 5-year relative survival rates for soft tissue of the trunk (5-year rolling average)

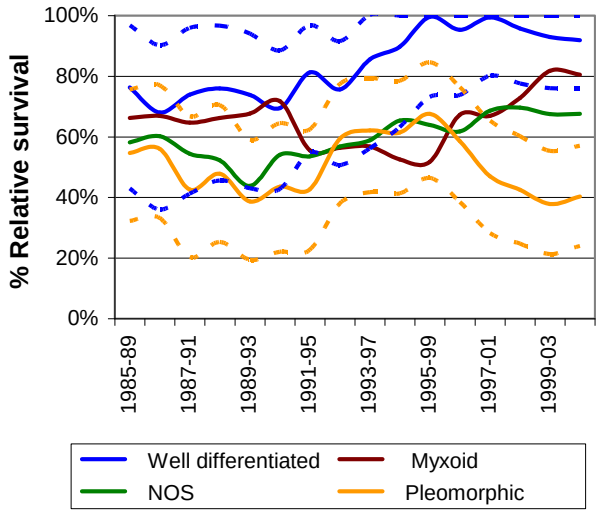
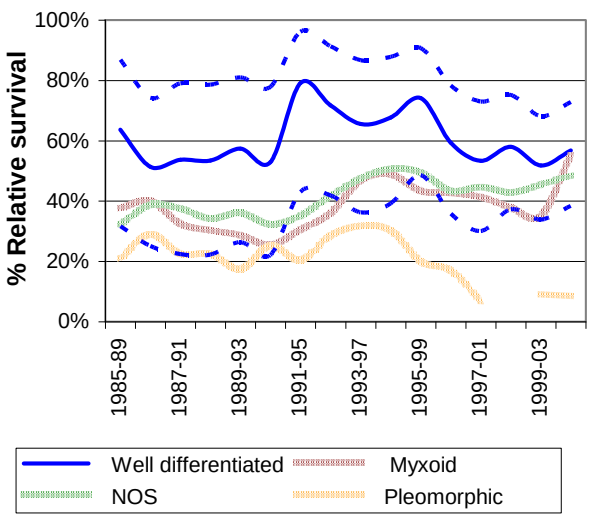


Figure 3.10 Liposarcoma 5-year relative survival rates for retroperitoneum (5-year rolling average)



Liposarcomas in the connective tissue of the trunk generally have higher 5-year relative survival rates than retroperitoneal liposarcomas (Figures 3.9 and 3.10). No significant improvements in 5-year relative survival were observed for any histological sub-group of liposarcomas occurring in the trunk over the time period examined. Well differentiated liposarcoma 5-year relative survival rates fluctuate around 90%, myxoid liposarcoma survival rates are approximately 70%, liposarcoma NOS survival rates are approximately 60%, and pleomorphic liposarcoma survival rates fluctuate around 50%.

The diagnosis of a retroperitoneal sarcoma tends to result in a poorer prognosis regardless of the liposarcoma sub-group (Figure 3.10). The well-differentiated liposarcomas have the

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highest 5-year relative survival, at around 60%, and patients with pleomorphic liposarcoma have the lowest 5-year relative survival at 20%. These results are considerably lower than the 60% overall 5-year retroperitoneal liposarcoma survival rate reported by Singer et al (2003)[16].

Although well-differentiated liposarcomas are usually associated with better prognosis and outcomes, well-differentiated liposarcomas arising in the retroperitoneum have the potential to "dedifferentiate" and metastasise and it is often impossible to obtain an adequate surgical resection margin, which eventually leads to a local recurrence that cannot be controlled.

Regardless of the cancer site of diagnosis, well-differentiated liposarcomas are usually associated with a better prognosis, although the differences between the well-differentiated, myxoid and NOS variants are not always statistically significant. Pleomorphic liposarcomas are at the extreme end of the liposarcoma survival spectrum with a typically poorer prognosis. However, the overall message is a positive one, in that overall 5-year relative survival rates for any liposarcoma diagnosis appear to be improving.

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3.5 References

1. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 35-46. Geneva: WHO Press.

2. Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

3. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 35. Geneva: WHO Press.

4. Tos, A. P., 2006. Classification of pleomorphic sarcomas: where are we now? *Histopathology*, 48 (1), 51-62.

5. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 40. Geneva: WHO Press.

6. de Saint Aubain Somerhausen, N., 2012. *Lipomatous Tumours of Soft Tissues*. Available at: http://www.forpath.org/0001/part1.htm [Accessed 25/07/12].

7. Pollock, R. E., 2002. *Atlas of Clinical Oncology: Soft tissue sarcomas*. Ontario: BC Decker Inc.

8. Spittle, M. F., Newton, K. A. and MacKenzie, D. H., 1970. Liposarcoma: A review of 60 cases. British Journal of Cancer, 24 (4), 696-704.

9. Lahat, G., Anaya, D. A., Wang, X., Tuvin, D., Lev, D. and Pollock, R. E., 2008. Resectable well-differentiated versus dedifferentiated liposarcomas: Two different diseases possibly requiring different treatment approaches. *Annals of Surgical Oncology*, 15 (6), 1585-1593.

10. Spillane, A. J., Fisher, C. and Thomas, J. M., 1999. Myxoid liposarcoma: Frequency and the natural history of nonpulmonary soft tissue metastases. *Annals of Surgical Oncology*, 6 (4), 389-394.

11. Hornick, J. L., Bosenberg, M. W., Mentzel, T., McMenamin, M. E., Oliveira, A. M. and Fletcher, C. D. M., 2004. Pleomorphic liposarcoma: Clinicopathologic analysis of 57 cases. *American Journal of Surgical Pathology*, 28 (10), 1257- 1267.

12. Gebhard, S., Coindre, J.-M., Michels, J.-J., Terrier, P., Bertrand, G., Trassard, M., Taylor, S., Chateau, M.-C., Marques, B., Picot, V. and Guillou, L., 2002. Pleomorphic liposarcoma: Clinicopathologic, immunohistochemical and follow-up analysis of 63 cases: A study from the French Federation of Cancer Centers sarcoma group, *American Journal of Surgical Pathology*, 26 (5), 601-616.

3. Liposarcoma

13. Moore Dalal, K., Kattan, M. W., Antonescu, C. R., Brennan, M. F. and Singer, S., 2006. Subtype specific prognostic nomogram for patients with primary liposarcoma of the retroperitoneum, extremity or trunk. *Annals of Surgery*, 244 (3), 381-391.

14. Spillane, A. J., Fisher, C. and Thomas, J. M., 1999. Myxoid liposarcoma: Frequency and the natural history of nonpulmonary soft tissue metastases. Annals of Surgical Oncology, 6 (4), 389-394.

15. Eilber, F. C., Eilber, F. R., Eckardt, J., Rosen, G., Riedel, E., Maki, R. G., Brennan, M. F. and Singer, S., 2004. The impact of chemotherapy on the survival of patients with high- grade primary extremity liposarcoma. *Annals of Surgery*, 240 (4), 686-697.

16. Singer, S., Antonescu, C. R., Riedel, E. and Brennan, M. F., 2003. Histologic subtype and margin of resection predict pattern of recurrence and survival for retroperitoneal liposarcoma. *Annals of Surgery,* 238 (3), 358-371.

4. Fibroblastic sarcoma

Key Facts

- **Most common anatomical sites of diagnosis: the limbs, the skin (primarily due to dermatofibrosarcoma), and connective tissue of the trunk**
- **8,700 fibroblastic sarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 6.7 per million in 2007-2009**
- **Number diagnosed in 2008 and 2009: 378 and 400**
- **Sub-types:**
  - **Malignant fibrous histiocytoma: 3,673 diagnosed 1985-2009**
  - **Myxofibrosarcoma: 979 diagnosed 1985-2009**
  - **Fibrosarcoma: 1,380 diagnosed 1985-2009**
  - **Dermatofibrosarcoma: 2,668 diagnosed 1985-2009**

4.0 FIBROBLASTIC SARCOMA

Fibroblastic sarcomas arise in fibrous connective tissue within the body and can occur at any anatomical site. Collectively, fibroblastic sarcomas are among the most commonly diagnosed type of soft tissue sarcoma and account for approximately 16% of all soft tissue sarcomas diagnosed in England between 1985 and 2009. Fibroblastic sarcomas are more commonly diagnosed in the elderly, although infantile fibrosarcomas account for 6% of sarcomas diagnosed in children aged less than 5 years. Six different morphological sub-type variants of malignant fibroblastic sarcoma exist within the WHO classification of bone and soft tissue sarcomas. Incidence and survival rates are presented for the four most common sub-groups: malignant fibrous histiocytoma (MFH), myxofibrosarcoma, fibrosarcoma and dermatofibrosarcoma.

Table 4.1: Summary of fibroblastic sarcoma morphologies, anatomical sites, numbers and incidence rates

Name	ICD-O3 morphology code	Common anatomical sites of diagnosis	Number of tumours 1985-2009	Number of tumours 2008, 2009	Age-standardised incidence rate 2009 (per million)
Malignant fibrous histiocytoma	8830 (Malignant fibrous histiocytoma)	Soft tissue of limbs: 28% Skin: 4% Soft tissue of head: 8%	3,673	64, 91	1.4 (1.1, 1.7)
Dermatofibrosarcoma	8832 (Dermatofibrosarcoma) 8833 (Pigmented dermatofibrosarcoma protuberans)	Soft tissue of limbs: 45% Skin: 10% Soft tissue of head: 10%	2,668	159, 133	2.5 (2.1,3.0)
Fibrosarcoma	8810 (FS NOS) 8813 (fascial FS) 8814 (infantile FS) 8825 (inflammatory myofibroblastic tumour)	Soft tissue of limbs: 1% Skin: 96% Soft tissue of head: 1%	1,380	57, 47	0.8 (0.6, 1.1)
Myxofibrosarcoma	8811 (Myxofibrosarcoma)	Soft tissue of limbs: 67% Skin: 2% Soft tissue of head: 5%	979	98, 129	2.0 (1.7, 2.4)

4. Fibroblastic sarcoma

4.1 Fibroblastic Sarcoma Incidence

Between 1985 and 2009, 8,700 fibroblastic sarcomas were diagnosed in England, with an age standardised incidence rate of 6.7 per million persons in 2007 to 2009. The most common morphological type in the series is malignant fibrous histiocytoma (MFH) (Table 4.1), accounting for 42% of fibroblastic sarcomas between 1985 and 2009. Age standardised rates of fibroblastic sarcomas are generally higher in males (7.2 per million) than females (6.2 per million) although these differences are not significant. Incidence rates in males and females decreased significantly between 1985-1987 and 2007-2009 from 9.3 and 7.3 per million to 7.2 and 6.2 per million respectively. This is most probably a result of tumours previously diagnosed as MFH being assigned to a more specific morphology.

4.2 Fibroblastic Sarcoma Sub-groups

For the purpose of reporting incidence and survival rates, the six variants of fibroblastic sarcoma were aggregated into four sub-groups (Table 4.1).

4.2.1 Malignant Fibrous Histiocytoma Incidence

Malignant fibrous histiocytomas (MFH) were once among the most commonly diagnosed variants of soft tissue sarcoma. However, recorded incidence rates have decreased significantly due to improvements in histopathological techniques, and the differentiation of new sub-types within this group of poorly differentiated neoplasms[1] (for example myxofibrosarcoma).

Incidence rates of MFH decreased significantly between 1985 and 2009, from 5.8 to 1.5 per million in males and 4.1 to 0.9 per million in females. Incidence rates were significantly higher in males than females (Figure 4.1a). These rates are somewhat lower than the rate of 8.8 per million reported by Toro et al (2006)[2], but this may be because of the inclusion of earlier years within the SEER database before the reclassification of myxofibrosarcomas.

MFH is exceptionally rare in patients aged less than 20 years, with only 63 cases reported between 1985 and 2009 (Figure 4.1b). Age specific incidence rates of MFH vary according to gender. Male incidence rates increase rapidly with age, while female incidence rates increase more gradually, levelling off in those aged 80 years and above (Figure 4.1c).

4.2.2 Dermatofibrosarcoma Incidence

For the purpose of this analysis two distinct morphological sub-types, dermatofibrosarcoma (2,566) and pigmented dermatofibrosarcoma protuberans (102), have been combined into one sub-group. Dermatofibrosarcomas account for approximately 96% of diagnoses in this sub-group. Dermatofibrosarcomas are sarcomas in the dermis layer of the skin. They are very locally aggressive and recur often[3], but have a very high 5-year survival rate. Metastatic rates are exceptionally low (approximately 1%).

The incidence rates of dermatofibrosarcomas increased significantly between 1985 and 2009, from 1.4 to 2.8 per million in males and 1.2 to 3.1 per million in females (Figure 4.2a). Incidence rates are not significantly different in males and females. These rates are very different to those reported by Criscione and Weinstock (2007; 4.2 per million)[4], and Toro et al (2006; 5 per million)[2]. This could indicate that the incidence of dermatofibrosarcomas is under reported in England.

4. Fibroblastic sarcoma

Figure 4.1a: MFH age standardised incidence rates (3-year rolling average)

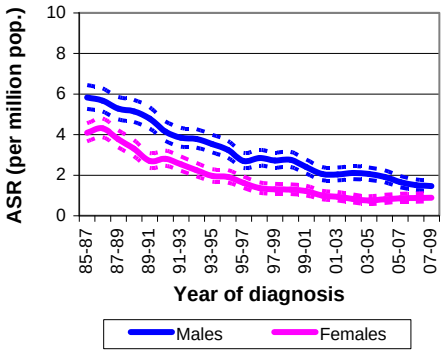


Figure 4.1b: Number of MFH tumours diagnosed in each age group and sex

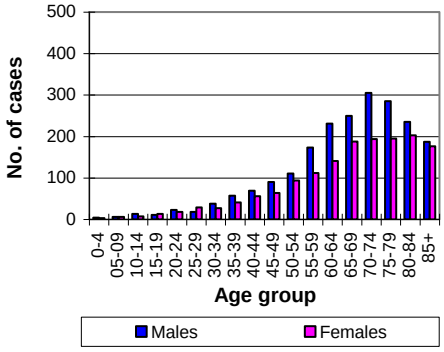


Figure 4.1c: MFH age specific incidence rates (England: 1985–2009)

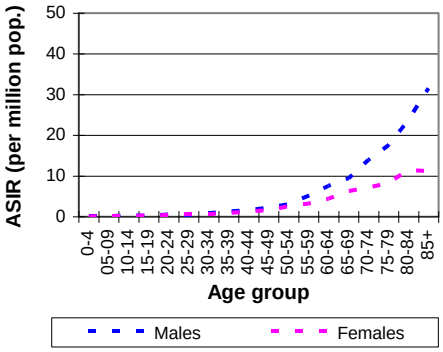


Figure 4.2a: Dermatofibrosarcoma age standardised incidence rates (3-year rolling average)

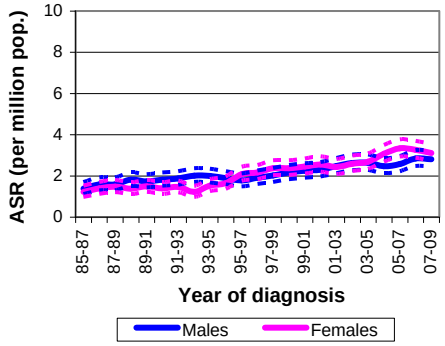


Figure 4.2b: Number of dermatofibrosarcomas diagnosed in each age group and sex

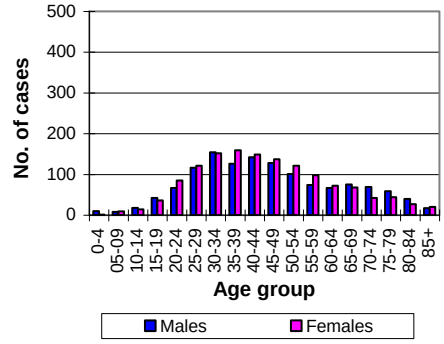


Figure 4.2c: Dermatofibrosarcoma age specific incidence rates (England: 1985–2009)

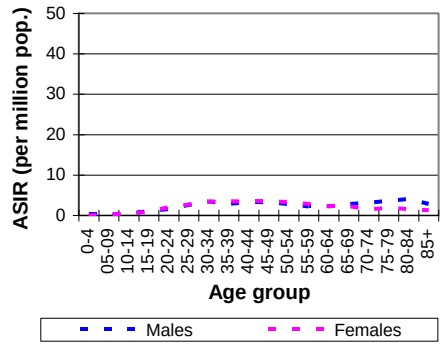


Figure 4.3a: Fibrosarcoma age standardised incidence rates (3-year rolling average)

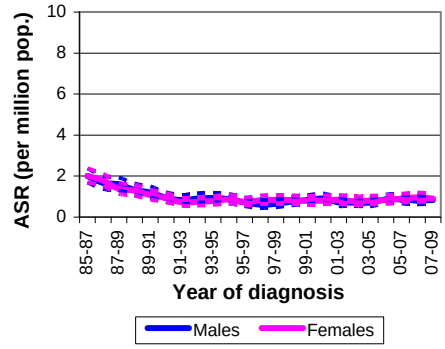


Figure 4.3b: Number of fibrosarcomas diagnosed in each age group and sex

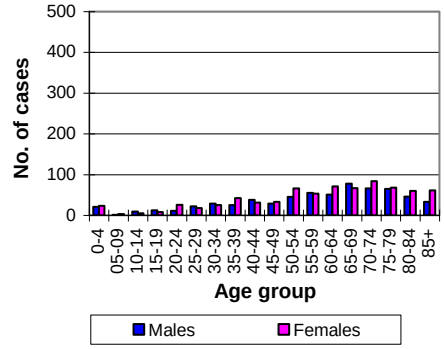


Figure 4.3c: Fibrosarcoma age specific incidence rates (England: 1985–2009)

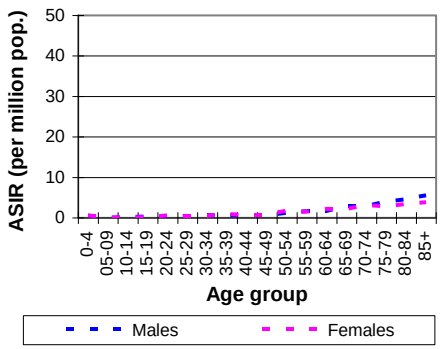


Figure 4.4a: Myxofibrosarcoma age standardised incidence rates (3-year rolling average)

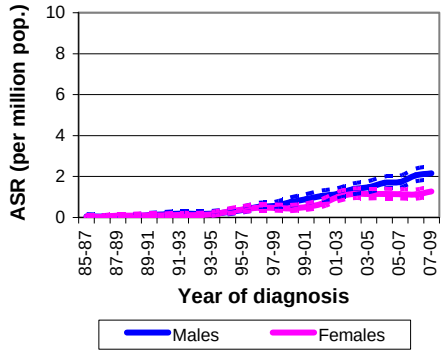


Figure 4.4b: Number of myxofibrosarcomas diagnosed in each age group and sex

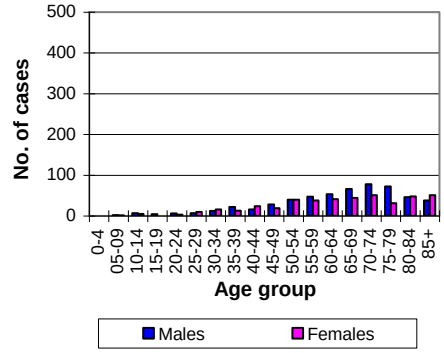
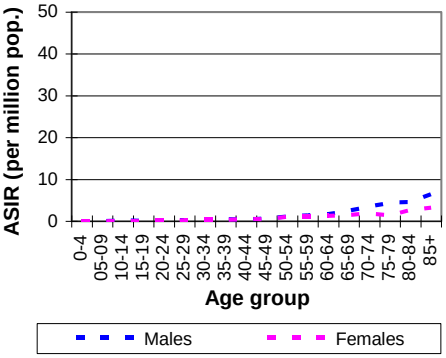


Figure 4.4c: Myxofibrosarcoma age specific incidence rates (England: 1985–2009)



4. Fibroblastic sarcoma

Dermatofibrosarcomas are exceptionally rare in patients aged under 15 years, with only 60 cases reported between 1985 and 2009 (Figure 4.2b). Unlike most other variants of soft tissue sarcoma, dermatofibrosarcoma rates appear to peak at 30 to 44 years. The age specific rate is bimodal in males, peaking at 30 to 49 years and at 80 years and over (Figure 4.2c) although there are relatively small numbers diagnosed in this age group.

4.2.3 Fibrosarcoma Incidence

The fibrosarcoma sub-group aggregates four distinct morphological sub-types: fibrosarcoma NOS (1,333), infantile fibrosarcoma, (33) inflammatory myofibroblastic tumour (9) and fascial fibrosarcoma (5). Fibrosarcomas NOS account for 97% of diagnoses in this sub-group.

Incidence rates of fibrosarcomas decreased significantly between 1985 and 2009, from 2.0 to 0.8 per million in males, and 2.0 to 0.9 per million in females (Figure 4.3a). There are no significant differences in the incidence rates in males and females. These decreases in incidence most probably result from changes in histopathology reporting; with a decrease into the use of the less precise term fibrosarcoma NOS being inversely correlated with the use of myxofibrosarcoma (see Section 4.2.2).

Fibrosarcoma age specific incidence rates show a small peak in children aged under 5 years (Figure 4.3b), due to the inclusion of infantile fibrosarcoma within this group[5]. Age specific rates for both males and females then increase gradually with increasing age (Figure 4.3c).

4.2.4 Myxofibrosarcoma Incidence

Many of the tumours that are now diagnosed and reported as myxofibrosarcoma were once diagnosed as myxoid fibrous histiocytoma. Historically, myxofibrosarcoma would have been recorded as MFH within the cancer registries (see Section 4.2.1). Myxofibrosarcomas now share a morphology code with fibromyxosarcoma (or low grade fibromyxoid sarcoma) although this term is no longer used.

Myxofibrosarcoma incidence rates increased significantly between 1985 and 2009 (Figure 4.4a), from 0.05 to 2.1 per million in males and 0.03 to 1.3 per million in females mainly because of changes in pathology reporting. The overall incidence rate appears to still be increasing, indicating that the true incidence rate of this type of sarcoma is not known for certain. From 2004 onwards, incidence rates in males were significantly higher than those in females.

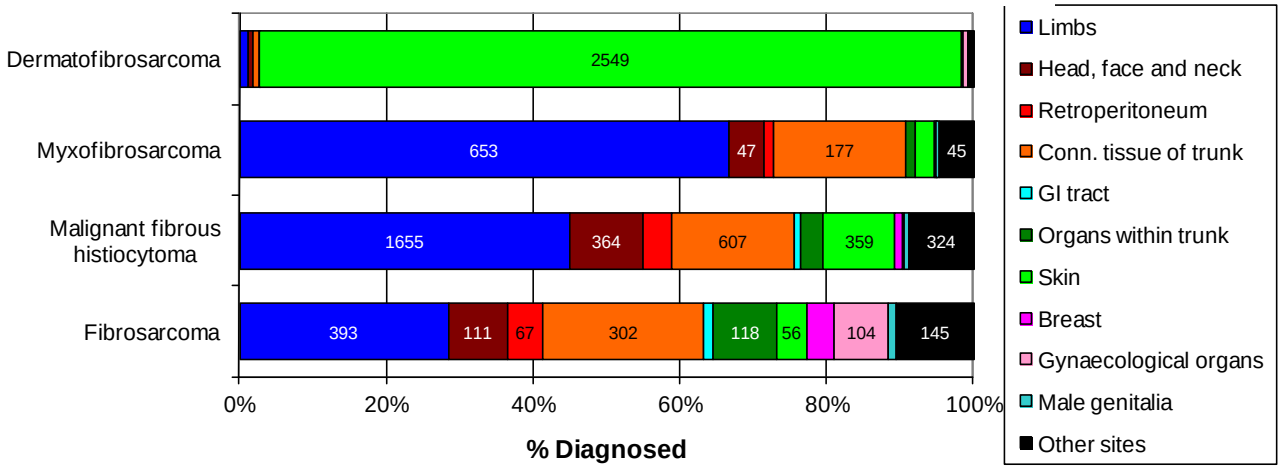
Myxofibrosarcomas are exceptionally rare in patients aged under 25 years, with only 28 cases reported between 1985 and 2009 (Figure 4.4b). Myxofibrosarcoma age specific incidence rates increase gradually with advancing age in both males and females (Figure 4.4c).

4.3 Variation in Fibroblastic Sarcoma Incidence with Anatomical Site

Fibroblastic sarcomas can arise at any anatomical site, but the distribution varies with histological sub-type (Figure 4.5). Dermatofibrosarcomas are almost exclusively confined to the skin (96%). Myxofibrosarcomas, MFH and fibrosarcomas most commonly arise in the limbs (67%, 45% and 28% respectively)[6].

4. Fibroblastic sarcoma

Figure 4.5: Fibroblastic sarcoma variants diagnosed in the most common anatomical sites (England: 1985–2009)



Myxofibrosarcomas also occur in the connective tissues of the trunk (18%) and the head, face and neck (5%), MFH in the connective tissues of the trunk (17%) and the skin (10%), and fibrosarcomas in the connective tissues of the trunk (22%), the organs within the trunk (9%), the head, face and neck (8%) and the gynaecological organs (8%).

