Ontario
Cancer Care Ontario
Action Cancer Ontario

Evidence Summary 11-9- EDUCATION AND INFORMATON 2014

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Multidisciplinary Specialist Care for Sarcoma

C. Catton, N. Coakley, S. Verma, H. Messersmith, and M. Trudeau

Report Date: October 28, 2013

An assessment conducted in October 2014 put Evidence Summary (ES) 11-9 in the Education and Information section. This means that the recommendations will no longer be maintained but may still be useful for academic or other information purposes. The PEBC has a formal and standardize process to ensure the currency of each document

(PEBC Assessment & Review Protocol)

Evidence Summary 11-9 is available on the CCO Website PEBC Sarcoma DSG page

For information about the PEBC and the most current version of all reports, please visit the CCO website at http://www.cancercare.on.ca or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: ccopgi@mcmaster.ca

Evidence Summary Citation (Vancouver Style): Catton C, Coakley N, Verma H, Messersmith H, Trudeau M. Multidisciplinary specialist care for sarcoma. Toronto (ON): Cancer Care Ontario; 2010 May 12. Program in Evidence-based Care Evidence Summary No.: 11-9.

cancer care ontario | action cancer ontario
program in evidence-based care | programme de soins fondé sur des preuves

Evidence Summary 11-9

Multidisciplinary Specialist Care for Sarcoma: Evidence Summary

C. Catton, N. Coakley, S. Verma, H. Messersmith, and M. Trudeau

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Report Date: May 12, 2010

INTRODUCTION

Sarcoma is a rare cancer of soft tissue and bone, with an estimated incidence in Ontario of approximately 700 adult cases per year. Because optimal management is often complex and multimodal, and requires both disease-specific and anatomy-specific expertise, sarcomas remain a significant cause of cancer morbidity and mortality in Ontario.

Sarcoma care in Ontario is presently provided in several specialized centres and in the community. However, the perception is that non-expert caregivers and patients often lack knowledge about best practice and how to access expert care.

In response to this concern, Cancer Care Ontario (CCO) initiated a review of the delivery of sarcoma care in Ontario. The goal of this review was to develop recommendations that, if implemented, would ensure higher quality and more efficient delivery of sarcoma care. An expert committee, the Sarcoma Review Panel, was formed to undertake this review. As part of this process, the Program in Evidence-based Care (PEBC) was asked to develop a summary of the available, relevant evidence regarding the advantages and implementation of expert multidisciplinary care for sarcoma. This evidence summary would be used, along with Ontario-level data on patient volumes, costs, and other aspects of sarcoma care and the expert opinion and consensus of the Sarcoma Panel itself, as the basis for the panel's recommendations.

Therefore, the PEBC conducted a systematic review for evidence regarding multidisciplinary care in sarcoma. This document represents the results of that review.

METHODS

For this project, the core methodology used to develop the evidentiary base was the systematic review. Evidence was selected and reviewed by one member of the PEBC Sarcoma Disease Site Group (DSG) and two methodologists. This systematic review is intended to promote evidence-based practice in Ontario, Canada. The PEBC is supported by the Ontario

Ministry of Health and Long-Term Care through CCO. All work produced by the PEBC is editorially independent from its funding source.

The overall strategy for this project was a two-stage systematic search for available evidence. First, a preliminary search was conducted to identify existing systematic reviews of the evidence on the original research question. The intent of this search was to capitalize on existing work in order to develop the necessary evidence base in the most efficient manner. If any existing systematic reviews of the evidence were identified, they would be evaluated for their completeness, timeliness, and quality. A decision would be made as to whether one or more of these reviews could be used as the basis of this evidence summary.

Second, a search for individual studies relevant to the research question would be conducted. This search would only cover the timeframes and content areas not addressed by any other identified systematic reviews. The methods for these two stages are described below.

Initial Search for Existing Systematic Reviews

Research Question

At the project's inception, only one research question was considered to be feasible, given the timeframes involved with the project and the volume of evidence that was expected to be identified. This question was:

- Are sarcoma patient outcomes improved in a high-volume centre with multidisciplinary management as opposed to a low-volume centre?

Initial Search Strategy for Existing Systematic Reviews

The MEDLINE (1950 through January [week two] 2009), Embase (1980 through week 3 2009), HealthSTAR (1966 through December 2008), and Cochrane Database of Systematic Reviews (CDSR) (4th Quarter 2008) databases were searched for relevant evidence. The search terms pertaining to sarcoma, healthcare access, and quality were combined in the search strategies. The full, combined MEDLINE, Embase, HealthSTAR, and CDSR literature search strategies can be found in Appendix 1. In addition, practice guideline organization websites were searched in January 2009, including the Scottish Intercollegiate Guidelines Network (SIGN), National Institute for Health and Clinical Excellence (NICE), National Health and Medical Research Council (NHMRC), New Zealand Guidelines Group (NZGG), and American Society of Clinical Oncology (ASCO).

Evaluation of Existing Systematic Reviews

Reviews identified through the search were to be evaluated using the AMSTAR tool (1) to assess their quality. In addition, the timeliness and relevance of the review were to be assessed, although no a priori standards were established for that assessment. Should a review be identified as relevant, timely, and of sufficient quality, it would serve as the basis for the next stage.

Search for Relevant Studies

Research Questions

As noted below in the Results section, the initial search for existing systematic reviews identified a comprehensive and recent systematic review published by the National Institute for Clinical Excellence (NICE) in the United Kingdom (UK) (2). Once this existing review was identified, the decision was that additional research questions could be addressed, given available timeframes and resources. The systematic review then focused on updating the evidence base surrounding the following research questions addressed in the NICE document:

- For people with lumps suspicious of sarcoma, does referral to a specialist sarcoma unit or multidisciplinary team (MDT) improve the rate of preoperative diagnosis?
- Does diagnosis by a specialist sarcoma pathologist compared with a general pathologist of sarcoma lead to greater diagnostic accuracy?
- Should all patients with sarcoma be reviewed by a specialist MDT?
- Does hospital case volume have an effect on outcomes for patients with sarcoma?
- Are outcomes better for patients with suspected bone sarcoma treated in specialist sarcoma units than for those treated in non-specialist units?
- Are outcomes (surgical margins, local control, patient experience, and survival) better for people with suspected limb, limb girdle, or truncal soft tissue sarcoma treated in specialist sarcoma units than for those treated in non-specialist units?
- Are outcomes better for patients with suspected abdominal or pelvic soft tissue sarcoma treated in specialist sarcoma units than for those treated in non-specialist units?

Update Search Strategy

The search strategies used by NICE in conducting their systematic review were obtained (Appendix 1). As the NICE systematic review covered evidence published up to 2006, these search strategies were used to identify evidence published from January 2006 to April 2009 in both MEDLINE and Embase. Relevant articles were selected and reviewed by one reviewer, and the reference lists from those sources were searched for additional studies.

Study Selection Criteria

Articles were selected for inclusion in the systematic review if they were published, English-language reports about the quality and care of sarcoma treatment. Letters, editorials, notes, case reports, and commentaries were not eligible. Translation capabilities were not available; therefore, articles published in a language other than English were excluded.

Synthesizing the Evidence

No meta-analysis was planned, as the a priori expectation was that no clinically homogenous studies with outcomes amenable to useful meta-analysis would be identified.

RESULTS

Initial Search for Existing Systematic Reviews

Literature Search Results

Two systematic reviews were identified that was relevant to the initial research question (2,3). The review by NICE (2) included all the studies in the review by Perez Romasanta et al (3), as well as additional studies. Therefore, the review by Perez Romasanta et al will not be discussed further in this document. The NICE review was conducted as part of the development of a practice guideline. The guideline portion of the NICE document was not formally evaluated or included in this systematic review; only its evidence base was considered.