4.4 Fibroblastic Sarcoma Survival

Figures 4.6 and 4.7 show 5-year relative survival rates for fibroblastic sarcomas in the most common anatomical sites and for each of the four fibroblastic sarcoma sub-groups. Overall 5-year relative survival rates and survival rates within each anatomical site increased significantly between 1985 and 2004 (Figure 4.6). As with other types of soft tissue sarcoma, tumours arising within the extremities tend to have higher 5-year relative survival rates (70%) than those arising in the trunk (fluctuates around 60%).

Figure 4.6: Fibroblastic sarcoma 5-year relative survival rates in the most common anatomical sites (5-year rolling average) (England: 1985–2004)

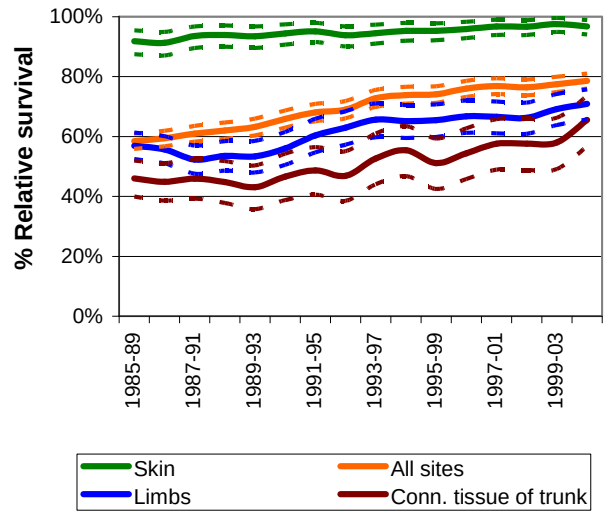
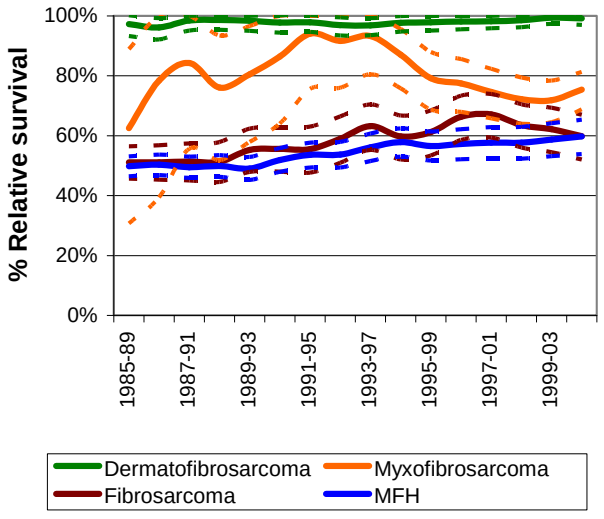


Figure 4.7: Fibroblastic sarcoma 5-year relative survival rates– variation with morphology (5-year rolling average) (England: 1985–2004)



4. Fibroblastic sarcoma

For patients diagnosed in 2000-2004, those with dermatofibrosarcoma have the highest 5-year relative survival rate at around 99%, and those with MFH the lowest at 60% (Figure 4.7). It is difficult to determine the true variations in survival for each morphological sub-type because of the changes in classification over the 25-year period studied. The MFH 5-year relative survival rate improved significantly, from 50% between 1985 and 1989, to 60% between 2000 and 2004. However, these increases will be distorted through the reclassification of high grade tumours such as myxofibrosarcoma which have relatively poor survival. The fibrosarcoma 5-year relative survival rate has also improved over the period of time studied (from 51% to 60%), although this increase is not statistically significant. This latter rate is the same as the rate reported by Pritchard, Soule, Taylor and Ivins (1974)[7].

The 5-year relative survival rate for myxofibrosarcoma oscillates between 1985 and 2004. This is also most likely to be due to classification changes over the time period; the decrease probably resulting from the increased contribution of high grade myxofibrosarcomas to the sub-group. The observed 5-year relative survival rate of 75% in patients diagnosed between 2000 and 2004 is consistent with the rate of 77% reported by Sanfilippo et al (2011)[8], based on 158 patients treated at an institution in Italy.

4.5 References

1. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 120. Geneva: WHO Press.

2. Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

3. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 122. Geneva: WHO Press.

4. Criscione, V. D. and Weinstock, M. A., 2007. Descriptive epidemiology of dermatofibrosarcoma protuberans in the United States, 1973-2002, *Journal of the American Academy of Dermatology*, 56 (6).

5. Chung, E. B. and Enzinger, F. M., 1976. Infantile fibrosarcoma. *Cancer*, 38 (2), 729-739.

6. Angervall, L., Kindblom, L.-G. and Merck, C., 1977. Myxofibrosarcoma. *Acta Pathologica*, 85a (2), 127-140.

7. Pritchard, D. J., Soule, E. H., Taylor, W. F. and Ivins, J. C., 1974. Fibrosarcoma: A clinicopathologic and statistical study of 199 tumours of the soft tissues of the extremities and trunk. *Cancer*, 33 (3), 888-897.

8. Sanfilippo, R., Miceli, R., Grosso, F., Fiore, M., Puma, E., Pennacchioli, E., Barisella, M., Sangalli, C., Mariani, L., Casali, P. G. et al, 2011. Myxofibrosarcoma: Prognostic factors and survival in a series of patients treated at a single institution. *Annals of Surgical Oncology*, 18 (3), 720-725.

5. Rhabdomyosarcoma

Key Facts

- **Most common anatomical sites of diagnosis: head, face and neck, soft and connective tissue of the trunk and limbs**
- **2,438 rhabdomyosarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 2 per million in 2007-2009**
- **Number diagnosed in 2008 and 2009: 91 and 100**
- **Sub-types:**
  - **Rhabdomyosarcoma NOS: 1,081 diagnosed 1985-2009**
  - **Embryonal rhabdomyosarcoma: 710 diagnosed 1985-2009**
  - **Alveolar rhabdomyosarcoma: 385 diagnosed 1985-2009**
  - **Pleomorphic rhabdomyosarcoma: 249 diagnosed 1985-2009**
  - **Mixed type, spindle cell and RMS with ganglionic differentiation: 13 diagnosed 1985-2009**

5.0 RHABDOMYOSARCOMA

Rhabdomyosarcomas (RMS) are sarcomas of the skeletal muscles. They are one of the rarer forms of soft tissue sarcoma, collectively accounting for approximately 4% of the total diagnosed in England between 1985 and 2009. Rhabdomyosarcomas account for 50% of all soft tissue sarcomas diagnosed in children less than 10 years of age. There are seven morphological variants of rhabdomyosarcoma in the WHO classification of bone and soft tissue sarcomas[1]. In this section, incidence and survival rates are presented separately for the three most common sub-groups, embryonic RMS, alveolar RMS and pleomorphic RMS. Incidence and survival rates for rhabdomyosarcoma NOS are reported along with mixed type RMS, spindle cell RMS and RMS with ganglionic differentiation, of which there were only 13 diagnoses between 1985 and 2009.

Table 5.1: Summary of rhabdomyosarcoma morphologies, anatomical sites, numbers and incidence rates

Name	ICD-O3 morphology code	Common anatomical sites of diagnosis	Number of tumours 1985-2009	Number of tumours 2008, 2009	Age-standardised incidence rate 2009 (per million)
Rhabdomyosarcoma NOS (plus aggregated rare types)	8900 (RMS NOS) 8902 (mixed type RMS) 8912 (spindle cell RMS) 8921 (RMS with ganglionic differentiation)	Head, face, neck: 21% Conn. tissue trunk: 19% Limbs: 17%	1,094	31, 42	0.9 (0.6, 1.2)
Embryonal RMS	8910 (Embryonal RMS)	Head, face, neck: 38% Conn. tissue trunk: 16% Limbs: 5%	710	26, 25	0.6 (0.4, 0.9)
Alveolar RMS	8920 (Alveolar RMS)	Head, face, neck: 31% Conn. tissue trunk: 21% Limbs: 21%	385	22, 24	0.5 (0.4, 0.8)
Pleomorphic RMS	8901 (Pleomorphic RMS)	Head, face, neck: 8% Conn. tissue trunk: 20% Limbs: 40%	249	12, 9	0.1 (0.1, 0.3)

5.1 Rhabdomyosarcoma Incidence

Between 1985 and 2009, 2,438 rhabdomyosarcomas were diagnosed in England, with an age standardised incidence rate of 1.94 per million in 2007-2009. Age

5. Rhabdomyosarcoma

standardised rates of rhabdomyosarcoma are higher in males (2.2 per million in 2007-2009) than females (1.7 per million in 2007-2009), but these sex specific differences are not statistically significant. The age-standardised incidence rate for all rhabdomyosarcomas has decreased significantly over the last 25 years, from 2.47 per million in 1985 to 1.94 per million in 2009. Rhabdomyosarcoma NOS is the most common diagnosis of rhabdomyosarcoma, accounting for 45% of diagnoses, with an age standardised incidence rate of 0.77 per million in 2007-2009.

5.2 Rhabdomyosarcoma Sub-groups

For the purpose of reporting incidence and survival rates, the seven variants of rhabdomyosarcoma were aggregated into four sub-groups (Table 5.1).

5.2.1 Rhabdomyosarcoma NOS Incidence

Rhabdomyosarcoma NOS accounts for 99% of the diagnoses in this sub-group. The remaining 1% consists of mixed type RMS, spindle cell RMS and RMS with ganglionic differentiation. The age standardised rate for rhabdomyosarcoma NOS decreased significantly between 1985 and 2009, from an incidence of 1.4 per million to 0.8 per million respectively. This most probably results from rhabdomyosarcoma NOS cases being given a more specific diagnosis such as pleomorphic or alveolar RMS. Age standardised incidence rates are higher in males than females, although these differences are not statistically significant. In 2007-2009, the age standardised incidence rates for males and females were 1.0 and 0.6 per million respectively (Figure 5.1a).

Tumours diagnosed as rhabdomyosarcoma NOS are uncommon in patients aged between 35 and 54 years (Figure 5.1b). The age specific incidence rates for rhabdomyosarcoma NOS also follow a bi-modal pattern, with higher incidence rates in both the youngest and the oldest age groups and the lowest incidence rates in the 35-39 to 50-54 year age groups (Figure 5.1c). While rates continue to increase in males aged over 80 years, female rates level off in those aged 70 years and over. These rates in elderly people may be a result of errors in coding. The bimodal incidence pattern probably reflects non-specific coding and/or reporting of diagnoses of embryonal RMS in the young, and pleomorphic RMS in the elderly.

5.2.2 Embryonal Rhabdomyosarcoma Incidence

Embryonal RMS is the second most common variant of RMS, accounting for approximately 30% of diagnoses between 1985 and 2009. Embryonal RMS resembles embryonic skeletal muscle in terms of biological and phenotypic features[2] and accounts for 26% of soft tissue sarcomas in children under 4 years old.

The age standardised incidence rate for embryonal RMS fluctuates around 0.8 cases per million and did not change significantly over the 25-year time period studied. Although embryonal RMS age standardised incidence rates in males are generally higher than those in females (0.5 per million and 0.3 per million respectively in 2006-2008, and 0.5 and 0.5 per million respectively in 2007-2009), the rates in males and females are not significantly different (Figure 5.2a). These incidence rates are somewhat lower than the rate of 1 per million reported by Toro et al (2006)[3]. The majority of embryonal RMS are diagnosed in patients less than 10 years of age, and these tumours are rarely diagnosed in patients aged 40 years and over, with only 44 cases reported between 1985 and 2009 (Figure 5.2b). Embryonal RMS age specific incidence rates peak in the 0-4 year age group and fall rapidly with increasing age (Figure 5.2c).

5. Rhabdomyosarcoma

Figure 5.1a: Rhabdomyosarcoma NOS age standardised incidence rates (3-year rolling average)

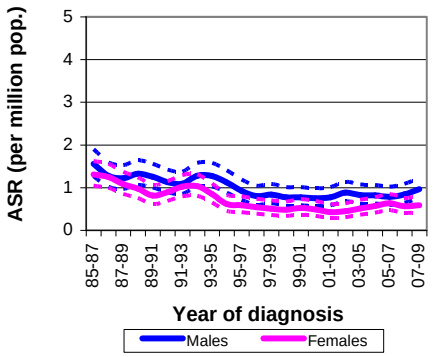


Figure 5.1b: Number of rhabdomyosarcoma NOS diagnosed in each age group and sex

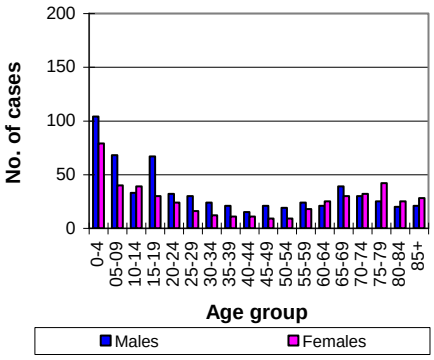


Figure 5.1c: Rhabdomyosarcoma NOS age specific incidence rates (England: 1985–2009)

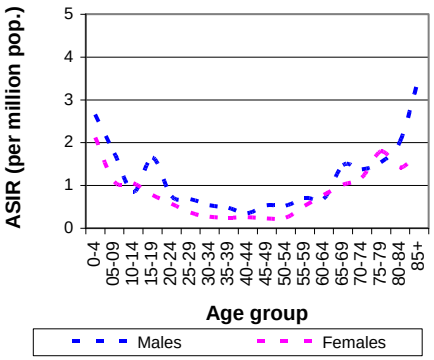


Figure 5.2a: Embryonal RMS age standardised incidence rates (3-year rolling average)

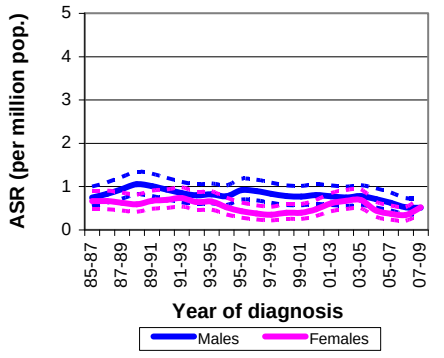


Figure 5.2b: Number of embryonal RMS diagnosed in each age group and sex

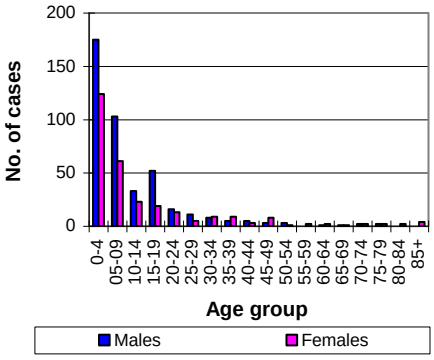


Figure 5.2c: Embryonal RMS age specific incidence rates (England: 1985–2009)

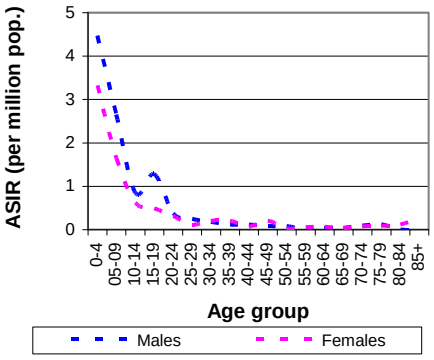


Figure 5.3a: Alveolar RMS age standardised incidence rates (3-year rolling average)

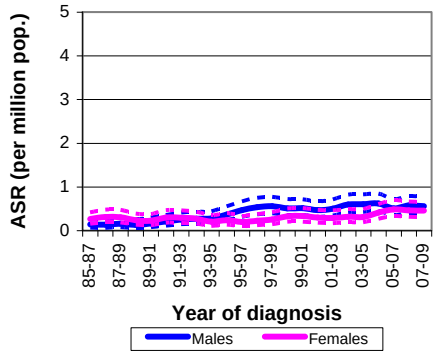


Figure 5.3b: Number of alveolar RMS diagnosed in each age group and sex

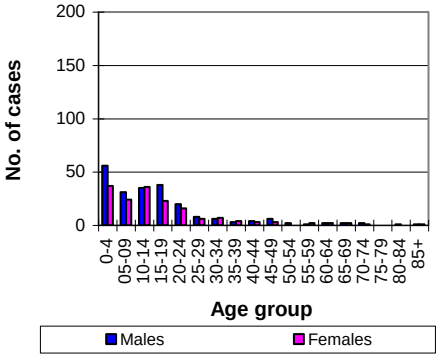


Figure 5.3c: Alveolar RMS age specific incidence rates (England: 1985–2009)

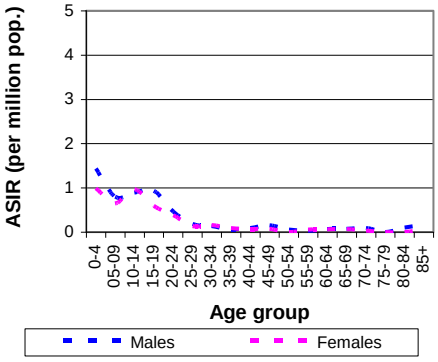


Figure 5.4a: Pleomorphic RMS age standardised incidence rates (3-year rolling average)

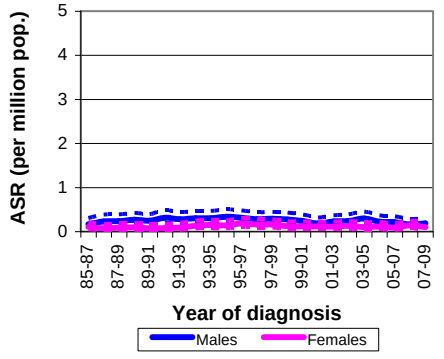


Figure 5.4b: Number of pleomorphic RMS diagnosed in each age group and sex

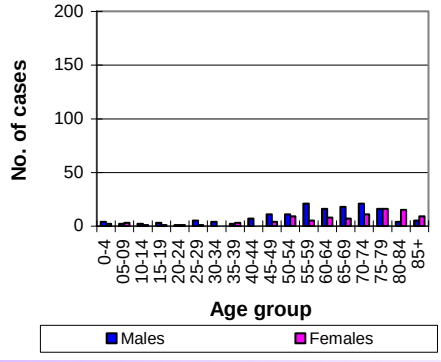
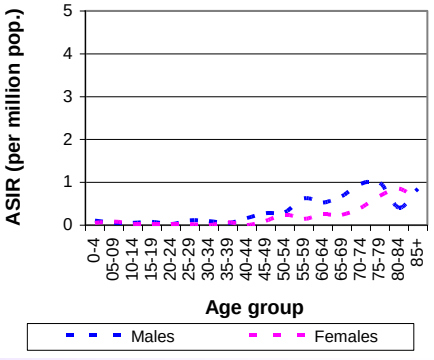


Figure 5.4c: Pleomorphic RMS age specific incidence rates (England: 1985–2009)



5. Rhabdomyosarcoma

5.2.3 Alveolar Rhabdomyosarcoma Incidence

Alveolar RMS resembles lymphoma[4] cytologically, and most commonly arises in children and adolescents. It is the third most common variant of RMS, accounting for approximately 16% of diagnoses between 1985 and 2009.

Alveolar RMS incidence rates increased significantly between 1985 and 2009, from 0.2 per million to 0.5 per million respectively (Figure 5.3a). This latter rate is similar to the 0.4 per million incidence rate reported by Toro et al (2006)[3] based on the SEER database. Alveolar RMS incidence rates do not vary significantly according to sex. Between 2007 and 2009 male and female incidence rates were 0.6 and 0.5 cases per million respectively.

Alveolar RMS are very rare in patients aged over 50 years, with only 19 cases in this age cohort between 1985 and 2009 (Figure 5.3b). Age specific incidence rates peak in patients aged under 5 years and 15-19 years and then fall rapidly with increasing age (Figure 5.3c).

5.2.4 Pleomorphic Rhabdomyosarcoma Incidence

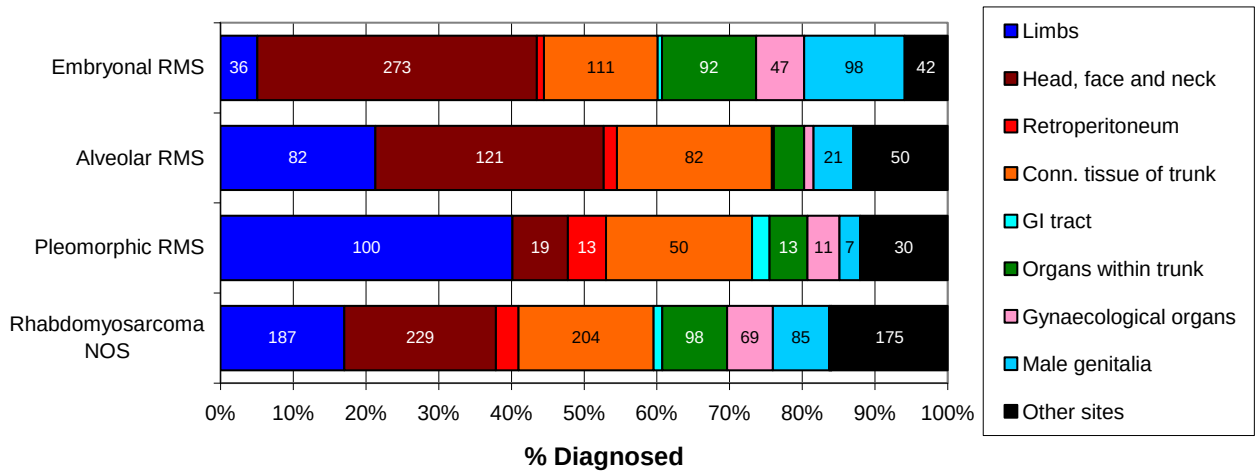
Pleomorphic RMS is a high grade sarcoma generally diagnosed in adults. It is the fourth most common variant of RMS, accounting for approximately 10% of diagnoses between 1985 and 2009.

The age standardised incidence rate for the pleomorphic RMS sub-group fluctuates around 0.2 per million and did not vary significantly over the 25-year time period studied. Although pleomorphic RMS age standardised incidence rates are generally higher in males than females (0.2 and 0.1 per million respectively in 2007-2009) they are not significantly different (Figure 5.4a). These incidence rates are very similar to the 0.2 per million incidence rate reported by Toro et al (2006)[3] based on the SEER database. Pleomorphic RMS is uncommon in patients aged 40 years and under, with 35 cases reported between 1985 and 2009 (Figure 5.4b).

Though overall sex-specific pleomorphic RMS rates are not significantly different, there is some variation in the incidence patterns for different age groups across men and women. Female age specific rates increase steadily between the ages of 45 and 80 years. Male age specific incidence rates peak in the 70-74 year age group (Figure 5.4c).

5.3 Variation in Rhabdomyosarcoma Incidence with Anatomical Site

Figure 5.5: Rhabdomyosarcoma variants diagnosed in the most common anatomical sites (England: 1985–2009)



5. Rhabdomyosarcoma

Rhabdomyosarcomas can arise within any anatomical site, but most commonly occur in the head, face and neck (26%), the connective and soft tissue of the trunk (18%) and the connective and soft tissue of the limbs (17%). The proportion of rhabdomyosarcomas diagnosed at each anatomical site varies with histological sub-type (Figure 5.5).

Embryonal RMS is most commonly diagnosed within the head, face and neck region (38%). It also occurs in connective and soft tissue of the trunk (16%), internal organs within the trunk (13%; the majority of which arise in the bladder) and within the male genitalia (14%). Unlike other variants of rhabdomyosarcoma, embryonal RMS is unlikely to arise in the connective and soft tissue of the limbs.

Alveolar RMS most commonly arises in the head, face and neck region (31%) and the connective and soft tissue of the trunk (21%). Unlike embryonal RMS, alveolar RMS also occurs in connective and soft tissue of the limbs (21%). Pleomorphic RMS, which tends to be diagnosed in more elderly patients, demonstrates a slightly different anatomical distribution, with 40% of tumours arising in the connective and soft tissue of the limbs and 20% in the connective and soft tissue of the trunk. Although the third most common site of diagnosis for pleomorphic RMS is the head, face and neck region (8%), occurrence at this site is much rarer than for other RMS variants.

Rhabdomyosarcoma NOS most commonly arises in the head, face and neck (21%), connective tissues of the trunk (19%) and the connective and soft tissue of the limbs (17%). It shows a more varied anatomical site distribution than the other RMS sub-types, being relatively common in the genital organs (14%) and the organs within the trunk (9%), and also having the highest percentage of tumours occurring at “other” sites (16%). This is likely to be due to the less specific coding of tumours in this morphology sub-group, in comparison to the embryonal, alveolar and pleomorphic RMS variants.

5.4 Rhabdomyosarcoma Survival

Figures 5.6 to 5.8 show 5-year relative survival rates for the four variants of rhabdomyosarcoma, and how 5-year relative survival rates vary with anatomical site and age group.

Figure 5.6: Rhabdomyosarcoma 5-year relative survival rates– variation with morphology (5-year rolling average) (England: 1985–2004)

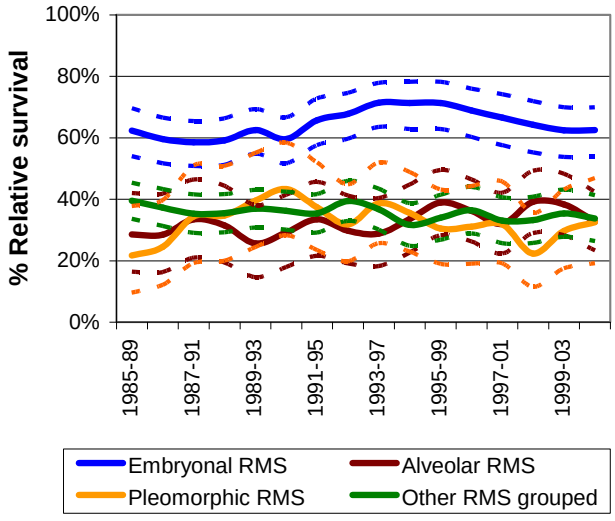
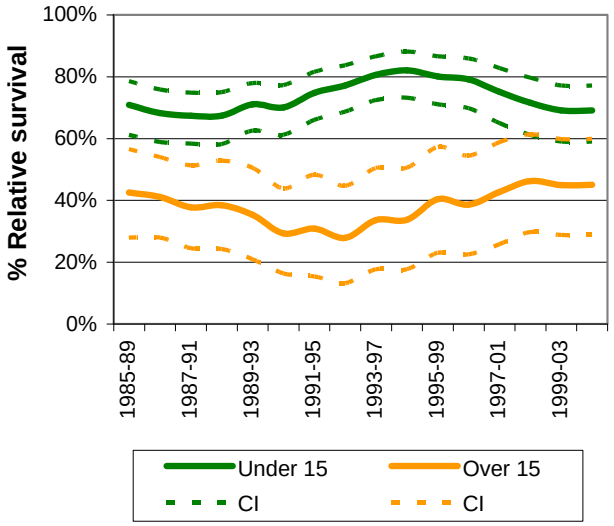
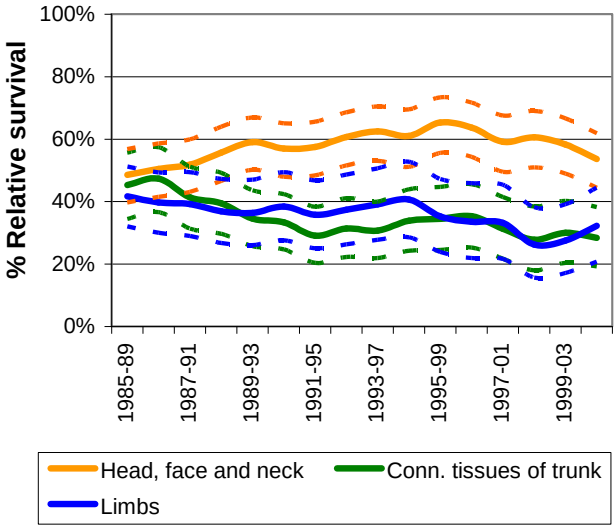


Figure 5.7: Embryonal Rhabdomyosarcoma 5-year relative survival rates– variation with age (5-year rolling average) (England: 1985–2004)



5. Rhabdomyosarcoma

Figure 5.8: Rhabdomyosarcoma 5-year relative survival rates in the most common anatomical sites (5-year rolling average) (England: 1985–2004)



With the exception of embryonal RMS, where the 5-year relative survival rates (60%) are significantly higher than those of the other three RMS variants, at 32%, the 5-year relative survival rates for patients with a diagnosis of RMS are amongst the poorest of all sarcoma sub-types (Figure 5.6). The 5-year relative survival rates observed for all four RMS histological sub-types did not improve across the time period studied. Age has a significant effect on embryonal RMS survival: 5-year relative survival rates are significantly higher amongst patients younger than 15 years old at diagnosis (70% compared with 45% for patients aged over 15 years; Figure 5.7). Embryonal RMS 5-year relative survival rates for patients younger than 20 years of age were 68% for patients diagnosed between 2000 and 2004. This is slightly lower the survival rate of 73% reported by Ognjanovic, Linabery, Charbonneau and Ross (2009)[5] for patients aged less than 20 years within the SEER database (1975 to 2005).

Five-year relative survival rates for patients with rhabdomyosarcomas arising in the head and neck region (54%) are significantly higher than for those with extremity (32%) or trunk (28%; Figure 5.8) tumours. Although these survival data are distorted by the fact that the majority of patients with rhabdomyosarcomas in the head and neck region are children, the results are consistent with previous reports: Simon, Paulino, Smith and Buatti (2002) found a 60% survival rate for all head and neck rhabdomyosarcomas[6] whereas Ghavimi, Mandell, Heller, Hajdu and Exelby (1989) found a 44% survival rate for extremity rhabdomyosarcomas[7].

5.5 References

1. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 141-154. Geneva: WHO Press.

2. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 146. Geneva: WHO Press.

5. Rhabdomyosarcoma

3. Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

4. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*. Geneva: WHO Press.

5. Ognjanovic, S., Linbery, A. M., Charbonneau, B. and Ross, J. A., 2009. Trends in childhood rhabdomyosarcoma incidence and survival in the United States (1975-2005). *Cancer*, 15 (18), 4218-4226.

6. Simon, J. H., Paulino, A. C., Smith, R. B. and Buatti, J. M., 2002. Prognostic factors in head and neck rhabdomyosarcoma, *Head & Neck*, 24 (5), 468-473.

7. Ghavimi, F., Mandell, L. R., Heller, G., Hajdu, S. I. and Exelby, P., 1989. Prognosis in childhood rhabdomyosarcoma of the extremity, *Cancer*, 64 (11), 2233-2237.

6. Ewing's sarcoma

Key Facts

- **Most common anatomical sites of diagnosis: brain (45%), connective and soft tissue of the trunk (15%) and in the limbs (12%)**
- **1,282 Soft Tissue Ewing's sarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 1.4 per million in 2007-2009**
- **Number diagnosed in 2008 and 2009: 61 and 69**
- **Sub-types:**
  - **Ewing's sarcoma: 438 diagnosed 1985-2009**
  - **Peripheral neuroectodermal tumour: 375 diagnosed 1985-2009**
  - **Primitive neuroectodermal tumour: 469 diagnosed 1985-2009**

6.0 SOFT TISSUE EWING'S SARCOMA

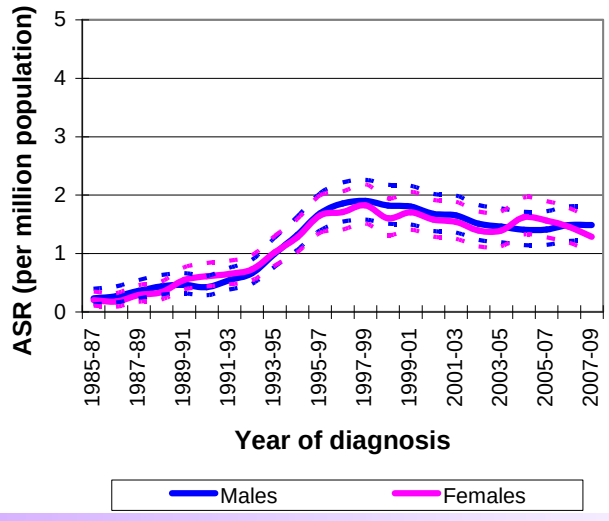
Ewing's sarcomas are round cell sarcomas which show varying degrees of neurodermal differentiation[1]. Though they occur at an equal rate within the bones and the soft tissue, the following analyses refer only to soft tissue sarcomas. For the purpose of the following analyses, the terms Ewing's sarcoma and pNET are used interchangeably as these tumours are discussed as a single entity in the WHO classification of bone and soft tissue sarcomas[1].

The soft tissue Ewing's sarcoma sub-group consists of three distinct morphological sub-types with very similar age profiles: Ewing's sarcoma which accounts for 34% of diagnoses, peripheral neuroectodermal tumour (29%) and primitive neuroectodermal tumour (37%). These sarcomas typically affect children rather than adults. It has been shown that Ewing's sarcomas and neuroectodermal tumours are clinically similar[2]. However, around 70% of primitive neuroectodermal tumours arise in the brain and central nervous system, so perhaps may not be considered sarcomas. They are included within the following analyses in line with the WHO classification system.

6.1 Ewing's Sarcoma/pNET Incidence

Between 1985 and 2009, 1,282 soft tissue Ewing's sarcomas were diagnosed in England. An average of 51 were diagnosed annually between 1985 and 2009, and 61 and 69 were diagnosed in 2008 and 2009 respectively.

Figure 6.1: Ewing's soft tissue sarcoma age standardised incidence rates (3-year rolling average) (England: 1985–2009)



6. Ewing's sarcoma

The incidence rates of soft tissue Ewing's sarcomas increased significantly during the 25 year time period studied (Figure 6.1). Advances in pathology may explain this significant increase. The chromosomal translocations which now identify Ewing's sarcomas (translocation t[11;22] and CD99) were not identified until the mid 1990's. Prior to this, Ewing's sarcomas may have been diagnosed as another round cell sarcoma type.

Ewing's soft tissue sarcoma incidence rates do not vary significantly according to sex. Over the 25-year period examined, the age standardised incidence rates in males and females increased from 0.2 per million to 1.5 per million and from 0.2 per million to 1.3 per million respectively. These rates are similar to the rate of 1.0 per million reported by Toro et al (2006)[3].

Ewing's sarcoma is most commonly diagnosed in patients under the age of 25 years (Figure 6.2)[4]. Age specific incidence rates decrease with age, and unlike Ewing's sarcoma of the bone, age specific rates do not vary according to sex (Figure 6.3).

Figure 6.2: Number of Ewing's soft tissue sarcoma diagnosed in each age group and sex (England: 1985–2009)

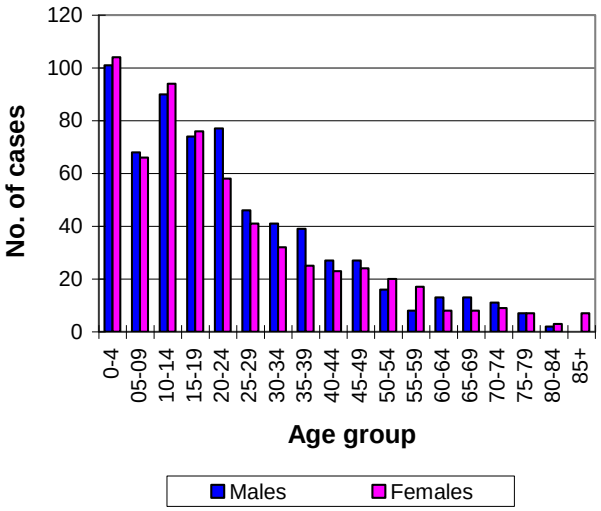
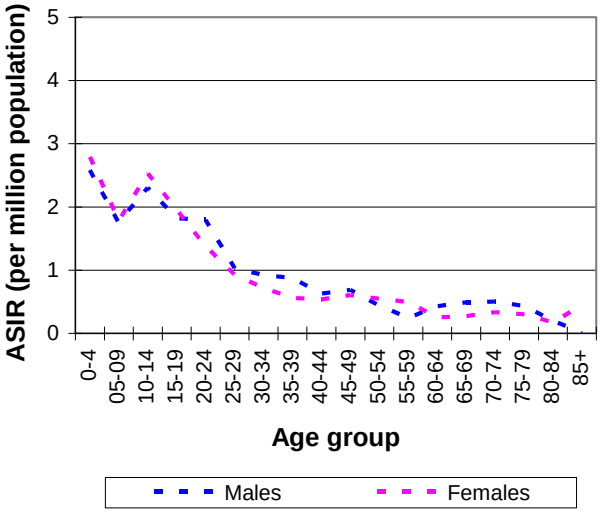


Figure 6.3: Ewing's soft tissue sarcoma age specific incidence rates (England: 1985–2009)



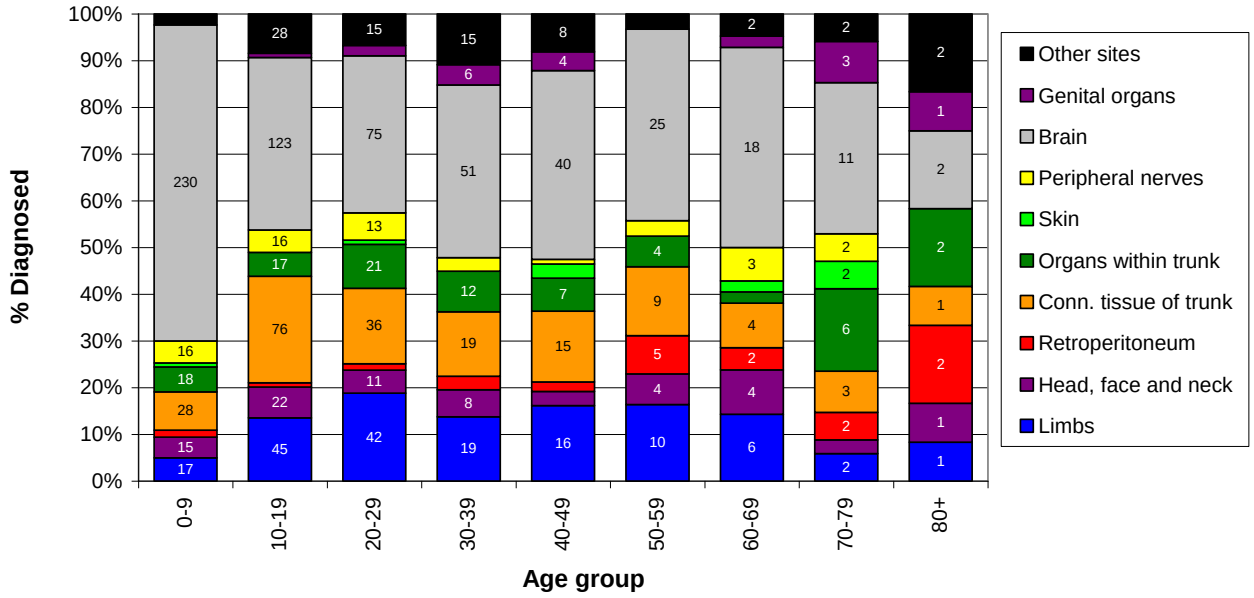
6.2 Variation in Ewing's Sarcoma/pNET Incidence with Anatomical Site

Forty five percent of soft tissue Ewing's sarcomas arise in the brain. These tumours are more likely to be a specific diagnosis of pNET (primitive/peripheral neuroectodermal tumours). Soft tissue Ewing's sarcomas also arise in other sites including the connective tissue of the trunk (15%) and the limbs (12%).

The proportion of soft tissue Ewing's sarcomas diagnosed at each anatomical site varies according to age, with the highest proportion of brain tumours arising in the youngest age group (0-9 years) (Figure 6.4). Soft tissue Ewing's sarcomas arise at other cancer sites across all the age groups, though Ewing's sarcomas of the brain continue to account for the greatest single proportion of tumours until the oldest age group (80 years and over). Sarcomas of the connective and soft tissue of the limbs and trunk also account for relatively high proportions of all soft tissue Ewing's sarcomas in patients under 60 years of age.

6. Ewing's sarcoma

Figure 6.4: Proportion of Ewing's sarcomas diagnosed in each age group and anatomical site (England: 1985–2009)



6.3 Ewing's Sarcoma/pNET Survival

There was no significant variation in the 5-year relative survival rates of soft tissue Ewing's sarcomas over the 25-year time period studied (Figure 6.5). In 1985-1989 the 5-year relative survival rate was 47%, and in 2000-2004 it was 41%. These 5-year relative survival rates are consistent with previously reported rates[2, 5].

Figure 6.5: Ewing's sarcoma 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

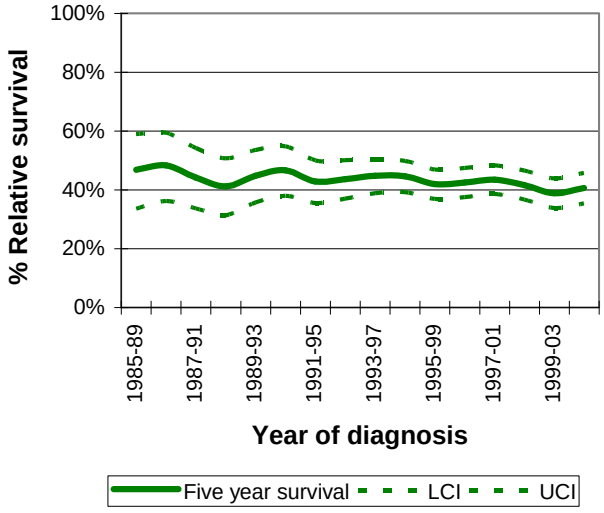
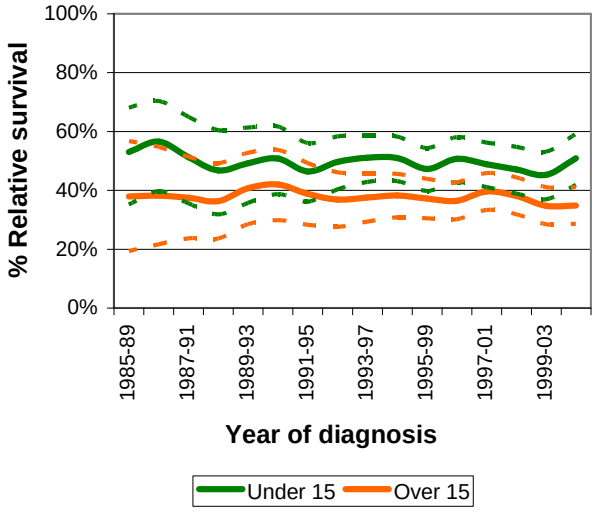


Figure 6.6: Ewing's sarcoma 5-year relative survival rates– variation with age (5-year rolling average) (England: 1985–2004)

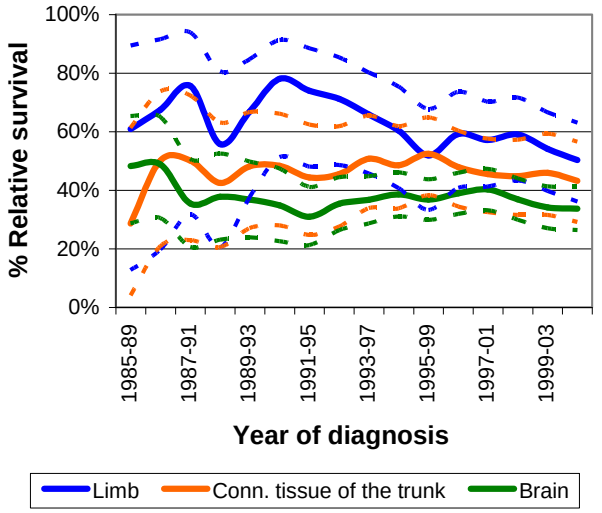


6. Ewing's sarcoma

Figure 6.6 shows how soft tissue Ewing's sarcoma 5-year relative survival rates vary with age at diagnosis. Previous studies have shown that age group (aged 15 years and above, and aged less than 15 years) is the strongest predictor of soft tissue Ewing's sarcoma survival[6]. However, in the present study, age had very little impact on the 5-year relative survival rates, with the difference between the two groups only becoming significant in the most recent diagnosis years (Figure 6.6).

The anatomical site of diagnosis also has very little impact on soft tissue Ewing's sarcoma 5-year relative survival rates. Five-year survival rates were slightly higher for Ewing's sarcomas diagnosed in the limbs and lowest for those diagnosed in the brain over the 25-year period studied (Figure 6.7), but these differences were not statistically significant. Ewing's sarcomas arising within the connective and soft tissue of the pelvis are usually associated with poor outcomes[7]. There is currently very limited published data with regards to primary sarcomas arising within the brain with which to compare these 5-year relative survival statistics, and most published articles tend to be case reports.

Figure 6.7: Ewing's sarcoma 5-year relative survival rates in the most common anatomical sites (5-year rolling average) (England: 1985 – 2004)



Important factors which could not be included within these analyses of soft tissue Ewing's sarcoma survival are the size of the tumour and whether metastases were present at the time of diagnosis. This information is not currently available, and further work is needed to investigate their impact.

6.4 References

1. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 298. Geneva: WHO Press.

2. Siebenrock, K. A., Nascimento, A. G. and Rock, M. G., 1996. Comparison of soft tissue Ewing's sarcoma and peripheral neuroectodermal tumour. *Clinical Orthopaedics & Related Research*, 329, 288-299.

3. Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

6. Ewing's sarcoma

4. Shimada, H., Newton, W. A., Soule, E. H., Qualman, S. J., Aoyama, C. and Maurer, H. M., 1988. Pathologic features of extraosseous Ewing's sarcoma: A report from the intergroup rhabdomyosarcoma study. *Human Pathology,* 19 (4), 442-453.

5. Rud, N. P., Reiman, H. M., Pritchard, D. J., Frassica, F. J. and Smithson, W. A., 1989. Extaosseous Ewing's sarcoma: A study of 42 cases. *Cancer*, 64 (7), 1548-1553.

6. Cotterill, S. J., Ahrens, S., Paulussen, M., Jurgens, H. F., Voute, P. A., Gadner, H. and Craft, A. W., 2000. Prognostic factors in Ewing's tumour of bone: Analysis of 975 patients from the European Intergroup Cooperative Ewing's Sarcoma Study Group. *Journal of Clinical Oncology,* 18 (17), 3108-3114.

7. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 300. Geneva: WHO Press.

7. Synovial sarcoma

Key Facts

- **Most common anatomical sites of diagnosis: connective and soft tissue of the limbs (65%) and the trunk (14%)**
- **1,318 synovial sarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 1.4 per million in 2007-2009**
- **Number diagnosed in 2008 and 2009: 76 and 60**
- **Sub-types:**
  - **Synovial sarcoma NOS: 1,107 diagnosed 1985-2009**
  - **Synovial sarcoma, biphasic: 123 diagnosed 1985-2009**
  - **Synovial sarcoma, spindle cell: 82 diagnosed 1985-2009**
  - **Synovial sarcoma, epithelioid cell: 6 diagnosed 1985-2009**

7.0 SYNOVIAL SARCOMA

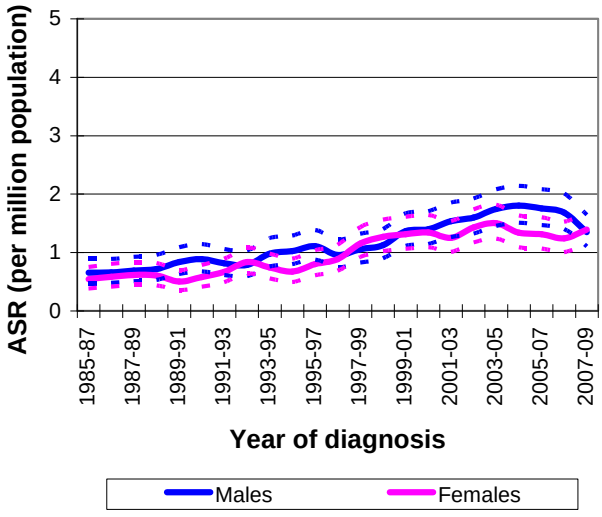
Synovial sarcomas are clinically and genetically distinct mesenchymal spindle cell tumours with variable epithelioid differentiation[1]. As a consequence it has been recommended that these tumours be renamed either carcinosarcoma or spindle cell carcinoma of soft tissue. There are no known factors predisposing patients to synovial sarcoma.

For the purposes of this report, four distinct morphological sub-types of synovial sarcoma, synovial sarcoma NOS, synovial sarcoma biphasic, synovial sarcoma: spindle cell and synovial sarcoma: epithelioid cell, all of which have similar age and anatomical site profiles[1], have been aggregated in the synovial sarcoma sub-group. Synovial sarcoma NOS accounts for 84% of diagnoses in the synovial sarcoma sub-group.

7.1 Synovial Sarcoma Incidence

In the present study, synovial sarcomas account for 2% to 3% of all soft tissue sarcomas diagnosed annually, slightly lower than the 5% to 10% stated in the WHO classification of soft tissue sarcomas[1].

Figure 7.1: Synovial sarcoma age standardised incidence rates (3-year rolling average) (England: 1985–2009)



7. Synovial sarcoma

Between 1985 and 2009, 1,318 synovial sarcomas were diagnosed in England. An average of 53 tumours were diagnosed annually between 1985 and 2009, and 76 and 60 were diagnosed in 2008 and 2009 respectively. There is no significant difference between the age standardised rates in males and females (Figure 7.1). Between 1985 and 2009 the synovial sarcoma age standardised incidence rate increased from 0.7 per million to 1.4 per million in males, and from 0.5 per million to 1.4 per million in females, with the most significant increases observed from 1997 onwards. The incidence rates seen in the most recent years are very similar to the incidence rate of 1.1 per million reported by Toro et al (2006)[2].

Synovial sarcoma is rarely diagnosed in patients under the age of 10 years, with only 25 cases reported between 1985 and 2009 (Figure 7.2). The greatest number of synovial sarcomas occurred in males aged 30-34 years, and the highest age specific rates were also observed in this age group. This is slightly older than the median age of 19 years for synovial sarcoma of the neck reported by Roth et al (1975)[3], although this study was based on a very small sample of 24 patients whose biopsies were carried out at the US Armed Forces Institute of Pathology. More recently, Okcu et al (2003)[4] reported an age standardised incidence rate of 0.7 per million in children and adolescents based on a sample of 219 children treated in four institutions in the US, Germany and Italy. This is similar to the rates seen in the present study for the younger age groups. Unlike the incidence rates for other sarcoma variants, which increase with age, the age specific rates for synovial sarcoma remain uniform from the age of 15 years onwards (Figure 7.3).