Table 1. AMSTAR evaluation of NICE systematic review.

1. **Was an 'a priori' design provided? Yes**
2. **Was there duplicate study selection and data extraction? No**
3. **Was a comprehensive literature search performed? Yes**
4. **Was the status of publication (i.e., grey literature) used as an inclusion criterion? No (all relevant literature was searched)**
5. **Was a list of studies (included and excluded) provided? No (no excluded list)**
6. **Were the characteristics of the included studies provided? Yes**
7. **Was the scientific quality of the included studies assessed and documented? Yes**
8. **Was the scientific quality of the included studies used appropriately in formulating conclusions? Yes**
9. **Were the methods used to combine the findings of studies appropriate? Not applicable (Due to the nature of the studies identified by NICE, a meta-analysis would not be appropriate.)**
10. **Was the likelihood of publication bias assessed? Not applicable (Due to the nature of the evidence identified by NICE, a formal evaluation of publication bias would not be feasible.)**
11. **Was the conflict of interest stated? No (The document states that the Guideline Development Group made "declarations of interest," but no reporting of this declaration was found in the document or on the NICE website.)**

The data reported in the NICE systematic review are summarized below. Based on the timeliness and quality of the NICE systematic review, it was used as the basis for this document, and additional research questions were considered as described above.

Update to the NICE Systematic Review

Four additional studies published in 2006 or later were identified in the update literature search that used the NICE search strategies (4-7). The newly identified studies are described in detail in Appendix 2. All of the newly identified studies were nonrandomized studies similar in design and size to those already identified by NICE.

OUTCOMES

In the summaries of the data identified in the NICE systematic review, below, the intent is not to provide a complete description of that data but to present a brief overview of the most important elements. The reader is encouraged to review the relevant tables and sections of the NICE systematic review directly to see all of the important evidence this review contains.

The NICE systematic review classified the vast majority of the studies it identified as "case series," with the majority of those being additionally classified as "retrospective." Very few were considered "prospective." Few studies were classified as "cohort" instead of "case series." The size of the included studies ranged from studies with fewer than 50 patients to large population-based studies with more than 1,000 patients.

For people with lumps suspicious of sarcoma, does referral to a specialist sarcoma unit or MDT improve the rate of preoperative diagnosis?

NICE Systematic Review

The NICE systematic review reported on eight studies that looked at the results of biopsies in relation to the type of centre in which the procedure was performed (2). These studies are described in detail in Table 2a of the NICE review. Complications or negative alternations in the treatment plan occurred more frequently in biopsies that were done outside specialist centres. However, none of these studies took into account the confounding effect of case mix between the centres. Some patients may have had superficial tumours that were not sarcoma, some patients may have initially been treated at the small centre and then transferred to a specialist centre, and patients with difficult tumours might not be representative of the patients treated at a smaller centre (2).

Table 2. Biopsy complication rates between specialist and non specialist centres.*

Author	Specialist centre	Non-specialist centre
Mankin 1996 (8)	4.1%	17.4%
Grimer 1990 (9)	5%	60%
Pollock 2004 (10)	2%	38%
Serpell 1998 (11)	0%	63%

* Source: NICE systematic review (2)

PEBC Update

No new studies relevant to this question were found in the updated search.

Does diagnosis by a specialist sarcoma pathologist compared with a general pathologist of sarcoma lead to greater diagnostic accuracy?

NICE Systematic Review

The NICE systematic review examined sixteen studies that analyzed whether a diagnosis by a specialist sarcoma pathologist led to greater accuracy than that by a general pathologist (2). These studies are described in detail in Table 3 of the NICE review. The change in diagnosis from sarcoma to that of non-sarcoma upon expert review ranged from 3-22% in the cases examined. The change in diagnosis of the subtype of sarcoma upon expert review ranged from 16-39% in the cases examined.

The NICE systematic review also reported that six studies examined how often the expert pathologist disagreed with the recorded tumour grade in the original histopathological report. These studies are also described in detail in Table 3 of the NICE review. The rate of disagreement was between 24 and 40%.

Finally, the NICE systematic review also reported on two studies that examined the change in diagnosis according to biopsy. The study by Mankin et al (8) reported that the lower diagnostic error rate was observed at musculoskeletal treatment centres (13%) compared to referring institutions (24%). The other study was part of the European Osteosarcoma intergroup clinical trial (9). They discovered that 2% of the subjects randomized were ineligible due to incorrect pathology.

Further data from the studies included in the NICE systematic review are summarized in Table 3, below.

Table 3: Change in diagnosis on review by specialist sarcoma pathologist.*

Authors Date (Reference)	Diagnosis changed on review		
	To non-sarcoma	Sarcoma subtype	Grade
Alvegard 1989 (13)	5%	20%	40%
Arbiser 2001 (14)	11%	-	-
Coindre 1986 (15)	-	39%	24%
Harris 1997 (16)	22%	39%	-
Meis-Kindblom 1999 (17)	5%	20%	25%
Presant 1986 (18)	6%	34%	24%
Shiraki 1989 (19)	10%	16%	-
Tetu 1984 (20)	-	35%	-
Randall 2004 (21)	3%	32%	25%
Remagen 1992 (22)	5%	19%	-
van Dalen 2000 (23,31)	4%	24%	36%
Grimer 2001 (9)	Major errors occurred in 4% of cases		
	Under-diagnosis occurred in 1% of cases		
	Over-diagnosis occurred in 2% of cases		
	Significant change in management of 3% of patients occurred		
Mankin 1996 (8)	Error in diagnosis (specialist centre vs. referring centre) 39/316 vs. 77/282 (13.3% vs. 27.4%, RR: 0.45)		
Stiller 2000 (24)	Diagnosis of 1317 patients reviewed. Error rate = 12%		
Barlow 1994 (25)	In 8% (11/145) of cases diagnosis differed with important clinical implications		
Souhami 1997 (12)	2% of patients referred to clinical trial ineligible due to pathology error		

Abbreviation: RR- relative risk; vs.- versus.
* Source: NICE systematic review (2)

PEBC Update

The updated search by the PEBC found one study additional study by Lenhardt et al (6) This study confirmed the proper primary diagnosis in 28.3% of cases for pathologists in private clinics, 29.6% for hospital pathologists, 36.8% for academic medical centres (university hospitals), and 70.5% for the department of pathology at the Name of Institution (Author's Initial. An improvement in diagnosis or confirmation of the correct primary diagnosis was seen in 73.1% of patients; on 2.5%, the second opinion was false.

Should all patients with sarcoma be reviewed by a specialist MDT? (NICE systematic review, Table 4a)

NICE Systematic Review

The NICE systematic review identified five studies that used cancer registries and/or hospital records to compare the outcomes of patients reviewed by a sarcoma MDT with those not reviewed by such an MDT (2). Only one study adjusted for differences in case mix in its analyses. The full details of these studies are included in Table 4a in the NICE systematic review.

NICE concluded from their systematic review that there was consistent evidence from these studies not only that outcomes are better in patients with soft tissue sarcoma (STS) managed by a specialist MDT, but also that it was unclear to what extent MDT management is

responsible for this difference. There was evidence of an overall survival advantage for those people with STS reviewed by a sarcoma MDT in the three retrospective studies that reported this outcome. Bhangu et al (26) reported a hazard ratio for death of 0.59 (95% confidence interval, 0.35 to 0.99) in patients treated by a MDT versus those that were not. Paszat et al (27) reported a relative risk of death of 1.4 (95% confidence interval, 1.1 to 1.7) in patients not receiving care from an MDT versus those that do. Finally, Wiklund et al (28) found a three-year, disease-free survival of 69% in patients treated at an institution after implementation of an MDT versus 36% in patients in the same institution before the implementation of the MDT.