Figure 7.2: Number of synovial sarcomas diagnosed in each age group and sex (England: 1985–2009)

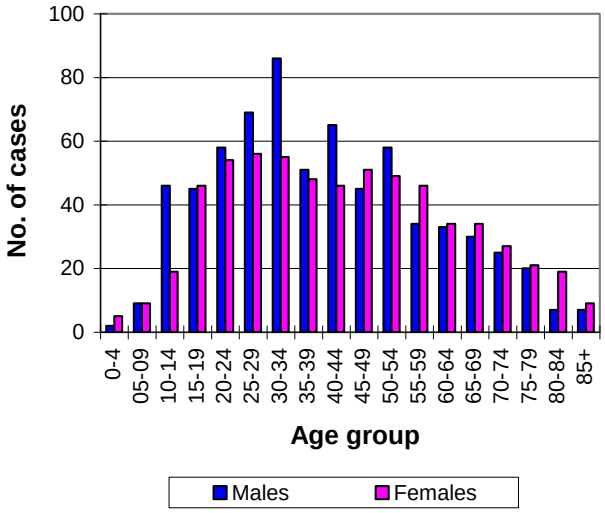
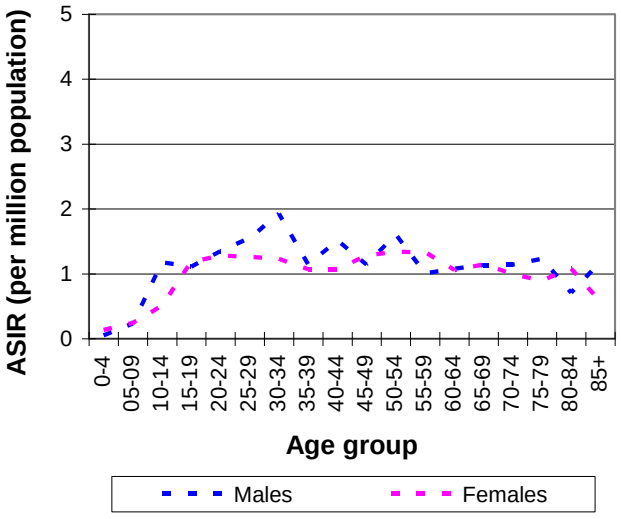


Figure 7.3: Synovial sarcoma age specific incidence rates (England: 1985–2009)

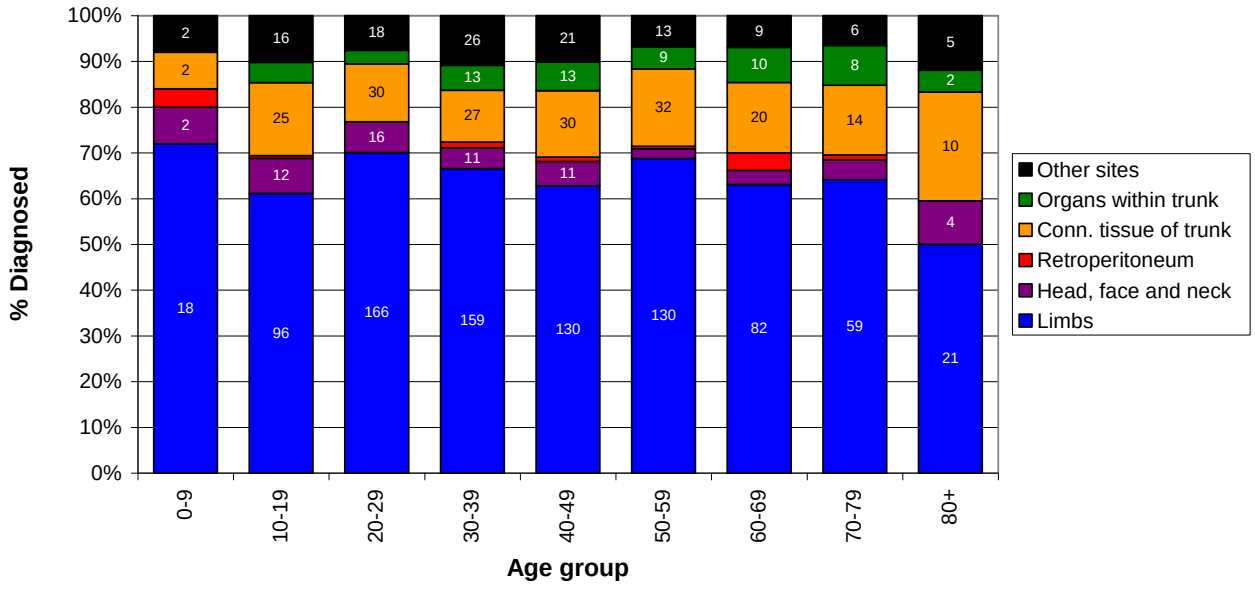


7.2 Variation in Synovial Sarcoma Incidence with Anatomical Site

Synovial sarcomas are most commonly diagnosed in the limbs (65%) and connective and soft tissue of the trunk (14%) (Figure 7.4). These proportions vary somewhat from those reported by Wright, Sim, Soule and Taylor (1982)[5], who found 94% in the extremities and 6% in the trunk, based on patients observed within one treatment centre. A small proportion of synovial sarcomas arise at other sites including the head, face and neck (5%) and internal organs (5%). The anatomical sites of diagnosis do not vary with age group.

7. Synovial sarcoma

Figure 7.4: Proportion of synovial sarcomas diagnosed in each age group and anatomical site (England: 1985–2009)



7.3 Synovial Sarcoma Survival

There was no significant variation in the 5-year relative survival rates for synovial sarcoma over the 25-year time period studied (Figure 7.5). The 5-year relative survival rate was 56% for patients diagnosed between 1985 and 1989, and 57% in the most recent diagnosis years (2000-2004). These rates are consistent with previously reported findings[6,7,8]. From 1993 onwards, 5-year relative survival rates were significantly higher for patients less than 30 years of age when compared to patients aged 30 years and over (74% and 50% respectively in 2000-2004) (Figure 7.6).

Figure 7.5: Synovial sarcoma 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

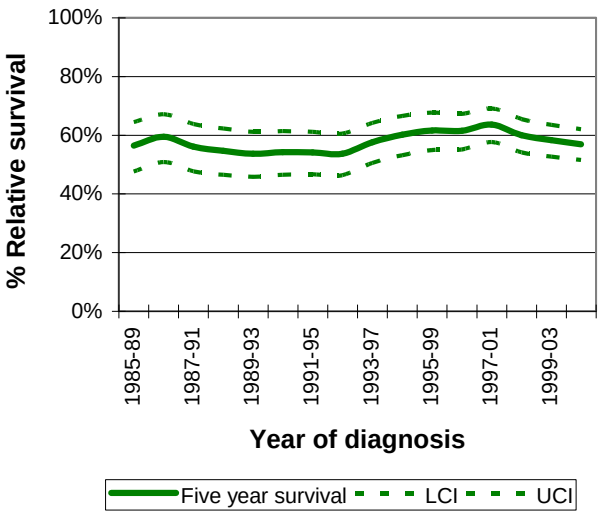
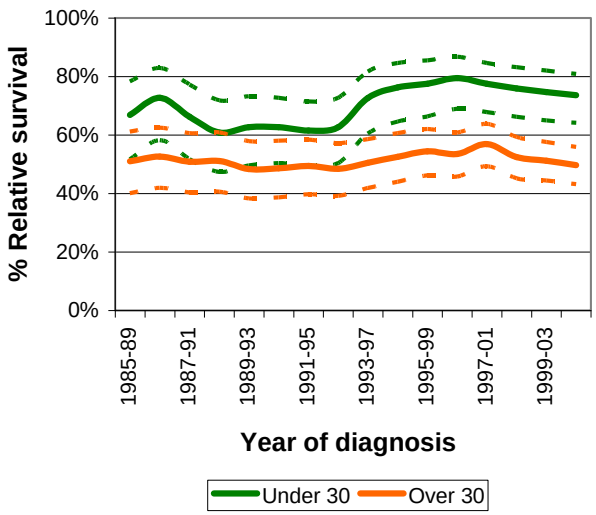


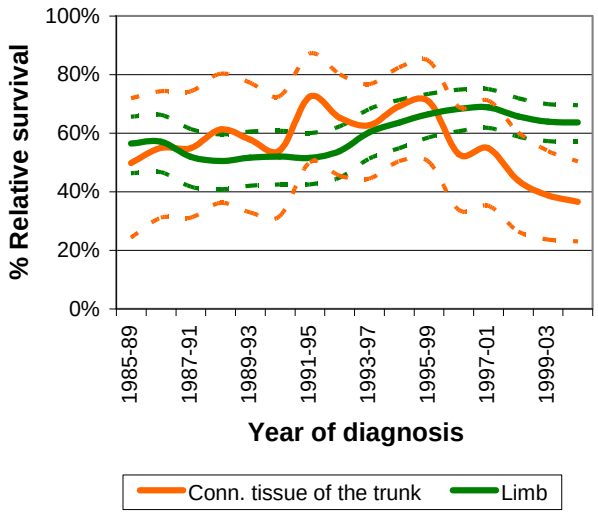
Figure 7.6: Synovial sarcoma 5-year relative survival rates– variation with age (5-year rolling average) (England: 1985–2004)



7. Synovial sarcoma

Five-year relative survival rates did not vary with the anatomical site for the majority of the 25-year period examined (Figure 7.7). However, in the most recent diagnosis years, 5-year relative survival rates for synovial sarcomas in the connective tissue of the limbs were significantly higher than those in the trunk (64% and 37% respectively in 2000-2004). The survival rates reported for the limbs in the present report are somewhat lower than those reported by Lewis et al (2000), who found a 75% survival rate for 112 patients with extremity synovial sarcoma[9]. Unlike other variants of sarcoma, such as liposarcoma and leiomyosarcoma, 5-year relative survival rates have not improved over the 25-year period studied.

Figure 7.7: Synovial sarcoma 5-year relative survival rates in the most common anatomical sites (5-year rolling average) (England: 1985–2004)



7.4 References

1. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 200. Geneva: WHO Press.

2. Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

3. Roth, J. A., Enzinger, F. M. and Tannenbaum, M., 1975. Synovial sarcoma of the neck: A follow-up study of 24 cases. *Cancer*, 35 (4), 1243-1253.

4. Okcu, M. F., Munsell, M., Treuner, J., Mattke, A., Pappo, A., Cain, A., Ferrari, A., Casanova, M., Ozkan, A. and Raney, B., 2003. Synovial sarcoma of childhood and adolescence: A multicenter, multivariate analysis of outcome. *Journal of Clinical Oncology*, 21 (8), 1602-1611.

5. Wright, P. H., Sim, F. H., Soule, E. H. and Taylor, W. F., 1982. Synovial sarcoma. *The Journal of Bone and Joint Surgery,* 64 (1), 112-122.

6. Bergh, P., Meis-Kindbolm, J. M., Gherlinzoni, F., Berlin, O., Bacchini, P., Bertoni, F., Gunterberg, B. and Kindbolm, L.-G., 1999. Synovial sarcoma: Identification of low and high risk groups. *Cancer*, 85 (12), 2596-2607.

7. Synovial sarcoma

7. Spillane, A. J., A'Hern, R., Judson, I. R., Fisher, C. and Thomas, J. M., 2000. Synovial sarcoma: A clinicopathologic, staging and prognostic assessment. *Journal of Clinical Oncology*, 18 (22), 3794-3803.

8. MacKenzie, D. H., 1966. Synovial sarcoma: A review of 58 cases. *Cancer*, 19 (2), 169-180.

9. Lewis, J. J., Antonescu, C. R., Leung, D. H. Y., Blumberg, D., Healey, J. H., Woodruff, J. M. and Brennan, M. F., 2000. Synovial sarcoma: A multivariate analysis of prognostic factors in 112 patients with primary localised tumours of the extremity. *Journal of Clinical Oncology,* 18 (10), 2087-2094.

8. Vascular sarcoma

Key Facts

- **Most common anatomical sites of diagnosis: organs within the trunk, head, face and neck, breasts and limbs**
- **2,050 vascular sarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 1.7 per million in 2007-2009**
- **Number diagnosed in 2008 and 2009: 125 and 116**
- **Sub-types:**
  - **Haemangiosarcoma: 1,808 diagnosed 1985-2009**
  - **Lymphangiosarcoma: 35 diagnosed 1985-2009**
  - **Haemangioendothelioma: 119 diagnosed 1985-2009**
  - **Epithelioid haemangioendothelioma: 88 diagnosed 1985-2009**

8.0 VASCULAR SARCOMA

Vascular sarcomas develop from endothelial cells in either the lymphatic vessels or the blood vessels. In most instances it is impossible to establish whether the tumour originated from the blood vessel endothelium (haemangiosarcoma) or from the vascular endothelium (lymphangiosarcoma)[1]. Kaposi's sarcomas are also vascular tumours, but these are presented separately in Section 9 due to their very different biology and incidence patterns.

Vascular sarcomas account for only 3% of all soft tissue sarcomas diagnosed in England between 1985 and 2009. Vascular sarcomas are very rarely diagnosed in children and tend to be relatively more common in elderly patients. Four different morphological sub-type variants (excluding Kaposi's sarcoma) exist within the WHO classification of bone and soft tissue sarcomas. For analysis purposes vascular sarcomas are divided into two sub-groups: angiosarcoma, comprised of haemangiosarcoma and lymphangiosarcoma, and haemangioendothelioma, comprised of haemangioendothelioma and epithelioid haemangioendothelioma.

Table 8.1: Summary of vascular sarcoma morphologies, anatomical sites, numbers and incidence rates

Name	ICD-03 morphology code	Common anatomical sites of diagnosis	Number of tumours 1985-2009	Number of tumours 2008, 2009	Age-standardised incidence rate 2009 (per million)
Angiosarcoma	9120 (haemangiosarcoma) 9170 (lymphangiosarcoma)	Head, face, neck: 22% Organs of trunk: 16% Breast: 16%	1,843	109, 109	1.5 (1.3, 1.9)
Haemangioendothelioma	9130 (haemangioendothelioma) 9133 (epithelioid haemangioendothelioma)	Head, face, neck: 10% Organs of trunk: 45% Breast: 0%	207	16, 7	0.1 (0.1, 0.3)

8.1 Vascular Sarcoma Incidence

Between 1985 and 2009, 2,050 vascular sarcomas were diagnosed in England, with an age standardised incidence rate of 1.7 per million persons in 2007 to 2009. Incidence rates increased significantly between 1985 and 2009, from 1.0 in 1985 to 1987, to 1.7 in 2007 to 2009. Rates do not vary significantly between males and females. Angiosarcomas are the most commonly diagnosed form of vascular sarcoma, accounting for 90% of

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diagnoses with an age standardised incidence rate of 1.5 per million in 2007 to 2009.

8.2 Vascular Sarcoma Sub-groups

For the purpose of reporting incidence and survival rates, the four variants of vascular sarcoma were aggregated into two sub-groups (Table 8.1).

Figure 8.1a: Angiosarcoma age standardised incidence rates (3-year rolling average)

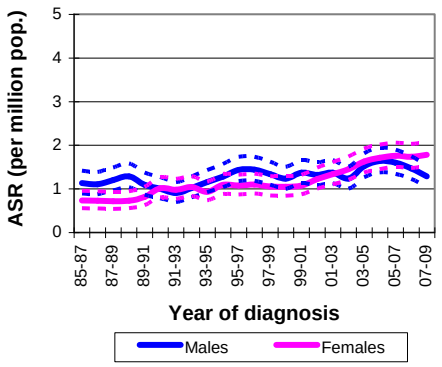


Figure 8.1b: Number of angiosarcomas diagnosed in each age group and sex

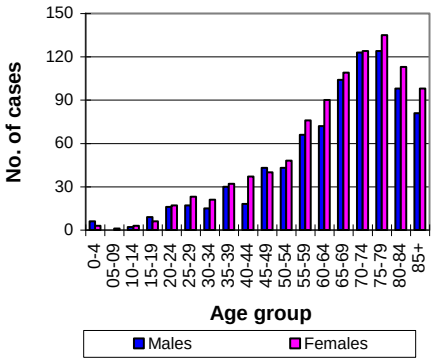


Figure 8.1c: Angiosarcoma age specific incidence rates (England: 1985–2009)

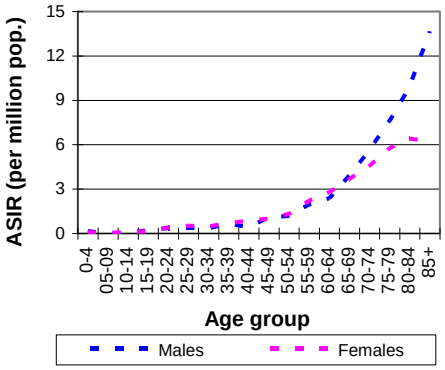


Figure 8.2a: Haemangioendothelioma age standardised incidence rates (3-year rolling average)

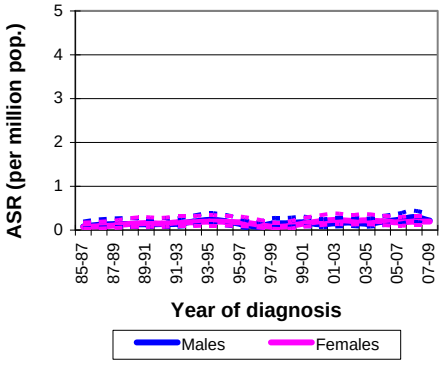


Figure 8.2b: Number of haemangioendotheliomas diagnosed in each age group and sex

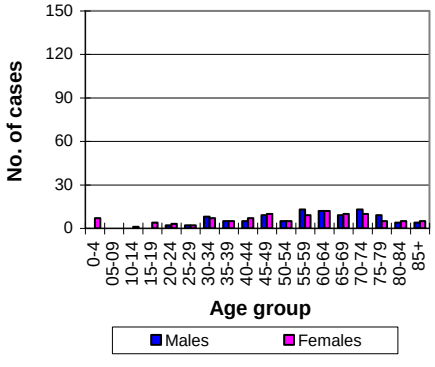
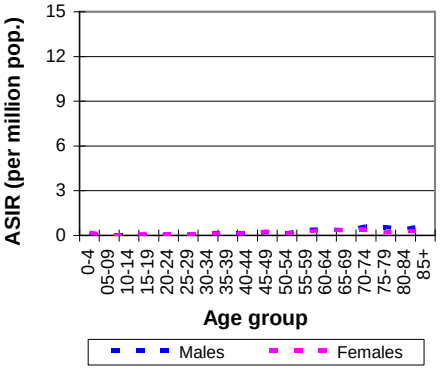


Figure 8.2c: Haemangioendothelioma age specific incidence rates (England: 1985–2009)



8.2.1 Angiosarcoma Incidence

The angiosarcoma sub-group aggregates two separate sub-types: haemangiosarcoma and lymphangiosarcoma. Haemangiosarcomas account for 98% of the diagnoses in this sub-group, although in most cases it is not possible to determine whether the true origin of the tumour was a blood vessel or a lymphatic vessel.

The age standardised incidence rate of angiosarcomas increased significantly between 1985 and 2009, from 0.9 per million in 1985 to 1987 to 1.5 per million in 2007 to 2009 (Figure 8.1a). The latter rate is comparable to the rate of 2.1 per million reported by Toro et al (2006)[2]. There were no significant differences between the age standardised angiosarcoma incidence rates for males and females. However, the angiosarcoma age standardised incidence rate

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in females in 2000-2004 was significantly above the rate in 1985-1987 while incidence rates in males have not increased significantly over this time period.

It has been suggested that the number of women diagnosed with angiosarcoma of the breast is increasing due to the greater number of women undergoing radiotherapy following breast conserving surgery as part of their treatment for a breast carcinoma[3]. Further examination of the current cohort found that, of the 365 patients who were recorded as having had a breast angiosarcoma, 184 (50%) had had a previous breast carcinoma diagnosis. Of these 184 women, 133 (72%) were recorded as having been treated with radiotherapy. The number of women diagnosed with an angiosarcoma who had a previous breast carcinoma is likely to be an underestimate because the 4-7[3] year time lag between breast irradiation and angiosarcoma development. This means that women diagnosed in the earlier years of the 1985-2009 period studied could have had a breast carcinoma prior to 1985. This interpretation is supported by the finding that significantly more women diagnosed with angiosarcomas in the most recent years had a previous breast carcinoma recorded. Further work is thus required to determine the true rate of angiosarcomas diagnosed after breast carcinomas.

Angiosarcomas are rarely diagnosed in patients under the age of 20 years, with only 30 cases reported between 1985 and 2009. The number of cases increases gradually with age in males and females, peaking in the 70-79 age group (Figure 8.1b). In males, angiosarcoma age specific incidence rates increase markedly with age from the 60-64 year age group onwards. In females, rates increase more gradually, levelling off from the age of 75 years (Figure 8.1c). In the over 85 year age group, consistent with previous findings[4], the male age specific incidence rate is over double that seen in females.

8.2.2 Haemangioendothelioma Incidence

The haemangioendothelioma sub-group consists of two distinct types of sarcoma: haemangioendothelioma and epithelioid haemangioendothelioma. Haemangioendotheliomas account for 58% of the diagnoses in this category. In the past, the term haemangioendothelioma has been applied to describe tumours of benign, intermediate and malignant behaviour. Only the “Composite” haemangioendothelioma of uncertain behaviour, and the malignant epithelioid haemangioendothelioma, are discussed in the WHO classification of bone and soft tissue sarcomas[5] and therefore only these are included in the present study.

The age standardised incidence rate of haemangioendotheliomas fluctuated around 0.16 per million and did not vary significantly over the 25-year time period studied. Although haemangioendothelioma age standardised incidence rates in males appear higher than those in females (0.22 per million and 0.19 per million respectively in 2007-2009) the incidence rates are not significantly different (Figure 8.2a). Haemangioendotheliomas are very rarely diagnosed in patients aged under 20 years of age, with only 12 cases diagnosed between 1985 and 2009. There were no cases diagnosed in males less than 15 years of age (Figure 8.2b). Age specific incidence rates are similar in males and females (Figure 8.2c).

8.3 Variation in Vascular Sarcoma Incidence with Anatomical Site

Vascular sarcomas can arise within any anatomical site in the body, but most commonly occur within the connective tissue of the head, face and neck (21%), the organs within the trunk (19%), the limbs (14%) and the breasts (14%) (Figure 8.3). Anatomical sites of diagnosis vary with tumour type, sex and age, with a greater proportion of angiosarcomas occurring in the breast and a greater proportion of haemangioendotheliomas occurring in the organs within the trunk.

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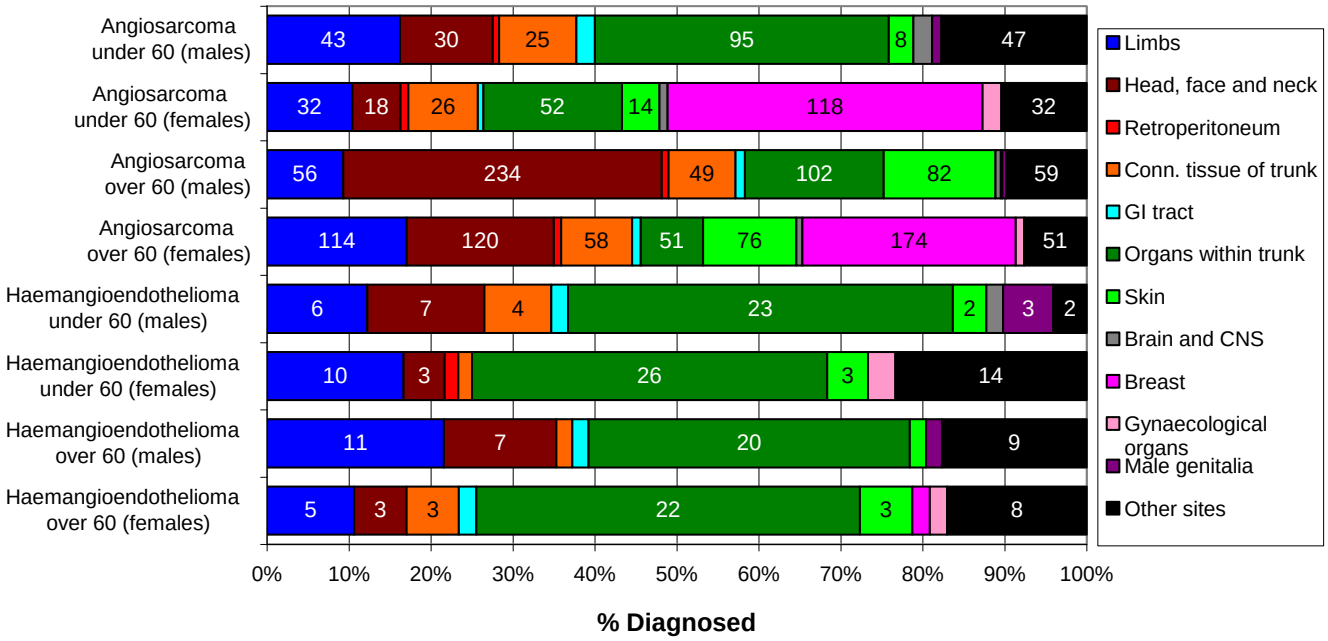
Figure 8.3: Vascular sarcoma variants diagnosed in the most common anatomical sites, by age and sex (England: 1985–2009)



Angiosarcoma patients less than 60 years of age are more predisposed to tumours in the organs within the trunk (26%; 12% in those aged 60 years and over) and the breasts (21%; 14% in those aged 60 years and over). Male patients aged 60 years and over have a higher proportion of tumours in the head, face and neck region (39%; 11% in men aged under 60 years). There are also some similarities between patients in both age groups, particularly with regard to tumours arising in the connective tissue in the trunk (9% and 8%), and in the connective tissue of the limbs (13% for both age groups). These results are somewhat different from a study by Fayette et al (2007)[6] who reported that 35% of the angiosarcomas in their cohort of 161 patients treated at three French hospitals were diagnosed in the breast, 20% in the skin and 13% in the soft tissues.

The anatomical sites of diagnosis for haemangioendotheliomas do not vary with age, with similar proportions of tumours occurring across all sites. The organs within the trunk were the most common site in both age groups, accounting for 45% in those aged under 60 years and 43% in those aged 60 years and above. The proportion of limb (15% and 16%), head, face and neck (9% and 10%), connective tissue of the trunk (5% and 4%) and skin (5% and 4%) haemangioendotheliomas diagnosed in the two age groups were also very similar.

8.4 Vascular Sarcoma Survival

Figures 8.4 to 8.6 show the overall 5-year relative survival rates for the two vascular sarcoma sub-groups, and how the 5-year relative survival rates of angiosarcomas vary with anatomical site. The survival curve for organs within the trunk is depicted by a fuzzy line, as it is based on fewer than ten cases.

8. Vascular sarcoma

Figure 8.4: Angiosarcoma 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

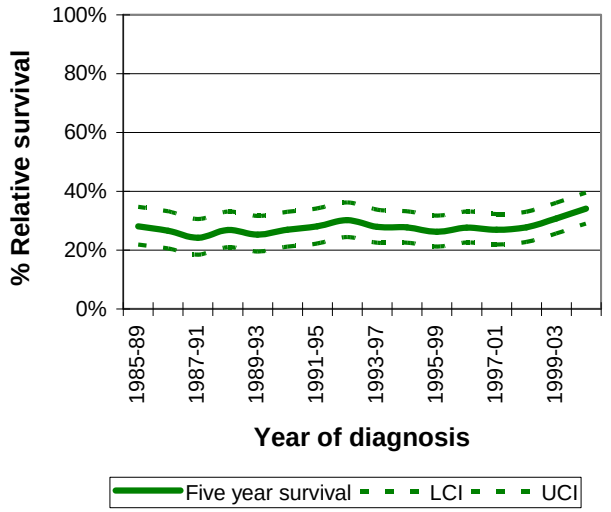


Figure 8.5: Haemangioendothelioma 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

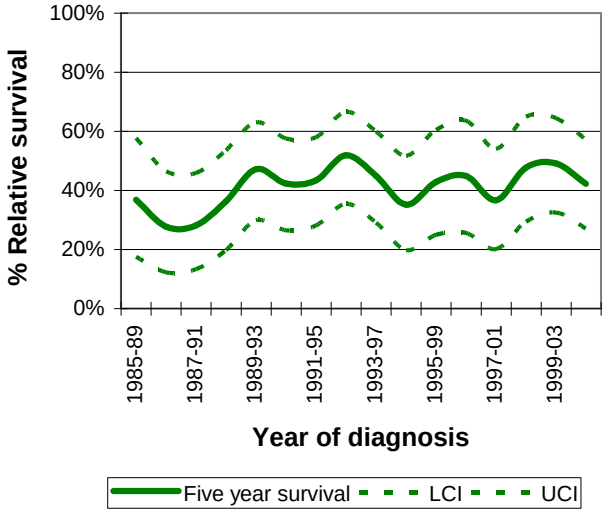
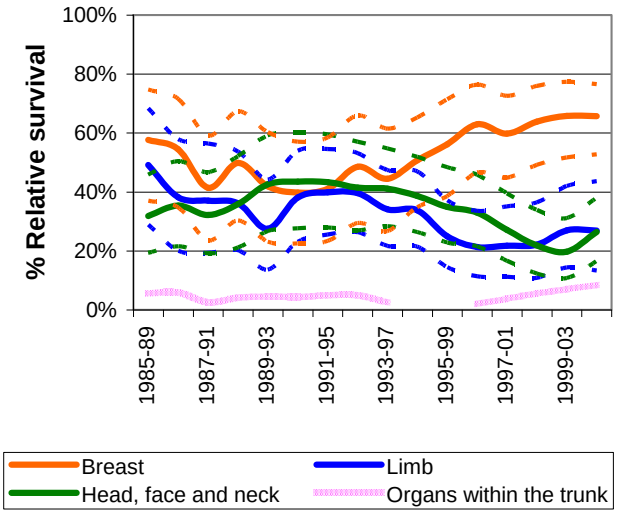


Figure 8.6: Angiosarcoma 5-year relative survival rates in the most common anatomical sites (5-year rolling average) (England: 1985–2004)



Five-year relative survival rates of patients with a diagnosis of angiosarcoma are amongst the poorest across all sarcoma sub-types. There was no significant variation in the 5-year angiosarcoma relative survival rate, which fluctuated around 30%, over the 25-year period studied (Figure 8.4). This is considerably lower than the 5-year disease specific survival rate of 60% reported by Abraham et al (2007)[7], based on 82 patients at one US institution, and somewhat lower than the 43% 5-year relative survival rate reported by Fayette et al (2007)[6], based on 161 patients treated in three French hospitals.

There was no significant variation in the 5-year haemangioendothelioma relative survival rate, which fluctuated around 40%, over the 25-year period studied (Figure 8.5). Partly because of this low survival rate, researchers have

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questioned the status of epithelioid haemangioendotheliomas. In a review of the files for 30 epithelioid haemangioendothelioma patients treated in the US and Germany[8], the authors concluded that these tumours should be regarded as malignant, rather than borderline neoplasms, a finding consistent with the survival rates reported in the present report.

The anatomical site of diagnosis had a significant impact on angiosarcoma survival rates (Figure 8.6). The survival rates shown for angiosarcomas arising in the organs within the trunk are based on small numbers, and this explains the small gap in the plotted survival rates between 1993-1997 and 1996-2000. The 5-year relative survival rates of patients with angiosarcomas arising within the organs within the trunk are significantly lower than the survival rates of patients with breast angiosarcomas (9% and 66% respectively). The survival rates reported here for angiosarcomas of the head, face and neck are somewhat higher than those reported by Holden, Spittle and Wilson Jones (1987)[9] who found that only 12% of the 72 face and scalp angiosarcoma patients diagnosed in a London hospital lived for five years. However, they are consistent with the rate of 22% reported by Panje, Moran, Bostwick and Kitt (1986)[10] based on 11 cases treated in a US hospital.

There are a number of reasons why 5-year relative survival rates in angiosarcomas of the breast may be higher than the rates at other sites. At least 50% of the breast angiosarcomas in the cohort arose in people who had already had breast cancer, thus it is possible that those patients were observed more closely for subsequent cancers, and so received treatment at an earlier stage. It has also been shown that radiation-induced angiosarcomas have a different genetic signature to spontaneously arising angiosarcomas[11], which may alter their survival patterns. Further work is needed to examine these potential influences on survival.

8.5 References

1. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 155. Geneva: WHO Press.

2. Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

3. Monroe, A. T., Feigenberg, S. J. and Mendenhall, N. P., 2003. Angiosarcoma after breast-conserving therapy. *Cancer*, 97 (8), 1832-1840.

4. Meis-Kindbolm, J. M. and Kindbolm, L.-G., 1998. Angiosarcoma of soft tissue: A study of 80 cases. *American Journal of Surgical Pathology*, 22 (6), 683-697.

5. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 168-175. Geneva: WHO Press.

6. Fayette, J., Martin, E., Piperno-Neumann, S,, Le Cesne, A., Robert, C., Bonvalot, S., Ranchere, D., Pouillart, P., Coindre, J. M. and Blay, J. Y., 2007. Angiosarcomas, a heterogeneous group of sarcomas with a specific behaviour depending on primary site: A retrospective study of 161 cases. *Annals of Oncology*, 18 (12), 2030-2036.

7. Abraham, J. A., Hornicek. F. J., Kaufman, A. M., Harmon, D. C., Springfield, D. S., Raskin, K. A., Mankin, H. J., Kirsch, D. G., Rosenberg, A. E. and Nielsen, G. P., 2007. Treatment and outcome of 82 patients with angiosarcoma. *Annals of Surgical Oncology*, 14 (6), 1953-1967.

8. Mentzel, T., Beham, A., Calonje, E., Katenkamp, D. and Fletcher, C., 1997. Epithelioid haemangioendothelioma of skin and soft tissues: Clinicopathologic and immunohistochemical study of 30 cases. *American Journal of Surgical Pathology*, 21 (4), 363-374.

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9. Holden, C. A., Spittle, M. F. and Jones, E. W., 1987. Angiosarcoma of the face and scalp, prognosis and treatment. *Cancer*, 59 (5), 1046-1057.

10. Panje, W. R., Moran, W. J., Bostwick, D. G. and Kitt, V. V., 1986. Angiosarcoma of the head and neck: Review of 11 cases. *The Laryngoscope*, 96 (12), 1381-1384.

10. Hadj-Hamou, N. S., Lae, M., Almeida, A., Grange, P. D. L., Kirova, Y., Sastre-Garau, X. and Malfoy, B., 2012. A transcriptome signature of endothelial lymphatic cells coexists with the chronic oxidative stress signature in radiation-induced post-radiotherapy breast angiosarcomas. *Carcinogenesis*, epublication.

9. Kaposi's sarcoma

Key Facts

- **Most common anatomical sites of diagnosis: skin, mouth, internal organs**
- **3,029 Kaposi's sarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 2.8 per million persons in 2007-2009**
- **Number diagnosed in 2008 and 2009: 171 and 114**

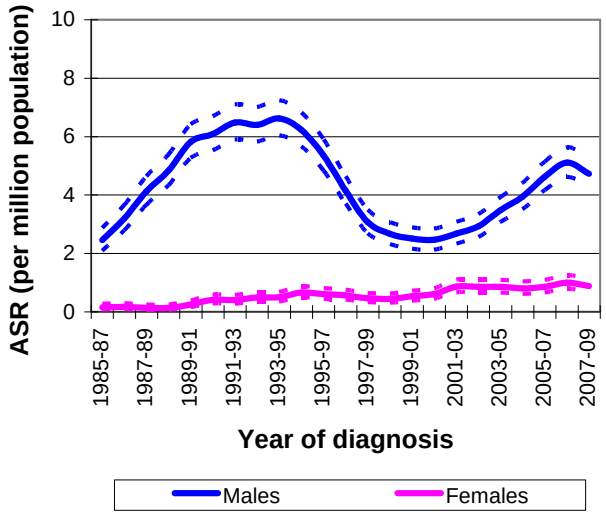
9.0 KAPOSI'S SARCOMA

Kaposi's sarcoma is caused by infection with the virus known as HHV-8 or Kaposi's sarcoma-associated herpes virus (KSHV)[1]. As the virus can be controlled by a healthy immune system, the majority of people who are infected do not experience any symptoms. However, when the immune system is compromised, as happens in the case of HIV infection, the virus can lead to the development of Kaposi's sarcoma[2]. It has been reported that, of UK Kaposi's sarcoma cases in 2010, 94% were caused by dual HHV-8 and HIV infection, with HHV-8, but not HIV, present in the remaining 6%[2].

9.1 Kaposi's Sarcoma Incidence

In 2007 to 2009 Kaposi's sarcoma incidence rates were 5 times higher in males than females (4.7 per million and 0.9 per million respectively). Kaposi's sarcoma age standardised rates increased significantly between 1985 and 2009 for both males and females. The male age standardised incidence rate was 1.5 per million in 1985, reaching an overall peak of 6.8 per million in 1993. By 2002 this rate had dropped dramatically to 2.2 per million males, before increasing for a second time to 5.3 per million in 2008 and decreasing again to 3.6 per million in 2009 (Figure 9.1).

Figure 9.1: Kaposi's sarcoma age standardised incidence rates (3-year rolling average) (England: 1985–2009)



Female Kaposi's sarcoma incidence rates increased linearly and gradually over the 25-year period from 1985 to 2009, from 0.03 per million in 1985, to 0.7 per million in 2009 (Figure 9.1). This is consistent with the findings of the European Centre for Disease Prevention and Control, which reported that the incidence of AIDS in UK women increased during the

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early 2000s, from 0.9 cases per million in 2001, to 1.4 cases per million in 2004[3]. Female HIV infection rates in the UK are now falling, and further work is needed to investigate whether this leads to reductions in female Kaposi's sarcoma incidence in the future.

Between 1971 and 1980, before the HIV/AIDS epidemic, the incidence rate of Kaposi's sarcoma in the UK was estimated to be 0.14 cases per million, with similar incidence in both males and females[4]. In contrast, in the current cohort of diagnoses in England between 1985 and 2009, 87% of Kaposi's sarcomas occurred in men. These significant differences in age standardised rates with sex have previously been described as "perplexing"[5] as the proportion of Kaposi's sarcoma in men is greater than the proportion of men with an HIV infection. It has been suggested that women may require a greater degree of immunosuppression than men to develop Kaposi's sarcoma[6], though this hypothesis needs further investigation.

Kaposi's sarcoma occurs almost exclusively in adults, with only 16 cases diagnosed in people under the age of 20 between 1985 and 2009 (Figure 9.2). Consistent with data from the Scottish Cancer Registry (1999)[7], the peak age for Kaposi's sarcoma diagnosis in England is 35-39 (Figure 9.3).

Figure 9.2: Number of Kaposi's sarcoma diagnosed in each age group and sex (England: 1985–2009)

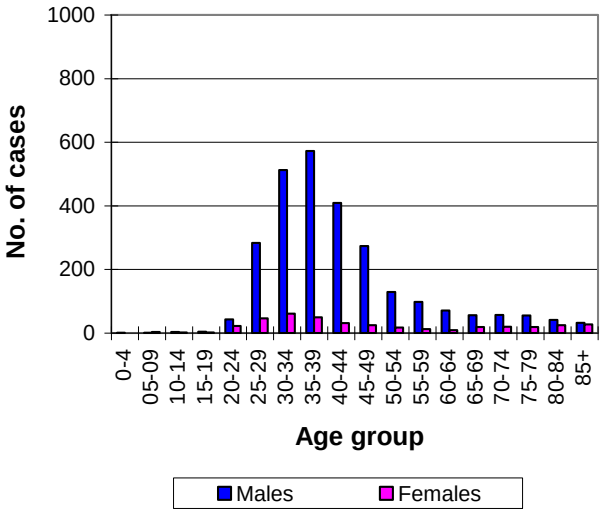
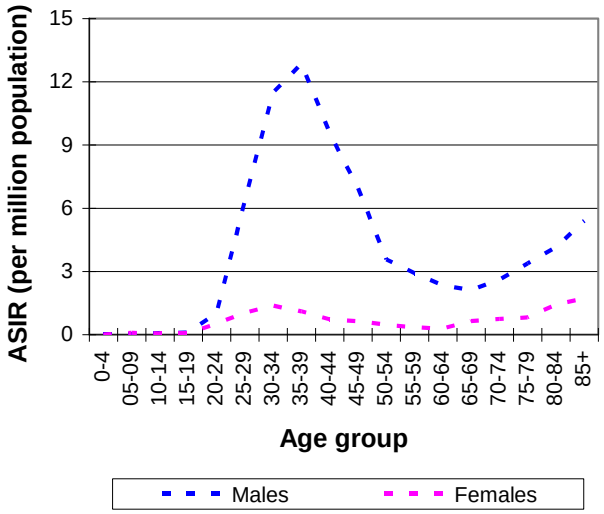


Figure 9.3: Kaposi's sarcoma age specific incidence rates (England: 1985–2009)



9.2 Kaposi's Sarcoma Survival

The 5-year relative survival rates for patients with Kaposi's sarcoma have increased significantly over the last 25 years, from 34% to 77% (Figure 9.4). The greatest increases in 5-year relative survival rates were for patients diagnosed between 1991 and 2001. The survival rate for patients diagnosed from 1999 and onwards is consistent with the 5-year relative survival rate reported by Armstrong et al (2012)[8] for classic Kaposi's sarcoma in the SEER database, but higher than the rate of 54% they reported for AIDS-related Kaposi's sarcoma. There were no significant increases in female 5-year relative survival over the 20-year period studied, with 52% survival for patients diagnosed between 1985 and 1989, and 66% survival for those diagnosed between 2000 and 2004. During the same period 5-year relative survival rates for males increased from 33% to 81%, reflecting an overall improved outlook for HIV/AIDS patients. From 1997 onwards, the 5-year relative survival rates for males with Kaposi's sarcoma became significantly higher than the 5-year relative

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survival rates in females (Figure 9.5). This is consistent with previously reported findings suggesting Kaposi's sarcoma is more aggressive in women than men, though it is rarer in women overall[10]. The reasons for this are still unclear, and further research is needed to understand these differences.

Figure 9.4: Kaposi's sarcoma 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

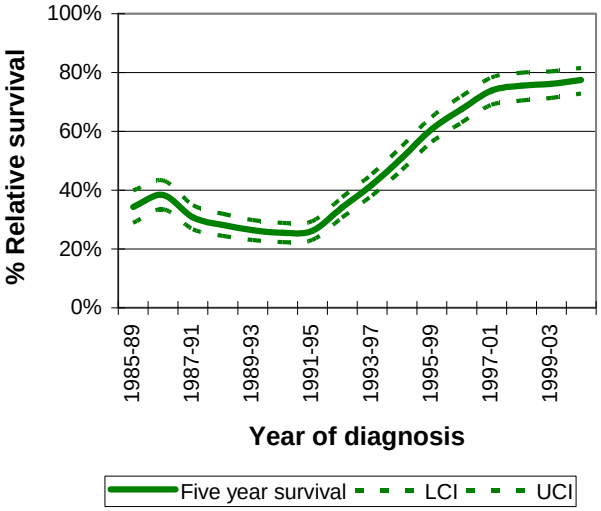
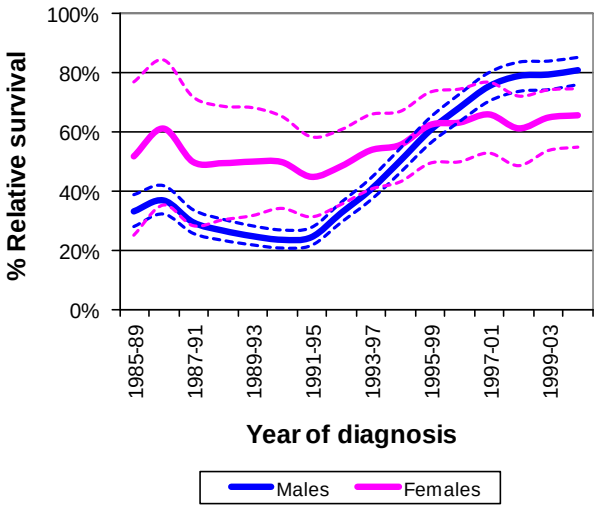


Figure 9.5: Kaposi's sarcoma 5-year relative survival rates in each sex (5-year rolling average) (England: 1985–2004)



9.3 References

1. Cancer Research UK, 2012. *Kaposi sarcoma-associated herpesvirus*. Available at: http://info.cancerresearchuk.org/cancerstats/causes/infectiousagents/kaposisarcoma/kaposi-sarcomaassociated-herpesvirus [Accessed 04/07/12].

2. Parkin, D. M., 2011. Cancers attributable to infection in the UK in 2010. *British Journal of Cancer*, 105, S49-S56.

4. European Centre for Disease Prevention and Control/ WHO Regional Office for Europe, 2011. HIV/AIDS surveillance in Europe: Surveillance report 2010. Stockholm: European Centre for Disease Prevention and Control. Available at: http://ecdc.europa.eu/en/publications/Publications/111129_SUR_Annual_HIV_Report.pdf

5. Grulich, A. E., Beral, V. and Swerdlow, A. J., 1992. Kaposi's sarcoma in England and Wales before the AIDS epidemic. *British Journal of Cancer*, 66, 1135-1137.

6. Colman, R. and Blackbourn, D. J., 2008. Risk factors in the development of Kaposi's sarcoma. *AIDS*, 22 (13), 1629-1632.

7. Phipps, W., Ssewankambo, F., Nguyen, H., Saracino, M., Wald, A., Corey, L., Orem, J., Kambugu, A. and Casper, C., 2010. Gender differences in clinical presentation and outcomes of epidemic Kaposi sarcoma in Uganda. *Plos One*, Vol 5, Iss 11, e13936.

8. Brewster, D. H., Harris, V., Black, R. J. and Goldberg, D. J., 1999. Epidemiology of Kaposi's sarcoma in Scotland, 1976-1996. British Journal of Cancer, 79 (11/12), 1938-1942.

9. Armstrong, A. W., Lam, K. H. and Chase, E. P., 2012. Epidemiology of classic and AIDS-related Kaposi's sarcoma in the USA: Incidence, survival and geographical distribution from 1975 to 2005. *Epidemiology and Infection*, 1-7.

10. Nasti, G., Serraino, D., Ridolfo, A., Antinori, A., Rizzardini, G., Zeroli, C., Nigro, L., Tavio, M., Vaccher, E. and Tirelli, U., 1999. AIDS-associated Kaposi's Sarcoma is more aggressive in women: A study of 54 patients. *Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology*, 20 (4), 337-341.

10. Nerve sheath tumours

Key Facts

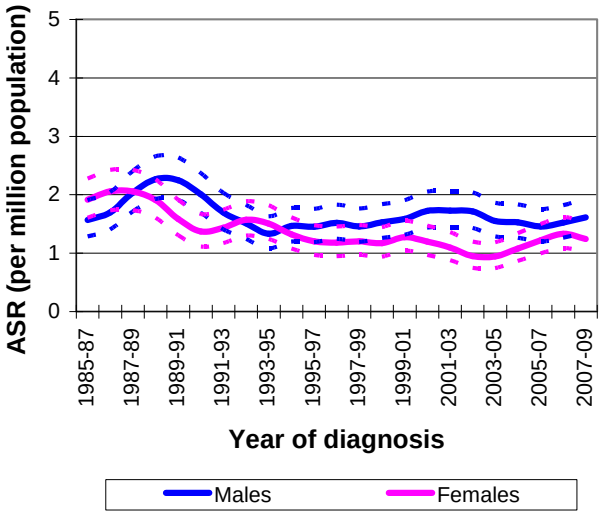
- **Most common anatomical sites of diagnosis: peripheral nerves, the limbs and the brain**
- **1,974 nerve sheath tumours diagnosed in England 1985-2009**
- **Age standardised incidence rate: 1.4 per million in 2007-2009**
- **Number diagnosed in 2008 and 2009: 87 and 75**
- **Sub-types:**
  - **Neurilemoma (malignant schwannomas): 1,065 diagnosed 1985–2009**
  - **Malignant peripheral nerve sheath tumours: 872 diagnosed 1985-2009**
  - **Malignant peripheral nerve sheath tumours with thabdomyoblastic differentiation: 37 diagnosed 1985–2009**

10.0 NERVE SHEATH TUMOUR

Nerve sheath tumours primarily develop in the peripheral nerves. They are rare in the general population, but occur more often in people with neurofibromatosis, a genetic disorder which causes nervous system tumours[1]. Malignant peripheral nerve sheath tumours (44%) and neurilemmomas (malignant schwannomas; 54%) account for the majority of diagnoses in this sub-group. The remainder of the diagnoses are malignant peripheral nerve sheath tumours with rhabdomyoblastic differentiation (triton tumours).

10.1 Nerve Sheath Tumour Incidence

Figure 10.1: Malignant nerve sheath tumour age standardised incidence rates (3-year rolling average) (England: 1985–2009)



Between 1985 and 2009, 1,974 nerve sheath tumours were diagnosed in England. An average of 79 were diagnosed annually between 1985 and 2009, and 87 and 75 were diagnosed in 2008 and 2009 respectively. The age standardised incidence rate fluctuates around 1.5 per million. This rate is similar to that of the 1.9 per million population reported by Toro et al (2006)[2]. It is also comparable to the diagnosis rate of 0.001% of the general population quoted by Ducatman et al (1986)[3] in their study of admissions to one US clinic

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between 1950 and 1982. Ducatman et al also noted that nerve sheath tumour incidence in people with neurofibromatosis is approximately 4.6% of the clinical population. Incidence rates in the present study were generally higher in males than females (1.6 per million and 1.2 per million respectively in 2007 to 2009). These differences were significant during 1990 to 1992 and between 2001 and 2005 (Figure 10.1).

Malignant nerve sheath tumours are very rare in children aged under 10 years of age, with only 31 tumours diagnosed in the 25-year period studied (Figure 10.2). The median age at diagnosis was 51 years. This is older than the median age reported by Anghileri et al (2006)[4] of 37 years, based on patients treated at a single institution in Italy between 1976 and 2003. The age specific incidence rates of malignant nerve sheath tumours are similar in males and females, increasing gradually to the age of 70 and then levelling off (Figure 10.3).