PEBC Update

One additional study by Aksnes et al (7). This study found that the sarcoma-specific, disease-free survival time for all patients treated by a MDT has increased from 39% to 53% at five years comparing the two subsequent 10-year periods (p=0.03)

Does hospital case volume have an effect on outcomes for patients with sarcoma?

NICE Systematic Review

The NICE systematic review identified four studies addressing the question of hospital volumes in relation to sarcoma care (2). These studies are described in detail in Table 4b of the NICE systematic review. NICE reported that they did not define high case volumes a priori in including these studies, but rather used the criteria of the studies themselves; as NICE reported, in reality sarcoma is a rare enough condition that few if any hospitals can be considered truly high volume. According to the study by Paszat et al (27), the case volume of the hospital providing treatment was not statistically associated with a risk of amputation or overall survival. Stiller et al (24) reported that the hospital case volume had a beneficial effect for people with Ewing's sarcoma but not with osteosarcoma. van Dalen et al (23) reported that retroperitoneal STS patients treated in higher volume hospitals were more likely to receive a complete resection of their tumour but no effect on survival was observed. However, this could be due to better preoperative assessment and selection of candidates for surgery in the higher volume hospitals. Nijhuis et al (29) reported that better adherence to guidelines for the diagnosis of soft tissue tumours greater than 3cm was seen in district hospitals treating more than two patients per year.

PEBC Update

One additional study by (4) was identified in the update search. This study reported on 4,205 STS cases and examined the differences in hospital case volumes and outcomes. The key findings regarding mortality and amputation rate from this study are described in Table 4, below. The study also reported on median, five-year, and ten-year survival, finding significant differences in ten-year survival between high- and low-volume centres for trunk and retroperitoneal sarcoma and lipsosarcoma, among other comparisons; see Appendix 2 for the details of these data.

Table 4. Mortality and amputation rates in low- versus high-volume centres.*

Outcome	Low-volume centre (n=2865; 68.1%)	High-volume centre (n=1340; 31.9%)	p value
30-day mortality	1.50%	0.70%	0.028
90-day mortality	3.60%	1.60%	<0.001
Amputation rate	13.80%	9.40%	0.048

* Source: Gutierrez et al (4)

Are outcomes better for patients with suspected bone sarcoma treated in specialist sarcoma units than for those treated in non specialist units?

NICE Systematic Review

The NICE systematic review identified three studies that reported patient outcomes for suspected bone sarcoma in relation to MDT care (2). These studies are described in detail in Table 5 of the NICE systematic review. Stiller et al (24) was a relatively large retrospective cohort study of 2,843 patients. It reported statistically significant differences in relative risk of death between specialist treatment centres and non-specialist centres in the UK for patients with osteosarcoma and Ewing's sarcoma. The limited evidence from one cohort and two observational studies suggested that overall survival was better for patients treated in specialist centres. Bergh et al (26) reported that, in patients with pelvic, sacral, and spinal chondrosarcomas, they found statistically significant differences in both local recurrence and tumour-related death in patients whose surgery was conducted at a specialist tumour centre compared to those whose surgery was conducted outside the tumour centre. Finally, Pollock and Stalley (10) found higher complication rates in patients treated in a specialist centre compared to those that were not.

PEBC Update

Two additional studies were found in the update (5,7). The data from the study by Aksnes et al were described above (7). Stiller et al reported in 2006 on five-year survival rates of patients with osteosarcoma or Ewing's sarcoma treated at several different types of institutions in the UK (5). This data is summarized in Table 5, below.

Table 5. Five-year survival of bone sarcoma patients treated at different types of institutions in the UK.*

Time period	N	Five-year survival					
		Bone tumour services	UK children's cancer study group	Other teaching	Non-teaching	Unknown	p
1980-1984	469	50%	51%	38%	37%	34%	0.0092
1985-1989	428	54%	58%	54%	37%	76%	0.077
1990-1994	400	49%	55%	55%	44%	56%	0.49

* Source: Stiller et al (5)

Are outcomes (surgical margins, local control, patient experience, and survival) better for people with suspected limb, limb girdle, or truncal STS treated in specialist sarcoma units than for those treated in non-specialist units?

NICE Systematic Review

The NICE systematic review identified twelve studies that reported patient outcomes for suspected limb, limb girdle, or truncal STS in relation to MDT care (2). These studies are described in detail in Table 6 of the NICE systematic review. Five of the six studies that reported on surgical margins found that adequate margins were more likely in patients treated at specialist centres; one study found no difference. Five studies reported on the local recurrence of sarcoma and found it to be less likely when the surgery was performed in

a specialist treatment centre. Two studies that adjusted for case mix reported that people with STS treated at specialist centres have better overall survival. Two studies that were unadjusted for case mix did not report a survival advantage for those treated at specialist centres. NICE suggested that this discrepancy might be caused by the fact that there were a greater proportion of patients with poor prognosis among those treated at specialist centres than among those treated at non-specialist centres (2).

PEBC Update

No additional studies were found that reported on differences in outcome between specialist MDT and non-specialist care for limb, limb girdle, or truncal STS.

Are outcomes better for patients with suspected abdominal or pelvic soft tissue sarcoma treated in specialist sarcoma units than for those treated in non specialist units? (NICE systematic review, Table 8)

NICE Systematic Review

The NICE systematic review identified one study that reported patient outcomes for suspected abdominal or pelvic soft tissue sarcoma in relation to MDT care (2). The study by van Dalen et al (31) found a statistically significant difference in overall survival between patients treated at a tertiary referral centre compared to those treated elsewhere. The NICE systematic review identified another study that it categorized as relevant to this question, but on review this study classifies the treatment centre according to high- versus low-volume, not specialist care, and therefore is not reported here. Due to the dearth of evidence, the NICE review also included data from 25 institutional case series; these data are not summarized here.

PEBC Update

No additional studies were found that reported on differences in outcome between specialist MDT and non-specialist care for abdominal or pelvic soft tissue sarcoma.

ONGOING TRIALS

As no studies identified to date have been prospectively planned clinical trials, it is difficult to search for studies that would meet the inclusion criteria for this review that might be ongoing or as yet unpublished, because there is no relevant registry or database. However, a search was conducted of the United States National Cancer Institute Clinical Trials Database (http://www.cancer.gov/clinicaltrials/search/) of multiple sarcomas, using the words "specialist", "multidisciplinary", and "volume," but no active or closed trials were identified.

DISCUSSION

The evidence identified by the NICE systematic review, as well as the update to this review performed by PEBC, is limited both in the number of studies and their quality. However, the evidence is consistent. A wide range of measures, including overall survival, have been reported as improved in patients with sarcoma who are treated with specialist care compared to those who do not received specialist care.

CONFLICT OF INTEREST

No conflicts of interest were declared for C. Catton, N. Coakley, S. Verma, H. Messersmith, or M. Trudeau.

ACKNOWLEDGEMENTS

The authors would like to thank S. Hertz and the members of the Sarcoma Expert Panel and the Working Group (Appendix 3) for their assistance in the development of this evidence summary.