Figure 10.2: Number of malignant nerve sheath tumours diagnosed in each age group and sex (England: 1985–2009)

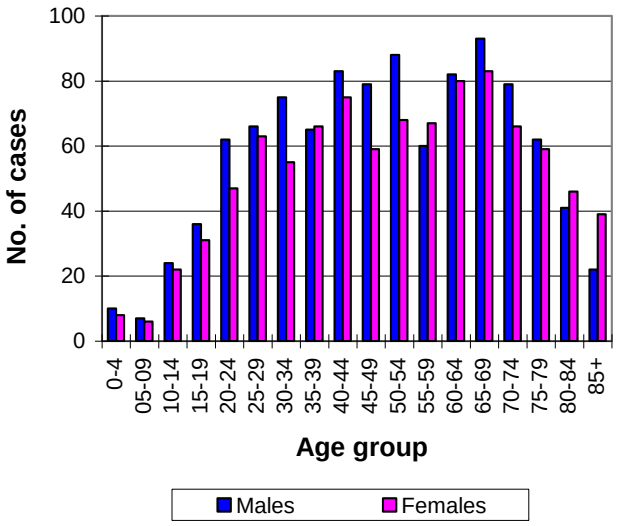
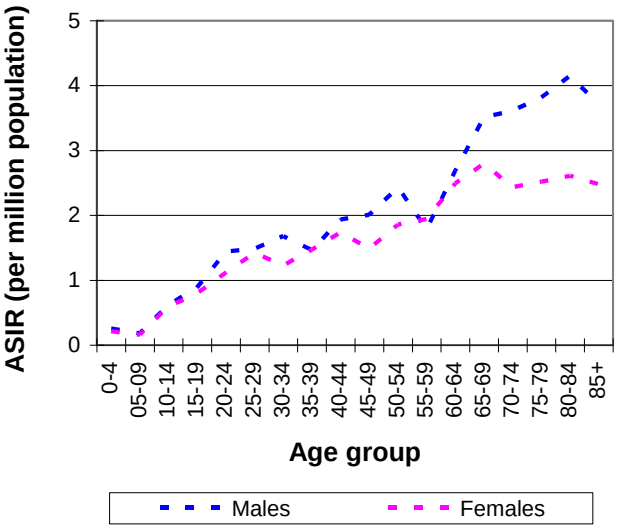


Figure 10.3: Malignant nerve sheath tumour age specific incidence rates (England: 1985–2009)



10.2 Variation in Malignant Nerve Sheath Tumour Incidence with Anatomical Site

Malignant nerve sheath tumours are most commonly diagnosed in the peripheral nerves (40%). However, they can also arise in connective and soft tissue of the limbs (28%) and the brain (16%). The anatomical site of diagnosis does not vary with age (Figure 10.4).

There are significant differences in malignant nerve sheath tumour age standardised incidence rates at different anatomical sites, with incidence rates in the peripheral nerves significantly higher than rates in the limbs and the brain in the most recent years (Figure 10.5). There has been a gradual significant increase in the age standardised incidence rate for malignant nerve sheath tumours in the peripheral nerves over the 25-year period studied; from 0.47 per million in 1985-1987 to 0.74 per million in 2007-2009. The age standardised incidence rate for malignant nerve sheath tumours in the brain has decreased over this time with the incidence rate in 1985-1987 being significantly higher than that in the most recent years.

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Figure 10.4: Proportion of malignant nerve sheath tumours diagnosed in each age group and anatomical site (England: 1985–2009)

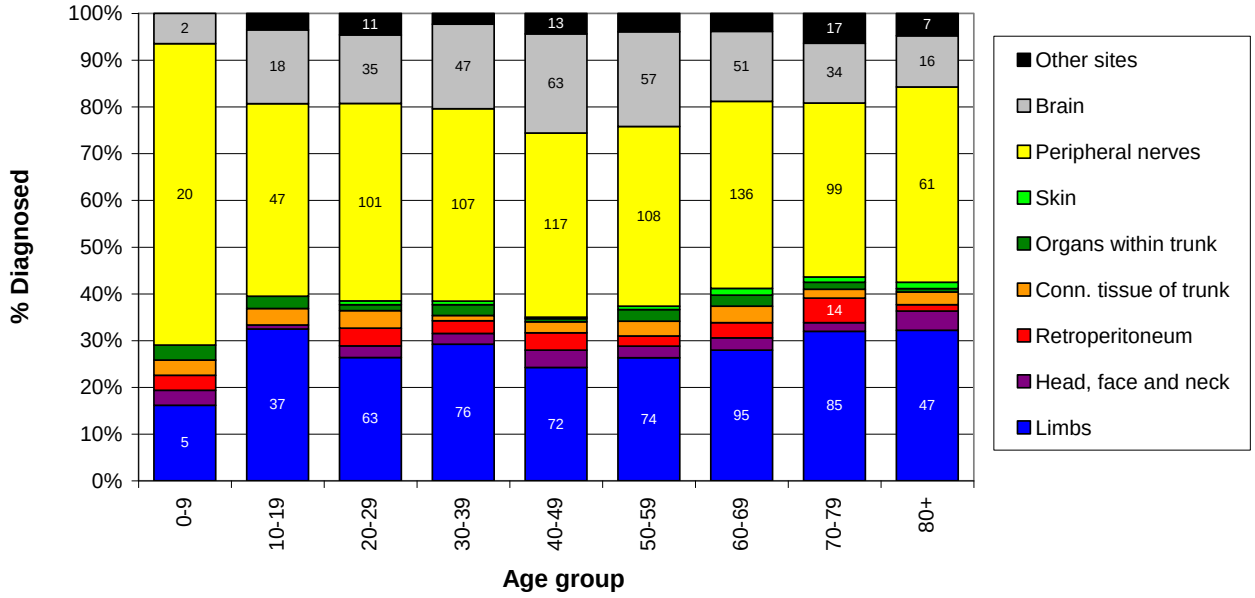


Figure 10.5: Malignant nerve sheath tumour age 3-year rolling age standardised incidence rates in the most common anatomical sites (England: 1985–2009)

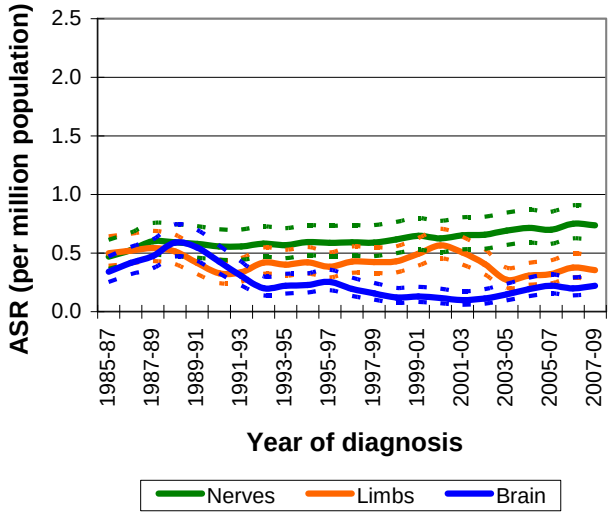
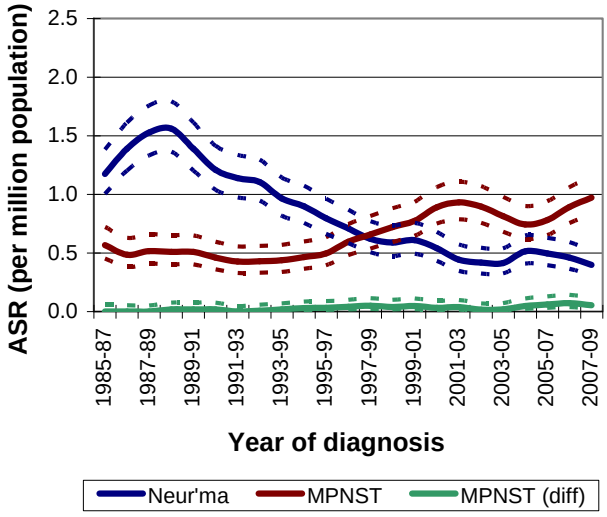


Figure 10.6: Malignant nerve sheath tumour age 3-year rolling age standardised incidence rates in the most common morphological types (England: 1985–2009)



These changes are consistent with the changes in morphological type over the 25-year period (Figure 10.6), with the age standardised incidence rate for neurilemmoma (malignant schwannoma) falling significantly from 1.17 per million in 1985-1991 to only 0.4 per million in 2006-2009, while the age standardised incidence rate for malignant peripheral nerve sheath tumour (MPNST) has risen significantly from 0.57 per million in 1985-1991 to 0.97 per million in 2006-2009.

10. Nerve sheath tumours

10.3 Nerve Sheath Tumour Survival

Malignant nerve sheath tumour 5-year relative survival has declined significantly over the 25-year period studied, from 64% to 53% (Figure 10.7). This is consistent with previously reported rates[5,6,7]. Five-year relative survival rates became significantly lower than the rate observed between 1985 and 1989 from 1991 onwards, and have remained stable ever since.

Figure 10.7: Malignant nerve sheath tumour 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

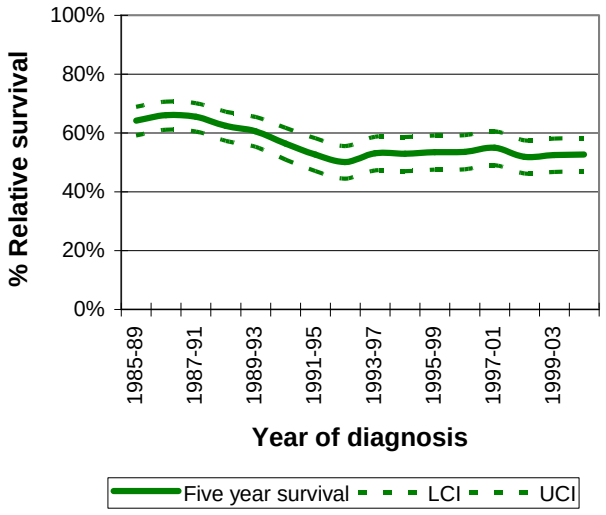


Figure 10.8: Malignant nerve sheath tumour 5-year relative survival rates– variation with age (5-year rolling average) (England: 1985–2004)

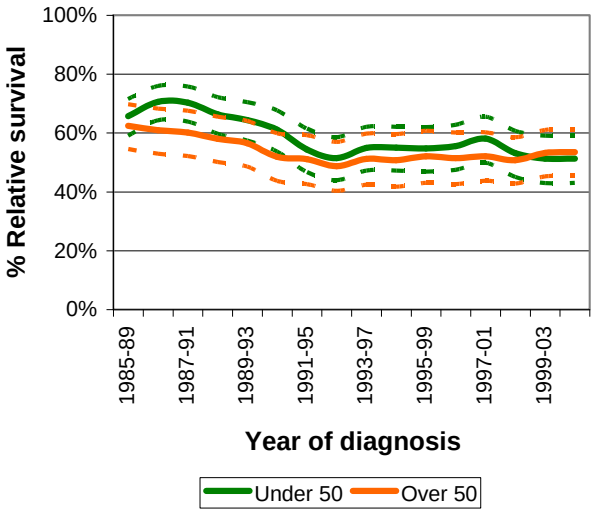
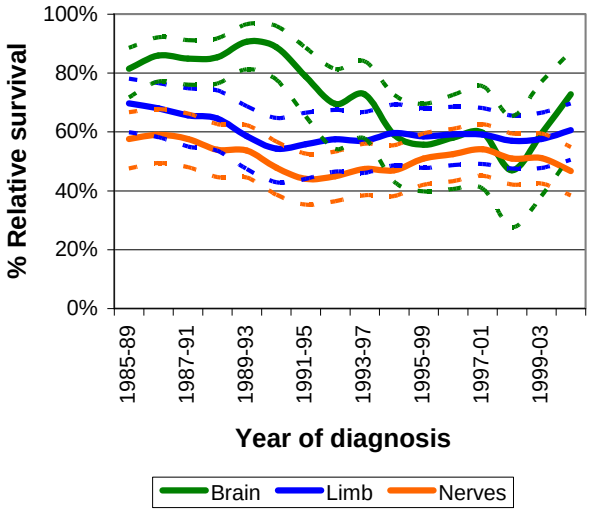


Figure 10.9: Malignant nerve sheath tumour 5-year relative survival rates in the most common anatomical sites (5-year rolling average) (England: 1985–2004)



Five-year relative survival rates have not varied significantly according to age, with 5-year relative survival rates decreasing between 1985 and 2009 for patients aged less than 50 years and those aged 50 years and over (from 66% to 51%, and 62% to 54% respectively) (Figure 10.8).

10. Nerve sheath tumours

The anatomical site of diagnosis also had very little impact on 5-year relative survival rates for patients with a diagnosis of a malignant nerve sheath tumour (Figure 10.9). There were no significant differences in the 5-year relative survival rates between diagnoses of nerve sheath tumours arising in the connective and soft tissue of the limbs, and those arising in the nerves, during the 25-year period examined. However, the most interesting observation is the decrease in survival rates for patients with nerve sheath tumours arising in the brain, the survival rates for which were around 90% in the mid 1990's and then decreased markedly. These decreases temporarily achieved significance in diagnosis years 1995-1999 and 1998-2002.

10.4 References

1. NHS Choices, 2012. Neurofibromatosis Type 1. Available at: http://www.nhs.uk/conditions/Neurofibromatosis/Pages/Introduction.aspx [Accessed 25/07/12].

2. Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

3. Ducatman, B. S., Scheithauser, B. W., Piepras, D. G., Reiman, H. M. and Ilstrup, D. M., 1986. Malignant peripheral nerve sheath tumours. A clinicopathologic study of 120 cases. *Cancer*, 57 (10), 2006-2021.

4. Anghileri, M., Miceli, R., Fiore, M., Mariani, L., Ferrari, A., Mussi, C., Lozza, L., Collini, P., Olmi, P., Casali, P. G., Pilotti, S. and Gronchi, A., 2006. Malignant peripheral nerve sheath tumours: Prognostic factors and survival in a series of patients treated at a single institution. *Cancer*, 107 (5), 1065-1074.

5. Stark, A. M., Buhl, R., Hugo, H. H. and Mehdorn, H. M., 2001. Malignant peripheral nerve sheath tumours: Report of 8 cases and review of the literature. *Acta Neurochirurgica*, 143, 347-364.

6. Kar, M., Deo, S. V. S., Kumar Shukla, N., Malik, A., DattaGupta, S., Kumar Mohanti, B. and Thulkarm S., 2006. Malignant peripheral nerve sheath tumours (MPNST)- Clinicopathological study and treatment outcome of twenty-four cases. *World Journal of Surgical Oncology*, 4, 55-63.

7. Anghileri, M., Miceli, R., Fiore, M., Mariani, L., Ferrari, A., Mussi, C., Lozza, L., Collini, P., Olmi, P., Casali, P. G., Pilotti, S. and Gronchi, A., 2006. Malignant peripheral nerve sheath tumours: Prognostic factors and survival in a series of patients treated at a single institution. *Cancer*, 107 (5), 1065-1074.

11. Phyllodes tumours

Key Facts

- **968 phyllodes tumours diagnosed in England 1985-2009**
- **Over 99% of phyllodes tumours are diagnosed in women, and arise in the breast**
- **Age standardised female incidence rate: 1.4 per million women in 2007-2009**
- **Number diagnosed in 2008 and 2009: 50 and 50**

11.0 MALIGNANT PHYLLODES TUMOUR

Phyllodes tumours have historically been classified as benign, borderline and malignant. Only phyllodes tumours with malignant behaviour are considered in the following analyses. Phyllodes tumours mainly occur in women who have not experienced the menopause[1,2]. Between 1985 and 2009, over 99% of phyllodes tumours in England were diagnosed in women.

Phyllodes tumours develop in the connective tissue and epithelial cells that line the breast and account for less than 1% of all breast tumours[3]. The most common site for phyllodes tumours to arise is within the upper outer quadrant of the breast[4,5]. Unlike angiosarcomas and other sarcomas of the breast, which have been linked to radiotherapy treatment for a previously diagnosed cancer, no factors have been identified as pre-disposing to the development of a phyllodes tumour.

Phyllodes tumours are curable through surgical excision with wide margins, and in some cases may be treated with post-operative radiotherapy. The local recurrence rate is reported to be in the region of 10% to 20%, and, although phyllodes tumours generally have high survival rates, they do have the potential to metastasise, with the lungs, liver and bones being the most common metastatic sites[3].

Population based incidence rates of phyllodes tumours are scarce, and most publications appear to focus on case reports or treatment centre follow up. This section therefore fills a gap within the existing research and information with regards to the incidence and survival of women with a diagnosis of malignant phyllodes tumour.

11.1 Phyllodes Tumour Incidence

Between 1985 and 2009, 968 phyllodes tumours were diagnosed in England (965 in women and 3 in men). All the tumours in females occurred in the breast. Two male patients had a diagnosis in the prostate and one in the breast. On average, 47 phyllodes tumours were diagnosed annually between 2000 and 2009, with 50 tumours diagnosed in both 2008 and 2009.

The female age standardised incidence rate in England fluctuates around 1.4 cases per million. This is slightly lower than the 2.1 per million reported by Bernstein et al (2003) based on patients registered in the Los Angeles County Cancer Registry[6]. There were increases in the female age standardised incidence rate at multiple points during the 25 years examined, which together give an overall statistically significant increase between 1985 and 2009 of 41% (Figure 11.1).

It is unclear what factors have contributed to these increases. It is possible that advances in pathology over the last two decades have led to more accurate classification of phyllodes tumours, and perhaps greater differentiation between malignant phyllodes tumours and those of uncertain behaviour. It is also possible that changes in the treatment of benign breast fibroadenomas have led to a greater number progressing to phyllodes tumours. During the 1980s and 1990s there was considerable

11. Phyllodes tumours

debate about the safety and desirability of conservative fibroadenoma management[7,8,9,10,11,12] and recent NICE guidelines state that, in general, fibroadenomas should not be excised unless the lump is very large or is causing discomfort[13]. Previous research has shown that a very small minority of fibroadenomas progress to phyllodes tumours[14]. Thus, it is possible that this reduced number of excisions of fibroadenomas has led to an increase in the number of phyllodes tumours.

Figure 11.1: Phyllodes tumour age standardised incidence rates (3-year rolling average) (England: 1985–2009)

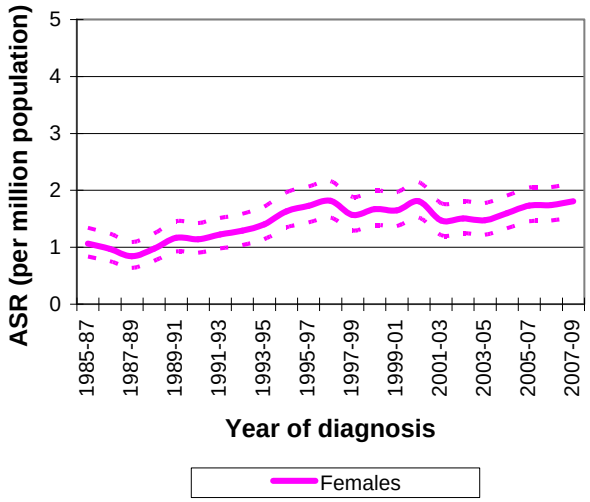


Figure 11.2: Number of phyllodes tumours diagnosed in each age group (England: 1985–2009)

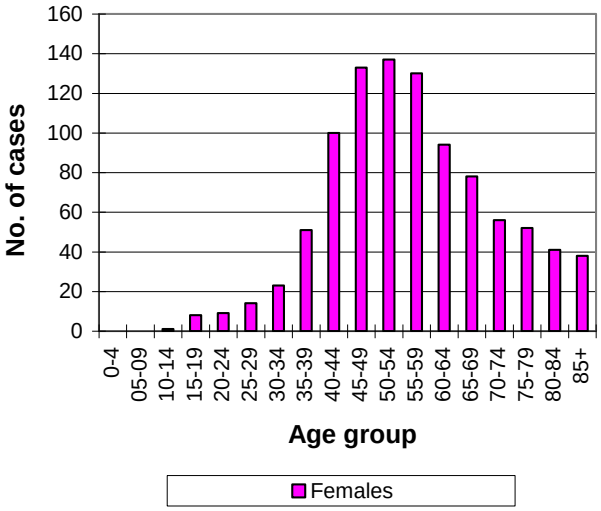
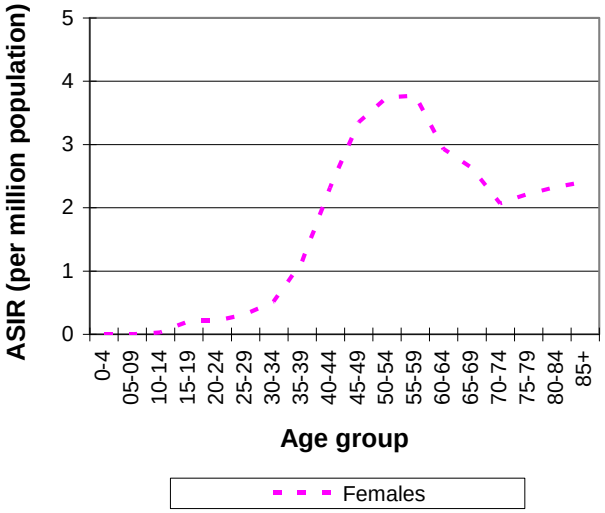


Figure 11.3: Phyllodes tumour age specific incidence rates (England: 1985–2009)



Phyllodes tumours are exceptionally rare in patients under the age of 20 years, with only 9 cases reported between 1985 and 2009 (Figure 11.2). Although patients under the age of 20 years are more likely to be diagnosed with fibroadenoma, with which phyllodes tumours can be confused, confirmed diagnoses of phyllodes tumour occur at any age above 12 years. Female age specific incidence rates for phyllodes tumours show a sharp increase

11. Phyllodes tumours

between the age groups of 40-44 and 50-54 years. This is consistent with previous publications which have reported mean patient ages of 40 to 50 years[1,15,16]. Incidence rates then fall and increase slightly in women aged 70 years and above (Figure 11.3).

11.2 Phyllodes Tumour Survival

The 5-year relative survival rate for phyllodes tumours has increased significantly over the last 25 years, from 68% to 91% (Figure 11.4), with the most significant increases observed from 1996 onwards. These 5-year relative survival rates are consistent with the 74% 5-year survival rate reported by Pandey et al (2001)[17], which was based on patients diagnosed and treated in India.

Between 1990 and 1998, the 5-year relative survival rates for patients aged 60 years and over was significantly lower than the rate observed in patients aged less than 60 years (Figure 11.5). There have been significant increases in the 5-year relative survival rates for patients in both age groups. Five-year relative survival rates increased over the twenty-year period from 76% to 93% for patients aged under 60 years, and from 57% to 88% for patients aged 60 years and over.

Figure 11.4: Phyllodes tumour 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

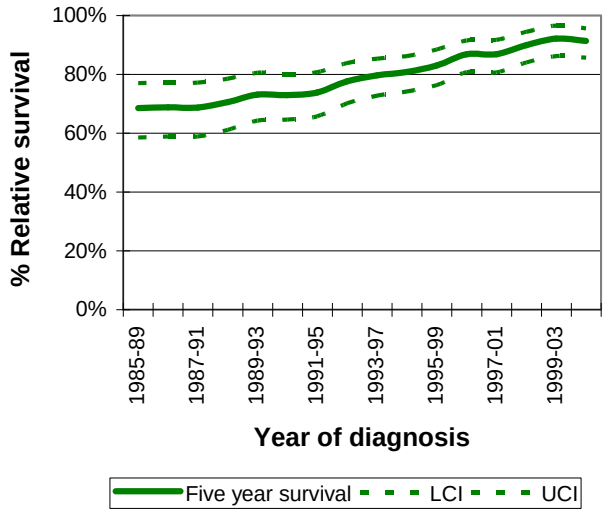
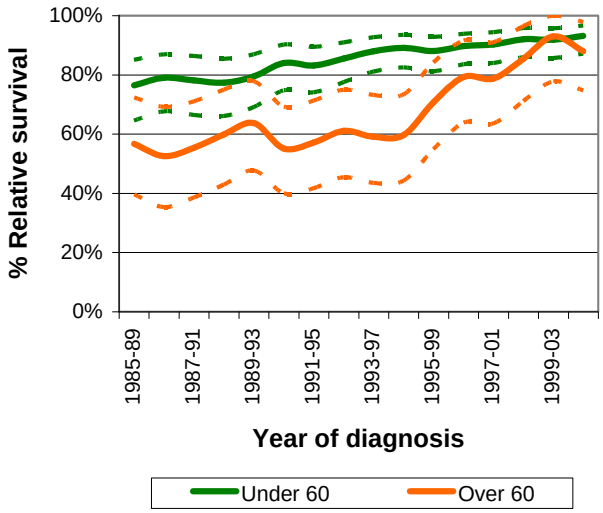


Figure 11.5: Phyllodes tumour 5-year relative survival rates– variation with age (5-year rolling average) (England: 1985–2004)



11.3 References

1. Iau, P. T., Lim, T. C., Png, D. J. and Tan, W. T., 1998. Phyllodes tumour: An update of 40 cases. *Annals of the Academy of Medicine in Singapore*, 27 (2), 200-203.

2. Holthouse, D. J., Smith, P. A., Naunton-Morgan, R. and Minchin, D., 1999. Cystosarcoma phyllodes: The Western Australian Experience. *Australian and New Zealand Journal of Surgery,* 69 (9), 635-638.

3. Pollock, R. E., 2002. *Atlas of Clinical Oncology: Soft tissue sarcomas*, p 150-151. Ontario: BC Decker Inc.

4. Stebbing, J. F. and Nash, A. G., 1995. Diagnosis and management of the phyllodes tumour of the breast: Experience of 33 cases at a specialist centre. *Annals of the Royal College of Surgeons of England*, 77 (3), 181-185.

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5. Alam, I., Awad, Z. T. and Given, H. F., 2003. Cystosarcoma phyllodes of the breast: A clinicopathological study of 11 cases. *Irish Medical Journal*, 96 (6), 179-180.

6. Bernstein, L., Deapen, D. and Ross, R. K., 1993. The descriptive epidemiology of malignant cystosarcoma phyllodes tumours of the breast, *Cancer*, 71 (10), 3020-3024.

7. Cant, P. J., Madden, M. V., Close, P. M., Learmonth, G. M., Hacking, E. A. and Dent, D. M., 1987. Case for conservative management of selected fibro-adenomas of the breast. *British Journal of Surgery*, 74 (9), 857-859.