For a complete list of the Sarcoma DSG members, please visit the CCO website at http://www.cancercare.on.ca/

Funding

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

Contact Information

For further information about this report, please contact:

Dr. Charles Catton, Princess Margaret Hospital
610 University Ave., Toronto, ON M5G 2L7
Phone: 416-946-2121 E-mail: charles.catton@rmp.uhn.on.ca
or
Dr. Maureen Trudeau, Cancer Care Ontario,
620 University Ave., Toronto, ON M5G 2L7
Phone: 416-480-5145 E-mail: maureen.trudeau@sunnybrook.ca

For information about the PEBC and the most current version of all reports, please visit the CCO website at http://www.cancercare.on.ca or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: ccopgi@mcmaster.ca

REFERENCES

1. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007;7(10).
2. National Institute for Health and Clinical Excellence (NICE). Improving outcomes for people with sarcoma: guidance recommendations [Internet]. London: National Institute for Health and Clinical Excellence; 2006 Mar [cited 2009 May 22]. Available from: http://www.nice.org.uk/nicemedia/pdf/CSG_sarcoma_recommendations.pdf.
3. Perez Romasanta LA, Luis AM, Capdevila RV, Cotelo AM, Rico Perez JM. Centralised treatment of soft tissue sarcomas in adults. Clin Transl Oncol. 2008;10(2):102-10.
4. Gutierrez JC, Perez EA, Moffat FL, Livingstone AS, Franceschi D, Koniaris LG. Should soft tissue sarcomas be treated at high-volume centers? An analysis of 4205 patients. Ann Surg. 2007;245(6):952-8.
5. Stiller CA, Passmore SJ, Kroll ME, Brownbill PA, Wallis JC, Craft AW. Patterns of care and survival for patients aged under 40 years with bone sarcoma in Britain, 1980-1994. Br J Cancer. 2006;94(1):22-9.
6. Lehnhardt M, Daigeler A, Hauser J, Puls A, Soimaru C, Kuhnen C, et al. The value of expert second opinion in diagnosis of soft tissue sarcomas. J Surg Oncol. 2008;97(1):40-3.
7. Aksnes LH, Hall KS, Folleraa G, Stenwig AE, Bjerkehagen B, Taksdal I, et al. Management of high-grade bone sarcomas over two decades: the Norwegian Radium Hospital experience. Acta Oncol. 2006;45(1):38-46.
8. Mankin HJ, Mankin CJ, Simon MA. The hazards of the biopsy, revisited. Members of the Musculoskeletal Tumor Society [see comment]. J Bone Joint Surg Am. 1996;78(5):656-63.
9. Grimer RJ, Carter SR, Spooner D, Sneath RS. Diagnosing musculoskeletal tumours. Sarcoma. 2001;2:89-94.
10. Pollock RE, Stalley PD. Biopsy of musculoskeletal tumours - beware. ANZ J Surg. 2004 Jul;74(7):516-9.
11. Serpell JW, Pitcher ME. Pre-operative core biopsy of soft-tissue tumours facilitates their surgical management. ANZ J Surg. 1998;68:345-349.
12. Souhami RL, Craft AW, Van der Eijken JW, Nooij M, Spooner D, Bramwell VH, et al. Randomised trial of two regimens of chemotherapy in operable osteosarcoma: a study of the European Osteosarcoma Intergroup [see comment]. Lancet. 1997;350(9082):911-7.
13. Alvegard TA, Berg NO. Histopathology peer review of high-grade soft tissue sarcoma: the Scandinavian Sarcoma Group experience. J Clin Oncol. 1989;7(12):1845-51.
14. Arbiser ZK, Folpe AL, Weiss SW. Consultative (expert) second opinions in soft tissue pathology. Analysis of problem-prone diagnostic situations. Am J Clin Pathol. 2001;116(4):473-6.
15. Coindre JM, Trojani M, Contesso G, David M, Rouesse J, Bui NB, et al. Reproducibility of a histopathologic grading system for adult soft tissue sarcoma. Cancer. 1986;58(2):306-9.
16. Harris M, Hartley AL. Value of peer review of pathology in soft tissue sarcomas. Cancer Treat Res. 1997;91:1-8.
17. Meis-Kindblom JM, Bjerkehage B, Bohling T, Domanski H, Halvorsen TB, Larsson O, et al. Morphologic review of 1000 soft tissue sarcomas from the Scandinavian Sarcoma Group (SSG) Register. The peer-review committee experience. Acta Orthop Scand. 1999;70(285):18-26.

18. Presant CA, Russell WO, Alexander RW, Fu YS. Soft-tissue and bone sarcoma histopathology peer review: the frequency of disagreement in diagnosis and the need for second pathology opinions. The Southeastern Cancer Study Group experience. J Clin Oncol. 1986;4(11):1658-61.
19. Shiraki M, Enterline HT, Brooks JJ, Cooper NS, Hirschl S, Roth JA, et al. Pathologic analysis of advanced adult soft tissue sarcomas, bone sarcomas, and mesotheliomas. The Eastern Cooperative Oncology Group (ECOG) experience. Cancer. 1989;64(2):484-90.
20. Tetu B, Hunt A, Mc Caughey WT, Lagace R. [Evaluation of the differences of opinion in the histopathologic diagnosis of soft tissue tumors] [French]. Ann Pathol.1984;4(4):267-71.
21. Randall RL, Bruckner JD, Papenhausen MD, Thurman T, Conrad EU, III. Errors in diagnosis and margin determination of soft-tissue sarcomas initially treated at non-tertiary centers. Orthopedics. 2004;27(2):209-12.
22. Remagen W. Importance of reference registries in bone tumor diagnosis [German]. Z Orthop Ihre Grenzgeb. 1992;130(4):267-8.
23. van Dalen T. Management of soft tissue sarcoma in the retroperitoneal space: a popluation based study in the Netherlands. Sarcoma. 2001;5:5-8.
24. Stiller CA, Passmore SJ, Brownbill PA, Kroll ME, Wallis JC, Craft AW. Patterns of care and survival for patients with bone sarcoma. Project NCP/E16. London: NHS National Cancer Research and Development Programme; 2000.
25. Barlow IW, Newman RJ. Primary bone tumours of the shoulder: an audit of the Leeds Regional Bone Tumour Registry. J R Coll Surg Edinb.1994;39(1):51-4.
26. Bhangu AA, Beard JAS, Grimer RJ. Should soft tissue sarcomas be treated at a specialist centre? Sarcoma. 2004;8(1):1-6.
27. Paszat L, o'Sullivan B, Bell R, Bramwell V, Groome P, Mackillop W, et al. Processes and outcomes of care for soft tissue sarcoma of the extremities. Sarcoma. 2002;6(1):19-26.
28. Wiklund T, Huuhtanen R, Blomqvist C, Tukiainen E, Virolainen M, Virkkunen P, et al. The importance of a multidisciplinary group in the treatment of soft tissue sarcomas. Eur J Cancer. 1996;32A(2):269-73.
29. Nijhuis PH, Schaapveld M, Otter R, Hoekstra HJ. Soft tissue sarcoma—compliance with guidelines. Cancer. 2001;91(11):2186-95.
30. Bergh P, Gunterberg B, Meis-Kindblom JM, al e. Prognostic factors and outcome of pelvic, sacral, and spinal chondrosarcomas: a center-based study of 69 cases. Cancer. 2001;91:1201-12.
31. van Dalen T, Hennipman A, van CF, Hoekstra HJ, van Geel BN, Slootweg P, et al. Evaluation of a clinically applicable post-surgical classification system for primary retroperitoneal soft-tissue sarcoma. Ann Surg Oncol. 2004;11(5):483-90.

Appendix 1. NICE search strategies.

MAIN SARCOMA SEARCH STRATEGY

MEDLINE and EBM Reviews

1. exp "Neoplasms, Connective and Soft Tissue"/
2. sarcoma$.tw.
3. Sarcoma, Alveolar Soft Part/
4. exp Myosarcoma/
5. myosarcoma$.tw.
6. rhabdomyosarcoma$.tw.
7. angiosarcoma$.tw.
8. (hemangiosarcoma$ or haemangiosarcoma$).tw.
9. lymphangiosarcoma$.tw.
10. (stewart-treves adj (tumo?r$ or sarcoma$ or syndrome)).tw.
11. (hemangiopericytoma$ or haemangiopericytoma$).tw.
12. adenosarcoma$.tw.
13. cystosarcoma$.tw.
14. phyllodes.tw.
15. fibroadenoma$.tw.
16. dermatofibrosarcoma$.tw.
17. fibrosarcoma$.tw.
18. gastrointestinal stromal tumo?r$.tw.
19. GIST.tw.
20. leiomyosarcoma$.tw.
21. liposarcoma$.tw.
22. malignan$ fibrous histiocytoma$.tw.
23. MFH.tw.
24. malignan$ peripheral nerve sheath tumo?r$.tw.
25. MPNST.tw.
26. myxosarcoma$.tw.
27. neurofibrosarcoma$.tw.
28. synovioma$.tw.
29. adamantinoma$.tw.
30. ewing$.tw.
31. primitive neuroectodermal tumo?r$.tw.
32. PNET$1.tw.
33. chondrosarcoma$.tw.
34. mesenchymoma$.tw.
35. osteoclastoma$.tw.
36. osteosarcoma$.tw.
37. malignan$ giant cell tumo?r$.tw.
38. sarcoma$.jw.
39. (chordoma adj sacrum).tw.
40. (retroperitoneal adj sarcoma$).tw.
41. (dermatofibrosarcoma protuberan$ or DFSP$1).tw.
42. uterine sarcoma$.tw.
43. (mullerian adenosarcom$ or malignant mullerian mixed tumo?r$ or MMMT or malignant mesoderm$ mixed tumo?r$).tw.
44. (endometrial stromal sarcoma$ or endometrial stromal tumo?r$).tw.
45. metaplastic carcin$.tw.
46. carcinosarcoma$.tw.
47. endometrial carcinoma$.tw.
48. (ovarian sarcoma$ or vulva$ sarcoma$).tw.
49. gyn?ecolog$ sarcoma$.tw.
50. or/1-49

EMBASE

1. exp Soft Tissue Tumor/
2. Gastrointestinal Stromal Tumor/
3. Osteosarcoma/
4. exp Connective Tissue Tumor/
5. exp Sarcoma/
6. sarcoma$.tw.
7. Alveolar Soft Part Sarcoma/
8. exp Myosarcoma/
9. myosarcoma$.tw.
10. rhabdomyosarcoma$.tw.
11. angiosarcoma$.tw.
12. (hemangiosarcoma$ or haemangiosarcoma$).tw.
13. lymphangiosarcoma$.tw.
14. (stewart-treves adj (tumo?r$ or sarcoma$ or syndrome)).tw.
15. (hemangiopericytoma$ or haemangiopericytoma$).tw.
16. adenosarcoma$.tw.
17. cystosarcoma$.tw.
18. phyllodes.tw.
19. fibroadenoma$.tw.
20. dermatofibrosarcoma$.tw.
21. fibrosarcoma$.tw.
22. gastrointestinal stromal tumo?r$.tw.
23. GIST.tw.
24. leiomyosarcoma$.tw.
25. liposarcoma$.tw.
26. malignan$ fibrous histiocytoma$.tw.
27. MFH.tw.
28. malignan$ peripheral nerve sheath tumo?r$.tw.
29. MPNST.tw.
30. myxosarcoma$.tw.
31. neurofibrosarcoma$.tw.
32. synovioma$.tw.
33. adamantinoma$.tw.
34. ewing$.tw.
35. primitive neuroectodermal tumo?r$.tw.
36. PNET$1.tw.
37. chondrosarcoma$.tw.
38. mesenchymoma$.tw.
39. osteoclastoma$.tw.
40. osteosarcoma$.tw.
41. malignan$ giant cell tumo?r$.tw.
42. sarcoma$.jw.
43. (chordoma adj sacrum).tw.
44. (retroperitoneal adj sarcoma$).tw.
45. (dermatofibrosarcoma protuberan$ or DFSP$1).tw.
46. uterine sarcoma$.tw.
47. (mullerian adenosarcom$ or malignant mullerian mixed tumo?r$ or MMMT or malignant mesoderm$ mixed tumo?r$).tw.
48. metaplastic carcin$.tw.
49. (endometrial stromal sarcoma$ or endometrial stromal tumo?r$).tw.
50. carcinosarcoma$.tw.
51. (ovarian sarcoma$ or vulva$ sarcoma$).tw.
52. gyn?ecolog$ sarcoma$.tw.
53. or/1-52

SARCOMA SPECIALIST SEARCH STRATEGY

MEDLINE and EBM Reviews – Sarcoma set plus

1. (specialist$ adj2 patholog$).tw.
2. ((speciali?ed or speciali?ing) adj2 patholog$).mp.
3. (experience$ adj2 patholog$).tw.
4. ((non-specialist$ or nonspecialist$ or general$ or inexperience$ or unexperience$) adj2 patholog$).tw.
5. ((histopatholog$ or cytopatholog$ or cellular) adj2 patholog$).tw.
6. ((musculoskeletal adj2 patholog$) or (cardiac adj2 patholog$)).tw.
7. or/1-6
8. exp Diagnosis/ or exp Early Diagnosis/
9. (diagnos$ or early diagnos$ or accurate diagnos$ or correct diagnos$).tw.
10. (misdiagnos$ or incorrect diagnos$ or missed diagnos$ or false diagnos$ or inaccurate diagnos$ or wrong diagnos$).tw.
11. complication$.tw.
12. exp Diagnostic Errors/
13. or/8-12
14. 7 and 13
15. sarcoma set and 14

EMBASE – Sarcoma set plus

1. (specialist$ adj2 patholog$).tw.
2. ((speciali?ed or speciali?ing) adj2 patholog$).mp.
3. (experience$ adj2 patholog$).tw.
4. ((non-specialist$ or nonspecialist$ or general$ or inexperience$ or unexperience$) adj2 patholog$).tw.
5. ((histopatholog$ or cytopatholog$ or cellular) adj2 patholog$).tw.
6. ((musculoskeletal adj2 patholog$) or (cardiac adj2 patholog$)).tw.
7. or1-7
8. exp Diagnosis/ or exp Early Diagnosis/
9. (diagnos$ or early diagnos$ or accurate diagnos$ or correct diagnos$).tw.
10. (misdiagnos$ or incorrect diagnos$ or missed diagnos$ or false diagnos$ or inaccurate diagnos$ or wrong diagnos$).tw.
11. complication$.tw.
12. exp Diagnostic Errors/
13. or/8-12
14. 7 and 13
15. sarcoma set and 14

SARCOMA DIAGNOSTIC SERVICES AND BONE SURGERY SEARCH STRATEGY

MEDLINE and EBM Reviews

1. exp bone neoplasms/su
2. exp neoplasms, bone tissue/su
3. (malignan$ and bone$).tw.
4. osteosarcom$.tw.
5. chondrosarcoma$.tw.
6. small round cell tumo?r$.tw.
7. ewing$.tw.
8. malignan$ giant cell tumo?r$.tw.
9. primary bone lymphoma$.tw.
10. malignan$ fibrous histiocytoma$.tw.
11. mesenchymal chondrosarcoma$.tw.
12. (hemangiothelioma$ or haemangiothelioma$).tw.
13. (hemangiopericytoma$ or haemangiopericytoma$).tw.
14. angiosarcoma$.tw.