8. Dixon, J. M., Dobie, V., Lamb, J., Walsh, J. S. and Chetty, U, 1996. Assessment of the acceptability of conservative management of fibroadenoma of the breast, *British Journal of Surgery*, 83 (2), 264-265.

9. Wilkinson, S., Anderson, T. J., Rifkind, E., Chetty, U. and Forrest, A. P. M., 1989. Fibroadenoma of the breast: A follow-up of conservative management. *British Journal of Surgery*, 76 (4), 390-391.

10. Alle, K. M., Moss, J., Venegas, R. J., Khalkhali, I. and Klein, S. R., 1996. Conservative management of fibroadenoma of the breast. British Journal of Surgery, 83 (7), 992-993.

11. Carty, N. J., Carter, C., Rubin, C., Ravichandran, D., Royle, G. T. and Taylor, I., 1995. Management of fibroadenoma of the breast. *Annals of the Royal College of Surgeons of England*, Vol 77, Iss 2, 127-130, 1995.

12. Cant, P. J., Madden, M. V., Colman, M. G. and Dent, D. M., 1995. Non-operative management of breast masses diagnosed as fibroadenoma. *British Journal of Surgery*, 82 (6), 792-794.

13. National Institute for Heath and Clinical Excellence, 2005. Interstital laser therapy for fibroadenomas of the breast. *Information About NICE Interventional Procedure Guidance 131*, 2005.

14. Noguchi, S., Yokouchi, H., Aihara, T., Motomura, K., Inaji, H., Imaoka, S. and Koyama, H., 1995. Fibroadenoma and Phyllodes tumour. Cancer, 76 (10), 1779-1785.

15. Parker, S. J. and Harries, S. A., 2001. Phyllodes tumours. *Postgraduate Medical Journal*, 77, 428-435.

16. Mokbel, K., Price, R. K., Mostafa, A., Wells, C. A. and Carpenter, R., 1999. Phyllodes tumour of the breast: A retrospective analysis of 30 cases. *The Breast*, 8 (5), 278-281.

17. Pandey, M., Mathew, A., Kattoor, J., Abraham, E. K., Mathew, B. S., Rajan, B. and Nair, K. M., 2001. Malignant phyllodes tumour. *The Breast Journal*, 7 (6), 411-416.

12. Rare STS variants

Key Facts

- **Rarer variants of soft tissue sarcoma with fewer than 11 cases diagnoses each year**
- **Cohort consists of 42 different morphologies which cannot be assigned to a larger sub-group**
- **2,457 rare sarcomas diagnosed in England 1985-2009**
- **Age standardised incidence rate: 2.9 per million (2007-2009)**
- **Number diagnosed in 2008 and 2009: 188 and 161**

12.0 RARE SOFT TISSUE SARCOMA VARIANTS

This sub-group includes all soft tissue sarcoma morphologies with fewer than 11 tumours diagnosed annually over the 25-year period 1985 to 2007, and which cannot be assigned to a sub-group previously described in this report. The most common diagnoses in the rare sarcoma sub-group are chordoma (261), haemangiopericytoma NOS (247), epithelioid sarcoma (241) and chondrosarcoma (205). A full list of the morphologies included in this section, together with the number of tumours diagnosed between 1985 and 2009, is provided in Appendix A. It must be noted, however, that this sub-group contains tumours where there may be coding issues within the National Cancer Data Repository. One anomaly is the presence of histologies that would normally be associated with primary bone sarcoma: telangiectatic osteosarcoma and other variants of osteosarcoma, ameloblastoma and giant cell sarcoma of the bone. Collectively, these variants account for 0.5% of this group of tumours.

12.1 Rare Variant Sarcoma Incidence

Rare sarcomas included in this sub-group account for less than 5% of all sarcomas diagnosed in England between 1985 and 2009, with 188 tumours diagnosed in 2008 and 161 in 2009. The age standardised incidence rate increased significantly between 1985 and 2009 for both males and females, from 1.5 and 1.2 per million in 1985 to 1987 to 3.0 and 2.8 per million in 2007 to 2009, respectively (Figure 12.1). Incidence rates did not vary by sex.

Seven percent of all rare variant soft tissue sarcomas are diagnosed in patients less than 5 years old (Figure 12.2a). Malignant rhabdoid tumours account for 55% of the incidence in this age group, and clear cell sarcomas of the kidney account for a further 24%. The age specific incidence rate decreases significantly in the 5-9 year age group before gradually increasing with age in both males and females (Figure 12.2b). From the age of 60 years, age specific incidence rates in males increase at a faster rate than those in females. In the oldest age groups (70 years and above), the age specific incidence rates in males are 150% higher than those in females.

It is not feasible to report the incidence of the rare variant sarcoma sub-types individually as in most instances fewer than 5 tumours are diagnosed annually. The incidence rates of the four most common variants, (chordoma, epithelioid sarcoma, haemangiopericytoma NOS and chondrosarcoma), which together account for 39% of rare soft tissue sarcoma diagnoses, are shown in Figures 12.4 to 12.6. There were no significant differences in any of the age-standardised incidence rates across the 25-year period studied, and only the incidence rates of epithelioid sarcoma increased significantly. Age-standardised incidence rates of haemangiopericytoma decreased in line with controversy about the existence of these types of tumours reported in published literature[1,2].

12. Rare STS variants

Figure 12.1: Rare soft tissue sarcoma age standardised incidence rates (3-year rolling average)

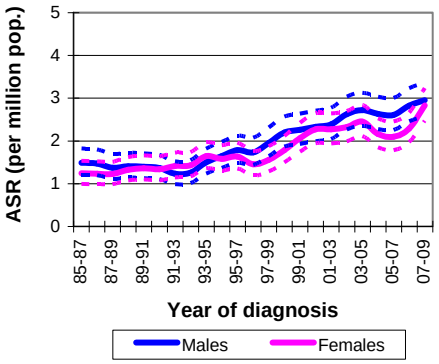


Figure 12.2a: Number of rare soft tissue sarcomas diagnosed in each age group and sex (England: 1985–2009)

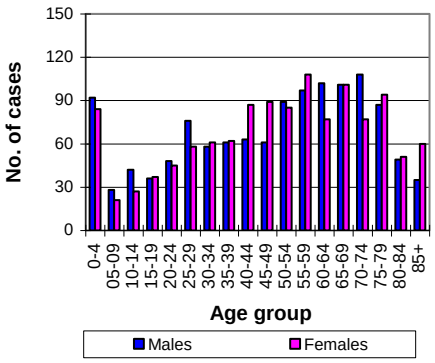


Figure 12.2b: Rare soft tissue sarcoma age specific incidence rates (England: 1985–2009)

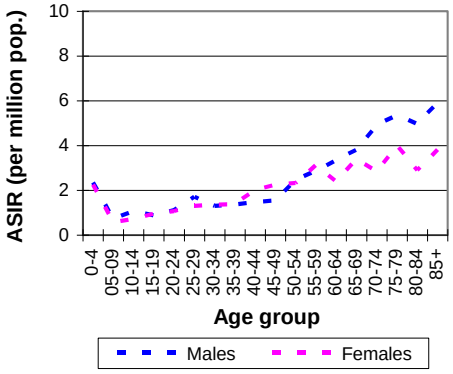


Figure 12.3: Chordoma age standardised incidence rates (3-year rolling average) (England: 1985–2009)

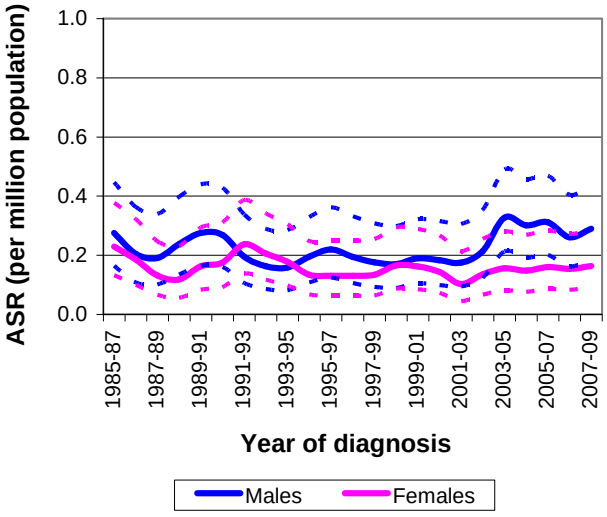


Figure 12.4: Epithelioid sarcoma age standardised incidence rates (3-year rolling average) (England: 1985–2009)

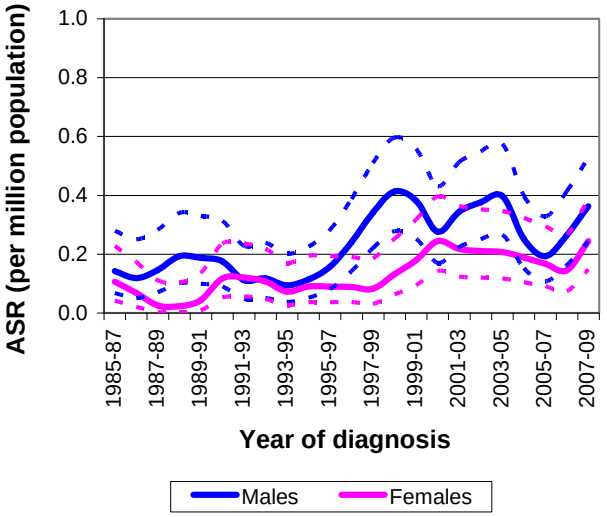


Figure 12.5: Haemangiopericytoma age standardised incidence rates (3-year rolling average) (England: 1985–2009)

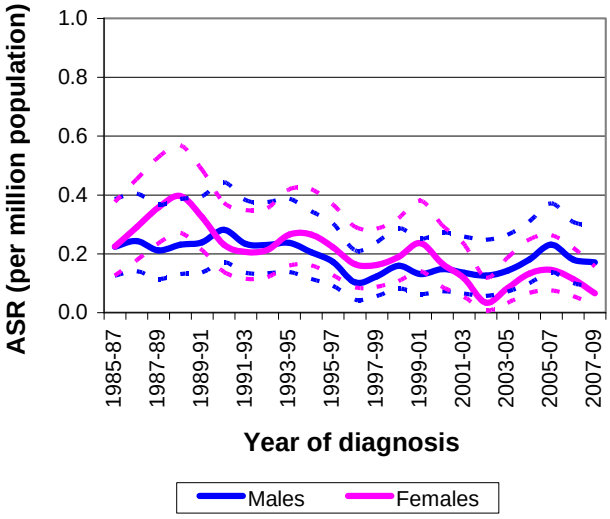
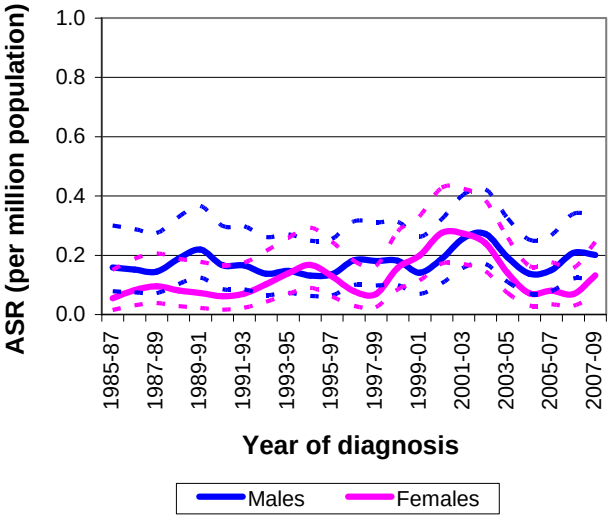


Figure 12.6: Chondrosarcoma age standardised incidence rates (3-year rolling average) (England: 1985–2009)



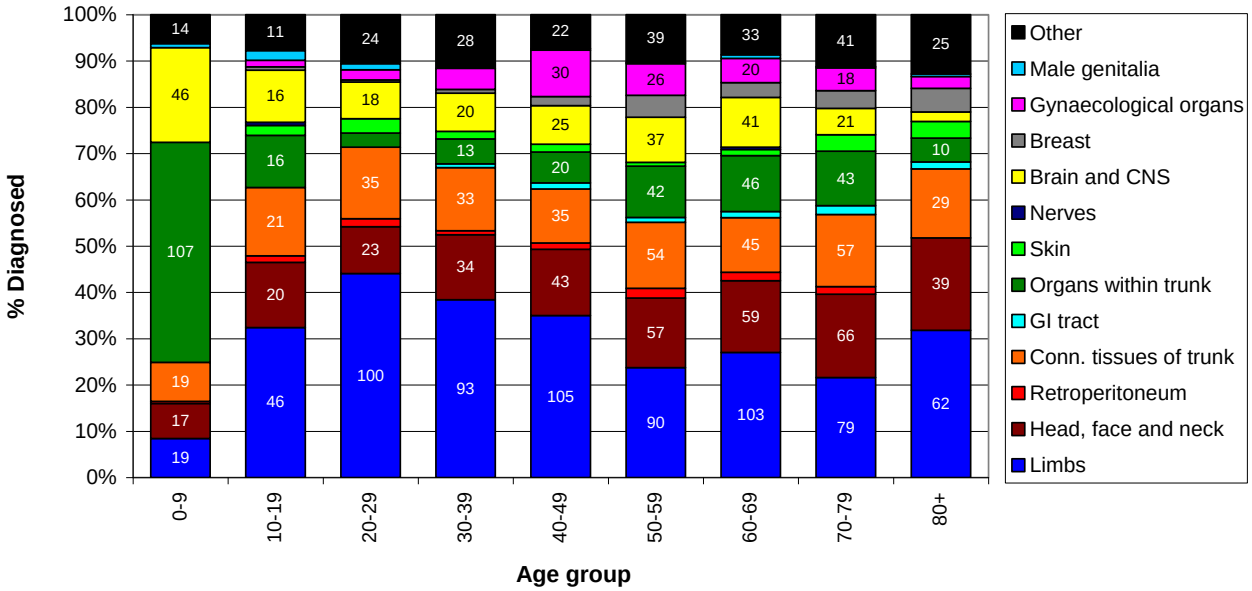
12. Rare STS variants

These results provide an interesting comparison with the gradually increasing incidence rates shown in Figure 12.1, and suggest that the increases in the overall rare variant sarcoma age-standardised incidence rates are driven by the greater number of rare variant sarcoma sub-types diagnosed and/or reported. Examination of the NCDR confirms this hypothesis, as only 15 separate rare variant soft tissue sarcoma morphologies were diagnosed in 1985, compared with 26 separate morphologies in 2009.

12.2 Variation in Rare Variant Sarcoma Incidence with Anatomical Site

Rare variant sub-types of soft tissue sarcoma are most commonly diagnosed in the limbs (28%) the head, face and neck (15%) and the connective tissue (13%) and organs (12%) of the trunk. These anatomical site breakdowns are less heterogeneous than in soft tissue sarcomas as a whole, with a greater proportion clustered in the most common sites. Diagnosis sites are quite consistent across the age groups, with only the 0-9 year age group showing any large differences (Figure 12.7). In this group 48% of all rare soft tissue sarcomas are diagnosed in the organs within the trunk. This is mainly driven by diagnoses in patients younger than 5 years old, who account for 85% of all rare soft tissue sarcoma in organs within the trunk diagnosed in the 0-9 year age group.

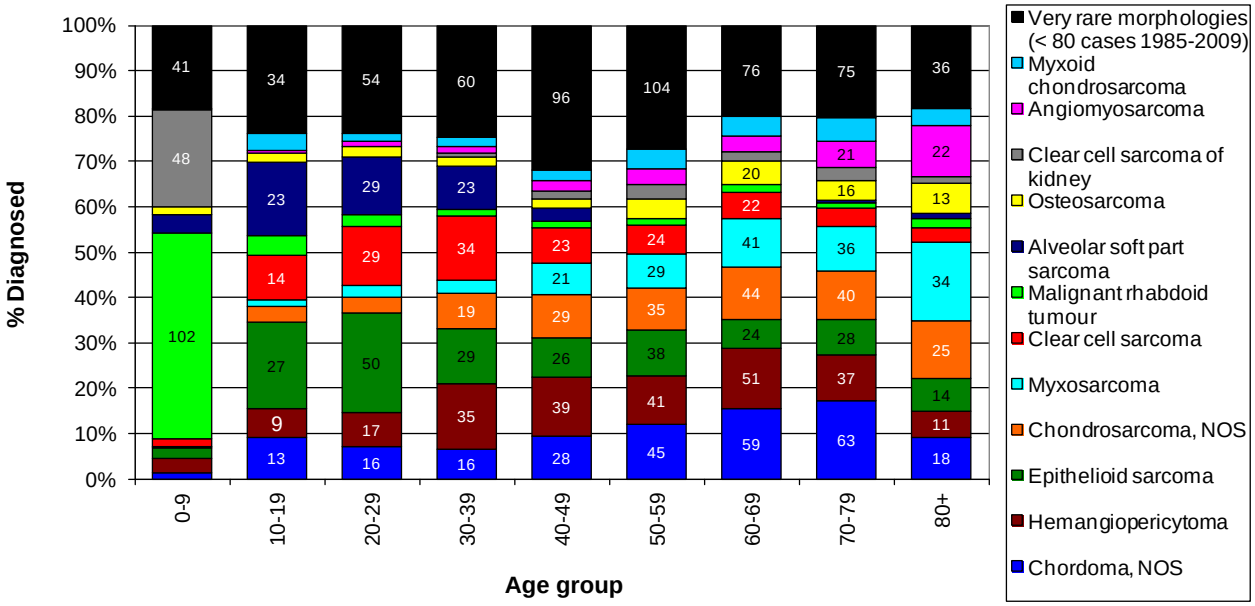
Figure 12.7: Proportion of rare variant soft tissue sarcomas diagnosed in each age group and anatomical site (England: 1985–2004)



Examining the distribution of cases by morphology provides an explanation for the high percentage of rare soft tissue sarcomas of the organs of the trunk in the 0-9 year age group (Figure 12.8). Malignant rhabdoid tumours are aggressive tumours commonly arising in the kidney[3], which are primarily diagnosed in young children. Malignant rhabdoid tumours account for 45% of all rare soft tissue sarcoma diagnoses in patients less than 10 years of age, compared with an average of 2% of all diagnoses all older age groups.

12. Rare STS variants

Figure 12.8: Proportion of rare variant soft tissue sarcomas diagnosed in each age group and main morphology (England: 1985–2004)



12.3 Rare Variant Sarcoma Survival

Figure 12.9: Rare variant soft tissue sarcoma 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

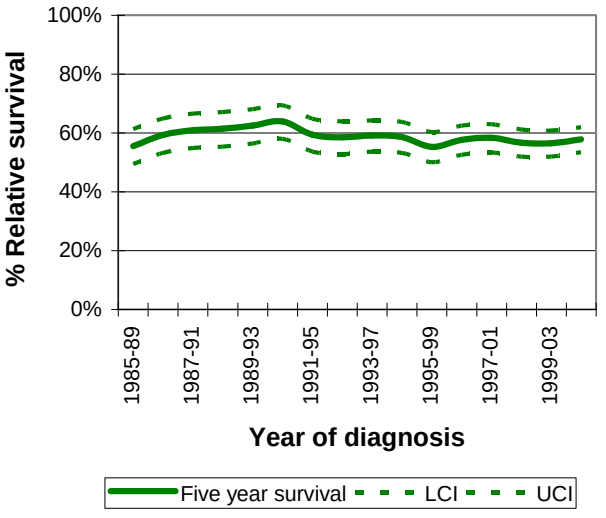
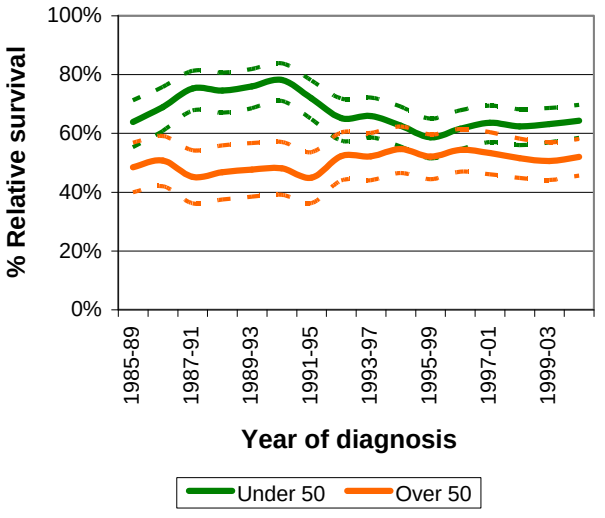


Figure 12.10: Rare variant soft tissue sarcoma 5-year relative survival rates– variation with age (5-year rolling average) (England: 1985–2004)



There was no significant variation in the 5-year relative survival rates of rare variant soft tissue sarcomas over the 20-year time period examined (Figure 12.9). In patients diagnosed in 1985-1989 the survival rate was 55%, and in patients diagnosed in 2000-2004 it was 58%.

Between 1985 and 1995, 5-year relative survival rates of patients aged less than 50 years (78%) were significantly higher than those of patients aged 50 years and over (50%) (Figure 12.10). From 1993 onwards, survival

12. Rare STS variants

rates of patients less than 50 years of age decreased significantly. These decreases directly correlate with the decrease in incidence rates of haemangiopericytoma (Figure 12.5) which is described as an intermediate grade tumour[4]. If haemangiopericytoma, alveolar soft part sarcomas and granular cell tumours are removed from the analyses, 5-year relative survival rates do not vary with age.

More specifically, from 2000 onwards 5-year relative survival rates for patients with chondrosarcoma (77%) were significantly higher than those of epithelioid sarcoma (46%). This 5-year relative survival rate for epithelioid sarcoma is considerably lower than previously published reports. In a review of 37 cases diagnosed at a UK hospital, the 5-year survival rate was 70%[5] and for 16 patients treated a US hospital, the 5-year survival rate was 66%[6]. The reasons for these differences are not clear.

The 5-year relative survival rates for patients with a diagnosis of either haemangiopericytoma or chordoma were between the observed rates for chondrosarcoma and epithelioid sarcoma (Figure 12.11). The 5-year relative survival rate for patients diagnosed with chordoma between 2000 and 2004 was 66%. This is consistent with the rate reported by McMaster et al (2001) based on the survival of patients in the SEER database[7]. The 5-year relative survival rate for patients diagnosed with haemangiopericytoma between 2000 and 2004 was 65%. This is consistent with the rate of 71% survival reported by Spitz et al (1998)[8], based on 36 adults treated at a single US cancer centre between 1975 and 1995.

Figure 12.11: Rare variant soft tissue sarcoma 5-year relative survival rates– variation with morphology (5-year rolling average) (England: 1985–2004)

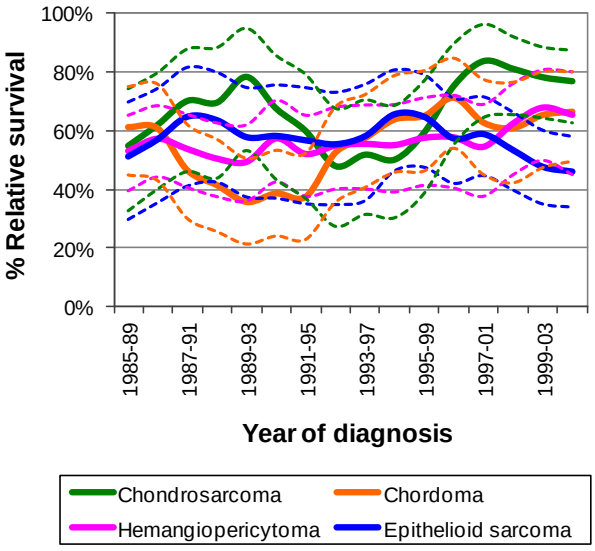
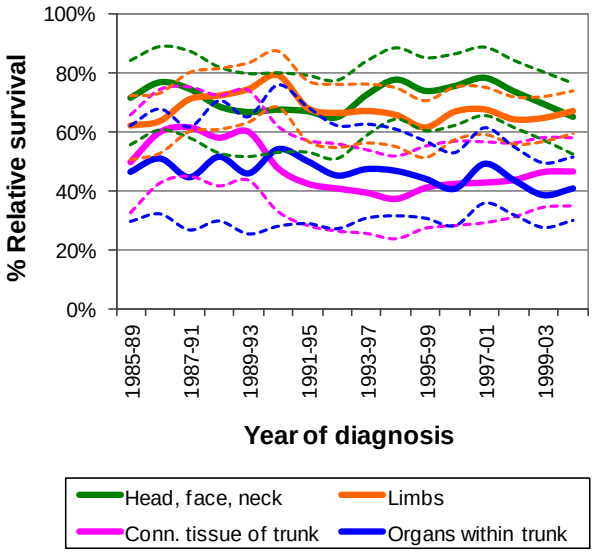


Figure 12.12: Rare variant soft tissue sarcoma 5-year relative survival rates– variation with anatomical site (5-year rolling average) (England: 1985–2004)



Five-year relative survival rates also varied significantly with anatomical site of diagnosis (Figure 12.12). In particular, the 5-year relative survival rates of sarcomas of the organs of the trunk (40%) were significantly lower than the survival rates of sarcomas of the head, face and neck (64%) in a number of year groups. There were also a number of significant differences between the 5-year relative survival rates of organs of the trunk sarcomas and sarcomas of the limbs. The differences in survival between sarcomas in the organs within the trunk and sarcomas in the limbs did not become significant until the diagnosis years 1998-2002, but these differences remained significant throughout the period analysed. For patients diagnosed in 2000-2004 the relative 5-year survival rate of rare soft tissue sarcomas of the limbs was 67%.