15. fibrosarcoma$.tw.
16. liposarcoma$.tw.
17. malignan$ mesenchymoma$.tw.
18. chordoma$.tw.
19. adamantinoma$.tw.
20. or/1-19
21. (surgery or surgical$ or operation$ or resection$ or excision$).tw.
22. 20 and 21
23. exp Sarcoma/ra
24. exp Diagnostic Imaging/
25. X-Rays/
26. (x-ray$ or xray$ or x ray$).tw.
27. exp Tomography, X-Ray Computed/
28. exp Tomography, Emission-Computed/
29. (ct scan$ or CT scan$).tw.
30. (computed tomography scan$ or computeri?ed tomography scan$).tw.
31. Magnetic Resonance Imaging/
32. (mri scan$ or magnetic resonance imaging$).tw.
33. isotope scan$.tw.
34. bone scan$.tw.
35. ultrasound$.tw.
36. exp Histological Techniques/
37. histopathol$.tw.
38. cytopathol$.tw.
39. (histol$ adj pathol$).tw.
40. staging.tw.
41. exp Diagnostic Techniques, Surgical/
42. exp Biopsy/
43. excision biops$.tw.
44. (core needle biops$ or needle biops$ or fine needle biops$).tw.
45. incisional biops$.tw.
46. bone biops$.tw.
47. aspiration.tw.
48. percutaneous needle$.tw.
49. or/23-48
50. (unit$ or centre$ or center$ or service$ or clinic1$ or facilit$).tw.
51. 49 and 50
52. 51 or (exp diagnostic services/ or diagnostic services.tw.)
53. 22 and 52

EMBASE

1. exp bone neoplasms/su
2. exp neoplasms, bone tissue/su
3. (malignan$ and bone$).tw.
4. osteosarcom$.tw.
5. chondrosarcoma$.tw.
6. small round cell tumo?r$.tw.
7. ewing$.tw.
8. malignan$ giant cell tumo?r$.tw.
9. primary bone lymphoma$.tw.
10. malignan$ fibrous histiocytoma$.tw.
11. mesenchymal chondrosarcoma$.tw.
12. (hemangiothelioma$ or haemangiothelioma$).tw.
13. (hemangiopericytoma$ or haemangiopericytoma$).tw.
14. angiosarcoma$.tw.

15. fibrosarcoma$.tw.
16. liposarcoma$.tw.
17. malignan$ mesenchymoma$.tw.
18. chordoma$.tw.
19. adamantinoma$.tw.
20. or/1-19
21. (surgery or surgical$ or operation$ or resection$ or excision$).tw.
22. 20 and 21
23. [exp Sarcoma/ra]
24. exp Diagnostic Imaging/
25. X-Rays/
26. (x-ray$ or xray$ or x ray$).tw.
27. exp Tomography, X-Ray Computed/
28. exp Tomography, Emission-Computed/
29. (ct scan$ or CT scan$).tw.
30. (computed tomography scan$ or computeri?ed tomography scan$).tw.
31. Magnetic Resonance Imaging/
32. (mri scan$ or magnetic resonance imaging$).tw.
33. isotope scan$.tw.
34. bone scan$.tw.
35. ultrasound$.tw.
36. exp Histological Techniques/
37. histopathol$.tw.
38. cytopathol$.tw.
39. (histol$ adj pathol$).tw.
40. staging.tw.
41. exp Diagnostic Techniques, Surgical/
42. exp Biopsy/
43. excision biops$.tw.
44. (core needle biops$ or needle biops$ or fine needle biops$).tw.
45. incisional biops$.tw.
46. bone biops$.tw.
47. aspiration.tw.
48. percutaneous needle$.tw.
49. or/23-48
50. (unit$ or centre$ or center$ or service$ or clinic1$ or facilit$).tw.
51. 49 and 50
52. 51 or (exp diagnostic services/ or diagnostic services.tw.)
53. 22 and 52

MULTIDISCIPLINARY TEAM SEARCH STRATEGY
MEDLINE and EMB Reviews – Sarcoma set plus

1. Physician's Practice Patterns/
2. exp Interprofessional Relations/
3. multiprofession$.tw.
4. (multi-profession$ or multi profession$).tw.
5. multidisciplinary.tw.
6. (multi-disciplinary or multi disciplinary).tw.
7. interprofession$.tw.
8. (inter-professional$ or inter profession$).tw.
9. crossdisciplinary.tw.
10. (cross-disciplinary or cross disciplinary).tw.
11. exp Nurses/
12. Oncologic Nursing/
13. nurs$ specialist$.tw.

14. oncology$ nurs$.tw.
15. exp Patient Care Team/
16. assessment$ team$.tw.
17. specialist$ team$.tw.
18. skill$ mix$.tw.
19. (skillmix$ or skill$-mix$).tw.
20. cancer network$.tw.
21. team meetings$.tw.
22. management plan$.tw.
23. Patient-Centered Care/
24. Continuity of Patient Care/
25. exp Delivery of Health Care, Integrated/
26. (integrated adj2 care).tw.
27. teamwork$.tw.
28. (team-work$ or team work$).tw.
29. or/1-28
30. sarcoma set and 29

EMBASE – Sarcoma set plus

1. Clinical Practice/
2. multiprofession$.tw.
3. multi-profession$.tw.
4. (multi adj profession$).tw.
5. multidisciplinary.tw.
6. multi-disciplinary.tw.
7. (multi adj disciplinary).tw.
8. interprofession$.tw.
9. inter-profession$.tw.
10. (inter adj profession$).tw.
11. crossdisciplinary.tw.
12. cross-disciplinary.tw.
13. (cross adj disciplinary).tw.
14. Nurse/ or Nursing/
15. (nurs$ adj specialist$).tw.
16. (specialist$ adj nurs$).tw.
17. (oncology$ adj1 nurs$).tw.
18. (assessment$ adj team$).tw.
19. (specialist$ adj team$).tw.
20. (patient adj care adj team$).tw.
21. (skill$ adj mix$).tw.
22. (skillmix$ or skill$-mix$).tw.
23. (cancer adj network$).tw.
24. (team adj meeting$).tw.
25. (patient-cent?red adj care).tw.
26. (patient adj cent?red adj care).tw.
27. (continuity adj2 patient adj care).tw.
28. (integrated adj2 care).tw.
29. teamwork$.tw.
30. team-work$.tw.
31. (team adj work$).tw.
32. or/1-31
33. sarcoma set and 32

SPECIALIST SERVICES SEARCH STRATEGY

MEDLINE and EBM Reviews – Sarcoma set plus

1. exp Hospitals, Special/
2. Oncology Service, Hospital/
3. Specialism/
4. specialist$.tw.
5. (speciali?ed or speciali?ing).tw.
6. (special$ adj (unit$ or centre$ or center$ or hospital$ or clinic$1)).tw.
7. (special$ adj (facilit$ or team$ or service$)).tw.
8. (single adj (unit$ or centre$ or center$ or clinic$1)).tw.
9. (sarcoma$ adj (unit$ or centre$ or center$ or clinic$1)).tw.
10. (sarcoma$ adj (facilit$ or team$ or service$)).tw.
11. ((specialist$ or speciali?ed) adj2 experience).tw.
12. (soft tissue adj (unit$ or centre$ or center$ or service$)).tw.
13. (bone tumo?r$ adj (unit$ or centre$ or center$ or service$)).tw.
14. ((cancer or oncology) adj (unit$ or centre$ or center$ or service$ or team$)).tw.
15. (non-specialist$ or nonspecialist$).tw.
16. or/1-16
17. plus main sarcoma set

EMBASE – Sarcoma set plus

1. Cancer Center/
2. Medical Profession/
3. specialist$.tw.
4. (speciali?ed or speciali?ing).tw.
5. (special$ adj (unit$ or centre$ or center$ or hospital$ or clinic$1)).tw.
6. (special$ adj (facilit$ or team$ or service$)).tw.
7. (single adj (unit$ or centre$ or center$ or clinic$1)).tw.
8. (sarcoma$ adj (unit$ or centre$ or center$ or clinic$1)).tw.
9. (sarcoma$ adj (facilit$ or team$ or service$)).tw.
10. ((specialist$ or speciali?ed) adj2 experience).tw.
11. (soft tissue adj (unit$ or centre$ or center$ or service$)).tw.
12. (bone tumo?r$ adj (unit$ or centre$ or center$ or service$)).tw.
13. ((cancer or oncology) adj (unit$ or centre$ or center$ or service$ or team$)).tw.
14. (non-specialist$ or nonspecialist$).tw.
15. or/1-16
16. plus main sarcoma set

BONE SPECIALIST SEARCH STRATEGY

MEDLINE and EBM Reviews

1. osteogenic sarcom$.tw.
2. exp osteosarcoma/
3. 1 or 2
4. exp Biopsy/
5. excision biops$.tw.
6. (core needle biops$ or needle biops$ or fine needle biops$).tw.
7. incisional biops$.tw.
8. bone biops$.tw.
9. aspiration$.tw.
10. percutaneous needle$.tw.
11. or/4-10
12. 3 and 11
13. exp Hospitals, Special/
14. Oncology Service, Hospital/
15. Specialism/

16. specialist$.tw.
17. (speciali?ed or speciali?ing).tw.
18. (special$ adj (unit$ or centre$ or center$ or hospital$ or clinic$1)).tw.
19. (special$ adj (facilit$ or team$ or service$)).tw.
20. (single adj (unit$ or centre$ or center$ or clinic$1)).tw.
21. (sarcoma$ adj (unit$ or centre$ or center$ or clinic$1)).tw.
22. (sarcoma$ adj (facilit$ or team$ or service$)).tw.
23. ((specialist$ or speciali?ed) adj2 experience).tw.
24. (soft tissue adj (unit$ or centre$ or center$ or service$)).tw.
25. (bone tumo?r$ adj (unit$ or centre$ or center$ or service$)).tw.
26. ((cancer or oncology) adj (unit$ or centre$ or center$ or service$ or team$)).tw.
27. (non-specialist$ or nonspecialist$).tw.
28. or/13-27
29. 12 and 28

EMBASE

1. exp Osteosarcoma/
2. osteogenic sarcom$.tw.
3. 1 or 2
4. exp Biopsy/
5. excision biops$.tw.
6. (core needle biops$ or needle biops$ or fine needle biops$).tw.
7. incisional biops$.tw.
8. bone biops$.tw.
9. aspiration$.tw.
10. percutaneous needle$.tw.
11. or/4-10
12. exp Hospitals, Special/
13. Oncology Service, Hospital/
14. Specialism/
15. specialist$.tw.
16. (speciali?ed or speciali?ing).tw.
17. (special$ adj (unit$ or centre$ or center$ or hospital$ or clinic$1)).tw.
18. (special$ adj (facilit$ or team$ or service$)).tw.
19. (single adj (unit$ or centre$ or center$ or clinic$1)).tw.
20. (sarcoma$ adj (unit$ or centre$ or center$ or clinic$1)).tw.
21. (sarcoma$ adj (facilit$ or team$ or service$)).tw.
22. ((specialist$ or speciali?ed) adj2 experience).tw.
23. (soft tissue adj (unit$ or centre$ or center$ or service$)).tw.
24. (bone tumo?r$ adj (unit$ or centre$ or center$ or service$)).tw.
25. ((cancer or oncology) adj (unit$ or centre$ or center$ or service$ or team$)).tw.
26. (non-specialist$ or nonspecialist$).tw.
27. or/12-26
28. 3 and 11 and 27

Appendix 2. Details on studies identified in update search.

Author	Applicable Tables in NICE review	Country	Aims	Design *	Population	Outcomes
Aksnes 2006 (7)	Table 4a, 5, 6	Norway	To report on the sarcoma program at the Norwegian Radium Hospital	Historically controlled trial	Osteosarcoma n= 196 Ewing's sarcoma n=56	To examine how high-grade bone sarcomas have been managed
Gutierrez 2007 (4)	Table 4b, 6, 7	US	To show the differences in cases of STS treated at high- and low-volume centres	Retrospective cohort study	4205 STS cases	Low- vs. high-volume centres, 30- and 90-day mortality rate. Limb amputation rate, 5- and 10-year survival: low- and high-grade, size, types of sarcoma and location
Lehnhardt 2008 (6)	Table 3a	Germany	To see how a second opinion changes the diagnosis of STS	Retrospective cohort study	603 patients with STS and aggressive fibromatosis	Second opinion of sarcoma diagnosis for 603 patients
Stiller 2006 (5)	Table 5, 6	UK	To calculate population-based survival rates for patients treated at specialist centres or clinical trials for osteosarcoma and Ewing's sarcoma in UK during 1980-1994.	Retrospective cohort study	1349 patients with osteosarcoma and 849 patients with Ewing's sarcoma	Survival

Abbreviations: STS- Soft Tissue Sarcoma; UK- United Kingdom; US, United States; vs.-versus.
* Classified according to the scheme presented in Chapter 13 of: Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions. Version 5.0.1. The Cochrane Collaboration; 2008 [updated 2008 Sep]. Available from: www.cochrane-handbook.org.