12. Rare STS variants

12.4 References

1. Fletcher, C. D. M., 1994. Haemangiopericytoma- A dying breed? Reappraisal of an “entity” and its variants: A hypothesis. *Current Diagnostic Pathology*, 1 (1), 19-23.

2. Gengler, C. and Guillou, L, 2006. Solitary fibrous tumour and haemangiopericytoma: Evolution of a concept. *Histopathology*, 48 (1), 63-74.

3. Batsakis, J. G. and Manning, J. T., 1988. Malignant rhabdoid tumour. *Annals of Ontology, Rhinology & Laryngology,* 97 (6), 690-691.

4. Fletcher, C. D. M., Unni, K. K. and Mertens, F. eds, 2002. *World Health Organisation Classification of tumours: Tumours of Soft Tissue and Bone*, p 90. Geneva: WHO Press.

5. Spillane, A. J., Thomas, J. M. and Fisher, C., 2000. Epithelioid sarcoma: The clinicopathological complexities of this rare soft tissue sarcoma. *Annals of Surgical Oncology*, 7 (3), 218-225.

6. Ross, H. M., Lewis, J. J., Woodruff, J. M. and Brennan, M. F., 1997. Epithelioid sarcoma: Clinical behaviour and prognostic factors of survival. *Annals of Surgical Oncology*, 4 (6), 491-495.

7. McMaster, M. L., Goldstein, A. M., Bromley, C. M., Ishibe, N. and Parry, D. M., 2001. Chordoma: Incidence and survival patterns in the United States, 1973-1995. *Cancer Causes and Control*, 12 (1), 1-11.

8. Spitz, F. R., Bouvet, M., Pisters, P. W. T., Pollock, R. E. and Feig, B. W., 1998. Haemangiopericytoma: A 20-year single-institution experience. *Annals of Surgical Oncology*, 5 (4), 350-355.

13. Sarcoma NOS

Key Facts

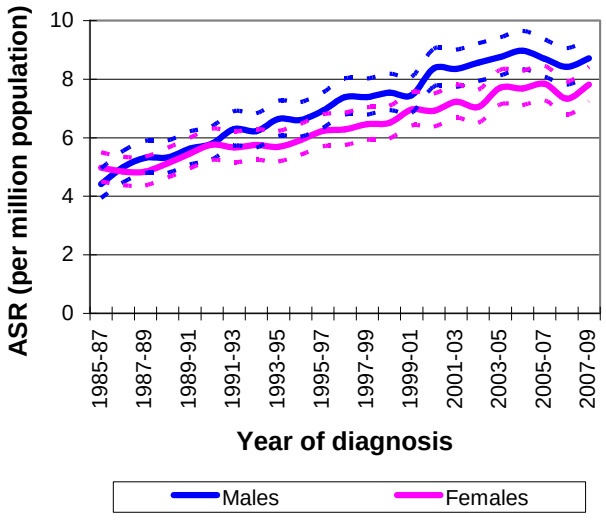
- **Sarcoma NOS: this term is used when:**
  - **A specific sarcoma diagnosis cannot be identified**
  - **The cancer registry which recorded the tumour did not enter a specific sarcoma morphology code**
- **Most common anatomical sites of diagnosis: organs within the trunk, soft and connective tissues of the trunk, limbs, gynaecological organs**
- **9,865 sarcoma NOS diagnosed in England 1985-2009**
- **Age standardised incidence rate: 8.2 per million persons in 2007-2009**
- **Number diagnosed in 2008 and 2009: 505 and 594**
- **Sub-types:**
  - **Sarcoma NOS: 7,024 diagnosed 1985-2009**
  - **Spindle cell sarcoma: 1,896 diagnosed 1985-2009**
  - **Giant cell sarcoma: 768 diagnosed 1985-2009**
  - **Small cell sarcoma: 157 diagnosed 1985-2009**
  - **Undifferentiated sarcoma: 20 diagnosed 1985-2009**

13.0 SARCOMA NOS

The sarcoma NOS group aggregates five distinct types of sarcoma: sarcoma NOS, spindle cell sarcoma, giant cell sarcoma, small cell sarcoma and undifferentiated sarcoma. Sarcoma NOS accounts for 71% of the diagnoses in this sub-group. Each of the variants possesses similar anatomical sites of diagnosis and 5-year relative survival. Therefore, cases of these morphological sub-types are aggregated for the purpose of reporting incidence and survival.

13.1 Sarcoma NOS Incidence

Figure 13.1: Sarcoma NOS age standardised incidence rates (3-year rolling average) (England: 1985–2009)



13. Sarcoma NOS

The sarcoma NOS age standardised incidence rate increased significantly in both males and females during the 25-year period studied; rising from 4.4 and 5.0 per million in 1985-1987 to 8.7 and 7.8 per million in 2007-2009 in males and females respectively (Figure 13.1). These earlier incidence rates are substantially higher than those reported by Hartley et al (1991) for Sarcoma NOS in the North West of England in 1982-1984[1]. The differences most probably result from changes in coding for tumours once referred to as malignant fibrous histiocytoma. Toro et al (2006), whose investigations of the SEER dataset included patients diagnosed more recently, found incidence rates consistent with those reported for the mid-1990s in the present study[2].

Sarcoma NOS is rarely diagnosed in patients aged 15 years and under, with only 161 cases reported between 1985 and 2009 (Figure 13.2). Sarcoma NOS age specific incidence rates increase gradually with age; with male incidence rates increasing more sharply than female incidence rates in those aged 65 years and over (Figure 13.3).

Figure 13.2: Number of sarcoma NOS tumours diagnosed in each age group and sex (England: 1985–2009)

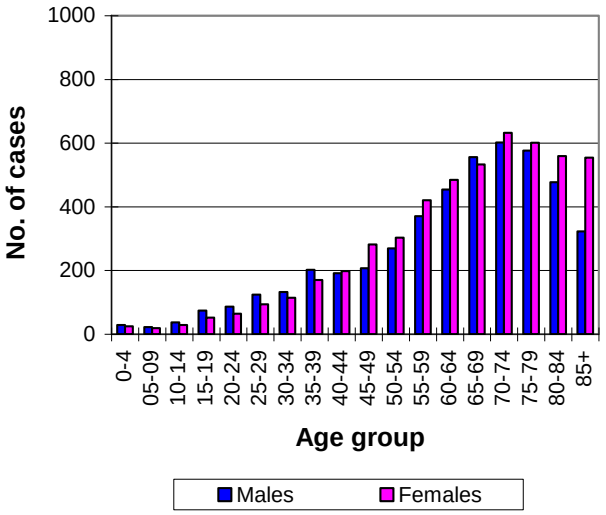
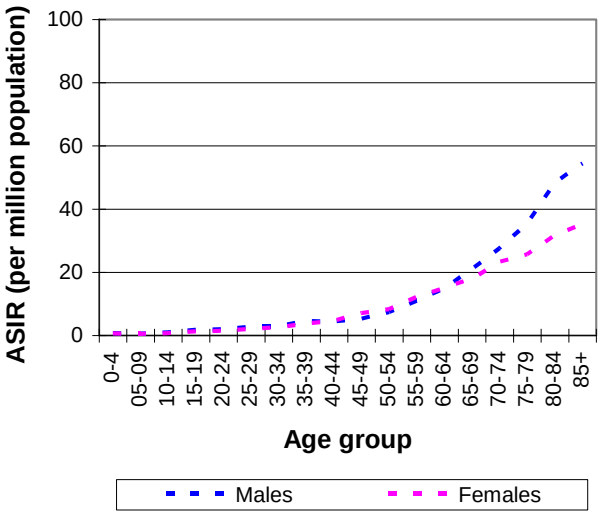


Figure 13.3: Sarcoma NOS age specific incidence rates (England 1985-2009)

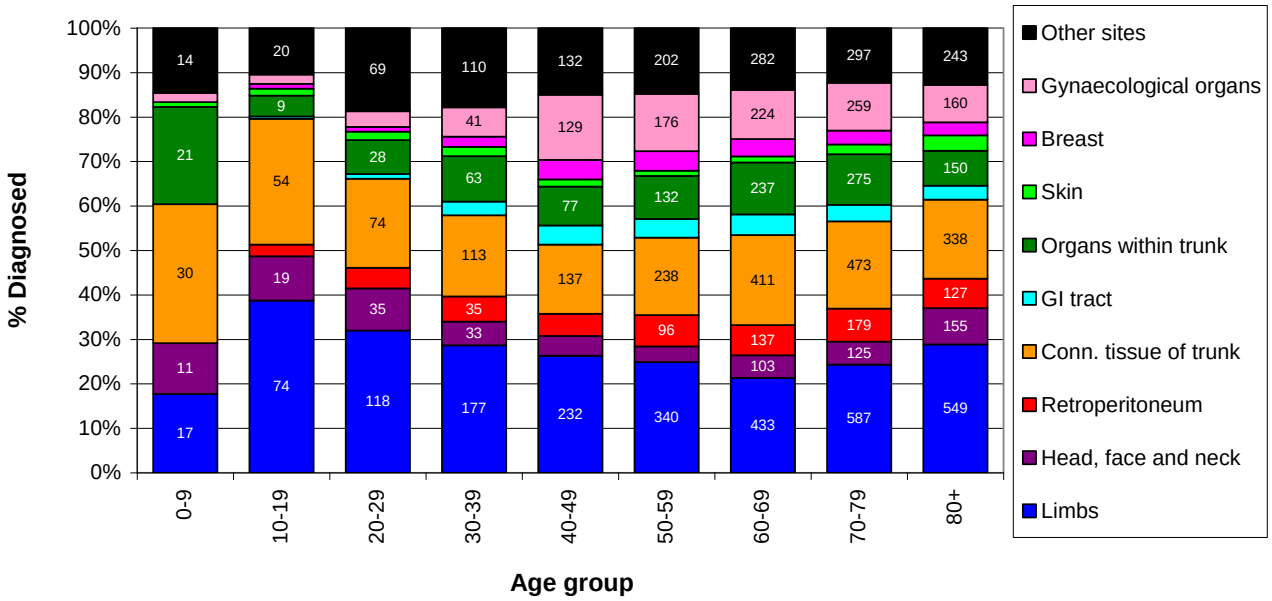


13.2 Variation in Sarcoma NOS Incidence with Anatomical Site

Sarcoma NOS is most commonly diagnosed in the limbs (26%) and the connective and soft tissue of the trunk (19%) (Figure 13.4). The anatomical sites of diagnosis are generally consistent across all age groups. However, patients under the age of 10 years are more likely to have a diagnosis within the internal organs, or the connective and soft tissue of the trunk.

13. Sarcoma NOS

Figure 13.4: Proportion of sarcoma NOS diagnosed in each age group and anatomical site (England: 1985–2009)



13.3 Variation in Sarcoma NOS Incidence Between Cancer Registries

The term sarcoma NOS may be applied when the pathologist cannot make a specific diagnosis, or when the cancer registry making the registration does not enter a specific sarcoma morphology code. The incidence of sarcoma NOS clearly differs by cancer registry, with the WMCIU displaying the lowest incidence rates (6.5 per million) (Figure 13.5h) and the OCIU the highest (10 per million) (Figure 13.5d) for tumours diagnosed in 2007-2009. In 6 of the 8 cancer registries there is a steady increase in the incidence of sarcoma NOS between 1985 and 2009. The TCR (Figure 13.5f) and the OCIU appear to have higher incidence rates in the late 1980's and mid 1990's, possibly indicating that fewer specific sarcoma morphology codes were used at this time.

A recent review of the WMCIU's cancer registration database demonstrated that a more specific morphology code could be derived from the pathology reports for a significant proportion of cases coded as sarcoma NOS. Thus, the relatively low rate of 6-6.5 per million recorded in the West Midlands is probably the most accurate reflection of the true incidence of sarcoma NOS.

13. Sarcoma NOS

Figure 13.5a: ECRIC Sarcoma NOS incidence rates (England: 1985–2009)

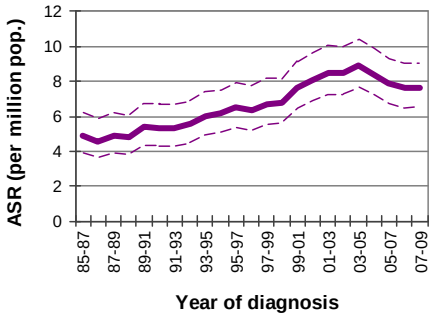


Figure 13.5b: NWCIS Sarcoma NOS Incidence rates (England: 1985–2009)

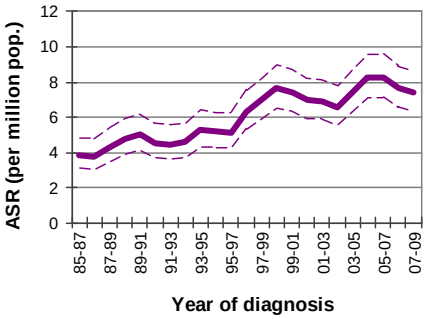


Figure 13.5c: NYCRIS Sarcoma NOS Incidence rates (England: 1985–2009)

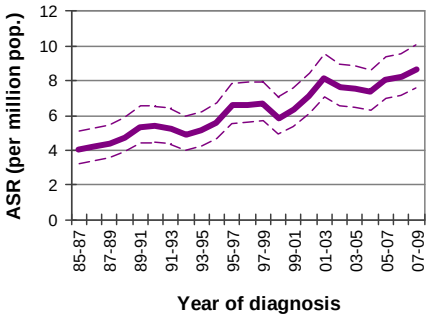


Figure 13.5d: OCIU Sarcoma NOS incidence rates (England: 1985–2009)

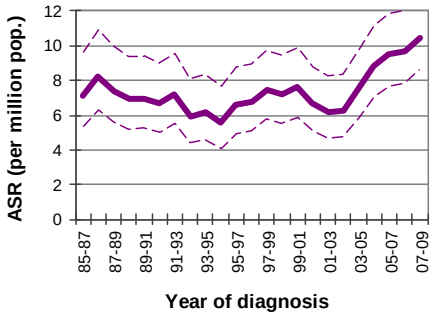


Figure 13.5e: SWCIS Sarcoma NOS Incidence rates (England: 1985–2009)

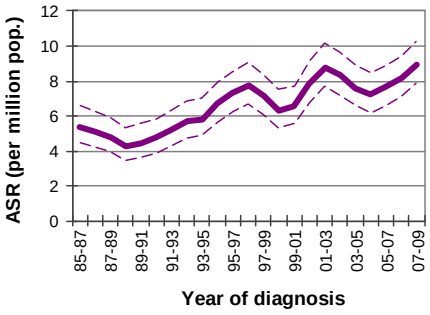


Figure 13.5f: TCR Sarcoma NOS Incidence rates (England: 1985–2009)

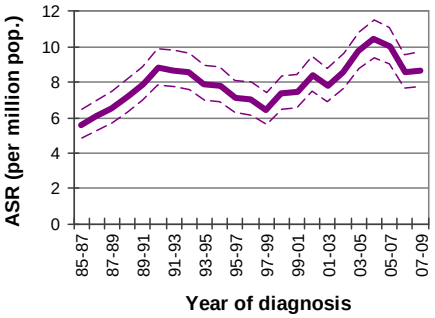


Figure 13.5g: TrCR Sarcoma NOS Incidence rates (England: 1985–2009)

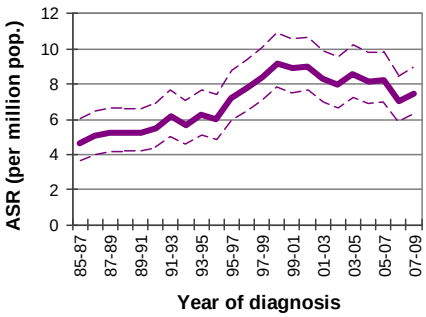
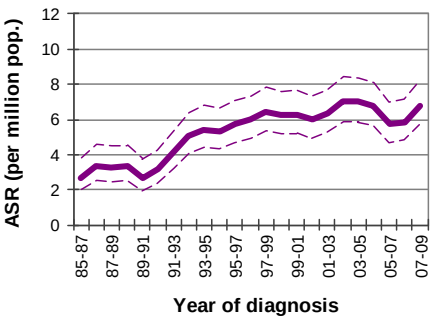


Figure 13.5h: WMCIU Sarcoma NOS Incidence rates (England: 1985–2009)



13. Sarcoma NOS

13.4 Sarcoma NOS Survival

There was no significant variation in the 5-year sarcoma NOS relative survival rates over the 25-year period studied, with survival rates of 32% and 35% for cases diagnosed in 1985-1989 and 1999-2003 respectively (Figure 13.6).

Figure 13.6: Sarcoma NOS 5-year relative survival rates (5-year rolling average) (England: 1985–2004)

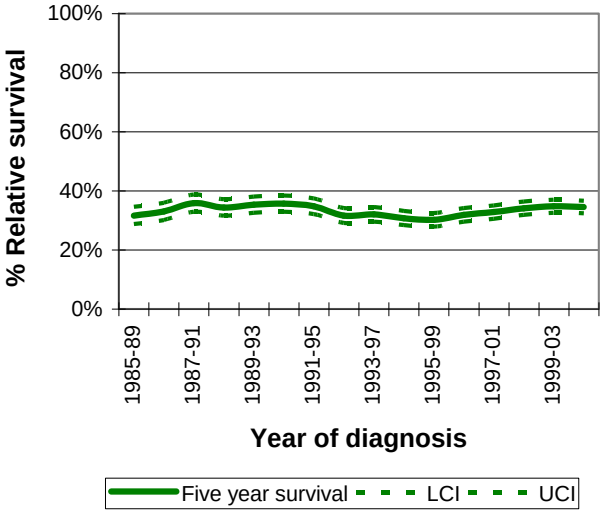


Figure 13.7: Sarcoma NOS 5-year relative survival rates– variation with age (5-year rolling average) (England: 1985–2004)

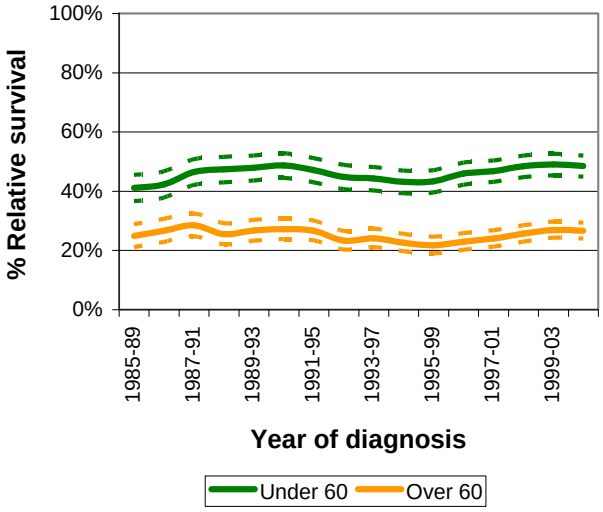
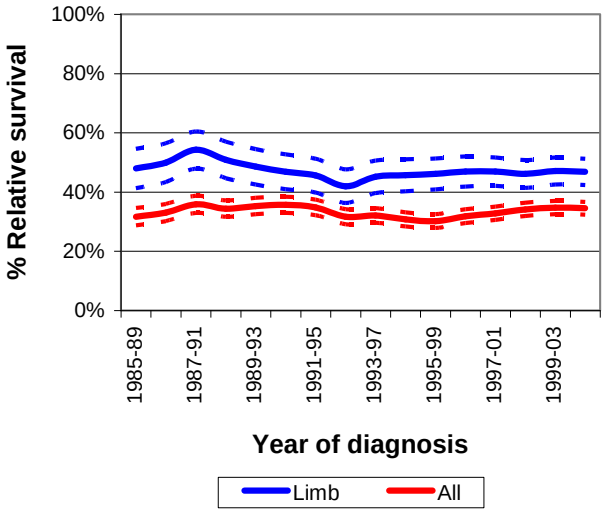


Figure 13.8: Sarcoma NOS 5-year relative survival rates in the most common anatomical sites (5-year rolling average) (England: 1985–2004)



Age has a significant impact on the 5-year relative survival rates of patients diagnosed with sarcoma NOS. Patients under the age of 60 years have significantly higher survival rates than patients aged 60 years and over (49% compared with 27% in those diagnosed in 2000-2004). No significant improvements in 5-year relative survival with time were observed in either cohort (Figure 13.7).

13. Sarcoma NOS

The anatomical site of diagnosis contributes significantly to the prognosis of 5-year sarcoma NOS relative survival rates. Sarcoma NOS arising in the limbs consistently showed a higher survival rate than sarcoma NOS arising in any of the other common sites: the connective tissues of the trunk, the organs within the trunk and the gynaecological organs (Figure 13.8). Sarcoma NOS tumours arising in the breast also had a significantly higher 5-year relative survival rate in the majority of year groups, but this finding is based on very few cases. No significant improvements in 5-year relative survival were observed for sarcoma NOS in any of the anatomical sites.

13.5 References

1. Hartley, A. L., Blair, V., Harris, M., Birch, J. M., Banerjee, S. S., Freemont, A. J., McClure, J. and McWilliam, L. J., 1991. Sarcomas in North West England: II Incidence. *British Journal of Cancer*, 64, 1145-1150.

2. Toro, J. R., Travis, L. B., Wu, H. J., Zhu, K., Fletcher, C. D. M. and Devesa, S. S., 2006. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the Surveillance, Epidemiology and End Results program, 1978-2001: an analysis of 26,758 cases. *International Journal of Cancer,* 119 (12), 2922-2930.

Appendix A
14. Rare sarcomas

Appendix A: Rare sarcomas and number of tumours diagnosed (1985 – 2009)

Morphology	Description	Cases diagnosed (England: 1985-2009)
9370	Chordoma	261
9150	Haemangiopericytoma, NOS	247
8804	Epithelioid sarcoma, epithelioid cell sarcoma	241
9220	Chondrosarcoma	205
8840	Myxosarcoma	177
9044	Clear cell sarcoma (except of kidney M8964/3)	170
8963	Rhabdoid sarcoma	142
9581	Alveolar soft part sarcoma	97
9180	Osteosarcoma, NOS	89
8964	Clear cell sarcoma of kidney	88
8894	Angiomyosarcoma	84
9231	Myxoid chondrosarcoma	80
8982	Myoepithelioma	72
9240	Mesenchymal chondrosarcoma	71
9251	Giant cell tumour of soft parts, NOS	70
9580	Granular cell tumour, malignant; granular cell myoblastoma, malignant	65
8895	Myosarcoma	59
8991	Embryonal sarcoma	57
8935	Stromal Sarcoma	54
8931	Endometrial stromal sarcoma, low grade	21
8815	Solitary fibrous tumour, NOS	19
8806	Desmoplastic small round cell tumour	15
9252	Malignant tenosynovial giant cell tumour (C49._)	12
8710	Glomangiosarcoma: Glomoid sarcoma	11
8711	Glomus tumour (and varients), malignant glomus tumour	9
8821	Aggressive fibromatosis, Desmoid tumour NOS	7
9310	Ameloblastoma	6
9270	Odontogenic tumour	4
9210	Osteochondromatosis	4
9250	Giant cell tumour of bone, NOS	4
8841	Angiomyxoma	3
8822	Abdominal fibromatosis (ICDO-2)	2
9181	Chondroblastic osteosarcoma	2
9182	Fibroblastic osteosarcoma ; osteofibrosarcoma	1
9183	Telangiectatic osteosarcoma	1
9184	Osteosarcoma in Paget's disease of bone	1
9242	Clear cell chondrosarcoma,	1
9243	Dedifferentiated chondrosarcoma	1
9290	Ameloblastic odontosarcoma: Ameloblastic fibrodentinosarcoma	1
8823	Desmoplastic fibroma (ICD-O-2)	1
9365	Askin tumour	1
9371	Chondroid chordoma	1

Appendix B
15. Glossary

Appendix B: Acronyms and descriptions

Abbreviation	Full text
AIDS	Acquired immunodeficiency syndrome
ASIR	Age specific incidence rate
ASR	Age standardised rate
CNS	Central nervous system
GI	Gastro-intestinal
GIST	Gastro-intestinal stromal tumour
HIV	Human immunodeficiency virus
HHV-8	Human herpes-virus 8, also known as KSHV
ICD-03	International Classification of Diseases for Oncology, 3rd Edition
ICD-10	International Classification of Diseases, 10th Revision
KSHV	Kaposi's sarcoma-associated herpes-virus, also known as HHV-8
LCI	Lower confidence interval
MFH	Malignant fibrous histiocytoma
MPNST	Malignant peripheral nerve sheath tumours
NCDR	National Cancer Data Repository
NCIN	National Cancer Intelligence Network
NICE	National Institute for Health and Clinical Excellence
NOS	Not otherwise specified
pNET	Primitive/ Peripheral neuroectodermal tumour
POP	Population
RMS	Rhabdomyosarcoma
SEER database	Surveillance, Epidemiology and End Results database
STS	Soft tissue sarcoma
UCI	Upper confidence interval
UK	United Kingdom
WHO	World Health Organisation

Cancer Registries

Abbreviation	Full text
ECRIC	East of England Cancer Registration and Information Centre
NWCIS	North West Cancer Intelligence Service
NYCRIS	Northern and Yorkshire Cancer Registration and Information Service
OCIU	Oxford Cancer Intelligence Unit
SWCIS	South West Cancer Intelligence Service
TCR	Thames Cancer Registry
TrCR	Trent Cancer Registry
WMCIU	West Midlands Cancer Intelligence Unit