<table>
<tr><th>Study</th><th>Results</th></tr>
<tr><td>Aksnes 2006 (7)</td><td>The sarcoma specific survival time for all patients has increased from 39% to 53% at 5 years comparing the two subsequent 10-year periods (p=0.03)</td></tr>
<tr><td>Gutierrez 2007 (4)</td><td>
<table>
<tr><th>Outcome</th><th colspan="3">Low-volume centre (n=2865; 68.1%)</th><th colspan="3">High-volume centre (n=1340; 31.9%)</th><th>p value</th></tr>
<tr><td>30-day mortality</td><td colspan="3">1.50%</td><td colspan="3">0.70%</td><td>0.028</td></tr>
<tr><td>90-day mortality</td><td colspan="3">3.60%</td><td colspan="3">1.60%</td><td><0.001</td></tr>
<tr><td>Amputation rate</td><td colspan="3">13.80%</td><td colspan="3">9.40%</td><td>0.048</td></tr>
<tr><td></td><td colspan="3">Low-volume centre</td><td colspan="3">High-volume centre</td><td>p value</td></tr>
<tr><td></td><td>Median Survival (mo)</td><td>5-year survival %</td><td>10-year survival %</td><td>Median Survival (mo)</td><td>5-year survival %</td><td colspan="2">10-year survival %</td></tr>
<tr><td>All pts</td><td>37</td><td>33.2</td><td>11.6</td><td>40</td><td>37.4</td><td>15.9</td><td>0.002</td></tr>
<tr><td>Low grade</td><td>48</td><td>42.7</td><td>10.6</td><td>48</td><td>43</td><td>19.6</td><td>0.099</td></tr>
<tr><td>High grade</td><td>24</td><td>20</td><td>4</td><td>30</td><td>25.1</td><td>7.6</td><td>0.001</td></tr>
<tr><td><10</td><td>30</td><td>15.2</td><td>1.6</td><td>30</td><td>19.1</td><td>0</td><td>0.345</td></tr>
<tr><td>>10</td><td>19</td><td>12.5</td><td>0</td><td>28</td><td>21.9</td><td>0</td><td>0.001</td></tr>
<tr><td>Fibrosarcoma</td><td>43</td><td>43</td><td>19.4</td><td>87</td><td>61.5</td><td>26.5</td><td>0.111</td></tr>
<tr><td>MFH</td><td>29</td><td>26.2</td><td>8</td><td>34</td><td>27.9</td><td>11</td><td>0.01</td></tr>
<tr><td>Liposarcoma</td><td>47</td><td>41.5</td><td>15.2</td><td>54</td><td>47</td><td>21.2</td><td>0.051</td></tr>
<tr><td>Leimyosarcoma</td><td>76</td><td>40</td><td>0</td><td>39</td><td>0</td><td>0</td><td>0.247</td></tr>
<tr><td>Trunk and retroperitoneum</td><td>31</td><td>31.9</td><td>11.6</td><td>39</td><td>35.6</td><td>16.3</td><td>0.011</td></tr>
<tr><td>Extremity</td><td>38</td><td>33.8</td><td>11.4</td><td>38</td><td>35</td><td>15.3</td><td>0.147</td></tr>
<tr><td>Head and Neck</td><td>43</td><td>30.7</td><td>8.2</td><td>64</td><td>47.4</td><td>14.3</td><td>0.117</td></tr>
</table>
</td></tr>
<tr><td>Lehnhardt 2008 (6)</td><td>The study confirmed the proper primary diagnosis in 28.3% for pathologists in private clinics, 29.6% for hospital pathologists, 36.8% for academic medical centres (university hospitals), and 70.5% for the department of pathology at the author's institution. An improvement in diagnosis or confirmation of the correct primary diagnosis was seen in 73.1% of patients. In 2.5%, the second opinion was false.</td></tr>
<tr><td>Stiller 2006 (5)</td><td>
<table>
<tr><th>5-year survival for patients treated at different centres</th><th>N</th><th>Bone tumour services</th><th>UK children's cancer study group</th><th>Other teaching</th><th>Non-teaching</th><th>Unknown</th><th>p</th></tr>
<tr><td>OS -1980-1984</td><td>469%</td><td>50%</td><td>51%</td><td>38%</td><td>37%</td><td>34%</td><td>0.0092</td></tr>
<tr><td>OS - 1985-1989</td><td>428</td><td>54%</td><td>58%</td><td>54%</td><td>37%</td><td>76%</td><td>0.077</td></tr>
<tr><td>OS - 1990-1994</td><td>400</td><td>49%</td><td>55%</td><td>55%</td><td>44%</td><td>56%</td><td>0.49</td></tr>
<tr><td>ES- 1980-1984</td><td>279</td><td>33%</td><td>40%</td><td>31%</td><td>21%</td><td>8%</td><td>0%</td></tr>
</table>
</td></tr>
</table>

	ES- 1985-1989	274	57%	52%	36%	22%	47%	0%
	ES- 1990-1994	278	57%	59%	42%	11%	56%	<0.0001
	OS patients entered into a clinical trial from 1983-1992			48%	survival was similar for trial and non-trial OS patients			
					5-year survival for ES trial vs. non-trial			
	ES patients entered into a clinical trial from 1980-1986			27%		42 vs. 30%		
	1987-1994			54%		59 vs. 42%		

Abbreviations: ES- Ewing's sarcoma; MFH- Malignant fibrous histiocytoma; mo- month; OS- overall survival; pts- patients; UK– United Kingdom; vs.- versus

Appendix 3. Sarcoma Multidisciplinary Care Project Team.

The following Project Team members were part of the Working Group *

Marcus Bernardini, MD, MSc, FRCSC Gynecologic Oncology University Health Network
Martin Blackstein, MD, PhD, FRCP(C), FACP Medical Oncology Mount Sinai Hospital
Judy Burns, BScN, MHSc, CHE Cancer Care Ontario
Charles Catton, MD, FRCPC * Chair, Sarcoma Expert Panel Associate Professor Department of Radiation Oncology Princess Margaret Hospital
Nadia Coakley, MLIS * Program in Evidence-based Care Cancer Care Ontario
Samy El Sayed, MD, FRCPC Radiation Oncology The Ottawa Hospital
Michelle Ghert, MD, FRCSC Orthopaedic Oncology Juravinski Cancer Centre (DSG) Assistant Professor Department of Surgery McMaster University
Abha Gupta, MD, MSc, FRCP(C) Haematology/Oncology Hospital for Sick Children
Eric Gutierrez, MRT (T), RTT, CMD, BSc Cancer Care Ontario
Alex Hammond, BSc, MBBCh, FRCPC, ABRT, MEd Professor Department of Oncology, Faculty of Medicine and Dentistry The University of Western Ontario London Regional Cancer Program
Jeremy Hamm Cancer Care Ontario
Sherrie Hertz, BScPhm * Cancer Care Ontario
Amber Hunter, MBA Cancer Care Ontario
Jonathan Irish, MD, MSc, FRCSC, FACS Provincial Head & Lead, Access to Care & Strategic Funding Surgical Oncology Program Cancer Care Ontario
Laurie Jenkins, RN, BScN, MBA Senior Director, Surgery & Oncology Mount Sinai Hospital

Rita Kandel, MD, FRCP(C) Pathology Mount Sinai Hospital
Korosh Khalili, MD, FRCPC Abdominal Imaging University Health Network
Cindy (Cynthia) McLennan, RN, BScN, CON (c), CPN (c) Nursing/Administration The Ottawa Hospital
Elaine Meertens, BScN Cancer Care Ontario
Hans Messersmith, (MPH) * Program in Evidence-based Care Cancer Care Ontario
Barry Rosen, MD, FRCSC Gynecologic Oncology University Health Network
Jill Ross, RN, MBA Cancer Care Ontario
Haim Sechter Cancer Care Ontario
Carol Swallow, MD, PhD, FRCS(C), FACS Professor, Department of Surgery Mount Sinai Hospital
Richard Tozer, BSc (Hon), PhD, MD, FRCPC Medical Oncology Juravinski Cancer Centre
Maureen Trudeau, BSc, MA, MD, FRCPC * Provincial Head Systemic Treatment Cancer Care Ontario
Shailendra Verma, MD, FRCPC, FACP * Medical Oncology The Ottawa Hospital
Padraig Warde, MB, MRCPI, FRCPC Provincial Head, Radiation Treatment Program Cancer Care Ontario
Ellie Wasserman, RN, BA Nursing Administrator Mt. Sinai Hospital
Jennifer Wiernikowski, RN(EC), NP-Adult, MN, CON(C) Nursing Juravinski Cancer Centre
Graham Woodward, MSc CCO Provincial and Corporate Planning Cancer Care Ontario
Joel Werier, MD,FRCS(C) Orthopaedic Oncology The Ottawa Hospital (DSG)

Lawrence M. White, MD, FRCPC Professor Department of Medical Imaging and Orthopaedic Surgery Mount Sinai Hospital
Jay Wunder, MD, MSC, FRCSC Orthopaedic Oncology Mount Sinai Hospital