Review Article

A Critical Review of the Impact of Sarcoma on Psychosocial Wellbeing

Lesley Storey,¹ Lorna A. Fern,² Ana Martins,² Mary Wells,³ Lindsey Bennister,² Craig Gerrand,⁴ Maria Onasanya,² Jeremy S. Whelan,² Rachael Windsor,² Julie Woodford,⁴ and Rachel M. Taylor²

¹School of Psychology, Queens University Belfast, Belfast BT7 1NN, UK
²Cancer Division, University College London Hospitals NHS Foundation Trust, London NW1 2PG, UK
³Nursing Directorate, Imperial College Healthcare NHS Trust, Charing Cross Hospital, London W6 8RF, UK
⁴Sarcoma Unit, The Royal National Orthopaedic Hospital NHS Trust, Stanmore, Middlesex HA7 4LP, UK

Correspondence should be addressed to Rachel M. Taylor; rtaylor13@nhs.net

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Background. Previous reviews of outcomes in specific sarcoma populations suggest patients have poor quality of life. In most of these reviews, there is a predominant focus on physical function rather than psychosocial outcome. The aim of this review was to describe the psychosocial impact of diagnosis and treatment on patients with all types of sarcoma.

Methods. Searches were conducted through six electronic databases for publications of any study design using a validated patient-reported outcome measure reporting the psychosocial impact in this population.

Results. Eighty-two studies fulfilled the inclusion criteria. Most (65%) were assessed of being of reasonable quality. The most common aspect of psychosocial wellbeing measured was quality of life (80%). Due to the heterogeneity of methods, outcomes, and populations, it was not possible to make definitive conclusions. It seems there is an improvement in the physical aspects of quality of life over time but not in psychosocial function or mental health. There was no change in mental health scores, but patients reported an improvement in adjusting to normal life. There are no differences according to the type of surgery patients receive, and psychosocial outcomes tend to be poorer than the general population. There is no consistency in identifying the factors that predict/influence psychosocial wellbeing.

Conclusion. The published literature does not provide a clear understanding of the impact of sarcoma diagnosis and treatment on psychosocial wellbeing. Instead, the review demonstrates a need for well-designed studies in this area and a more consistent approach to the measurement of patient-reported outcomes, which include psychosocial domains. Recommendations for future research have been proposed.

1. Introduction

Measurement of patient-reported outcome (PRO) and experience has become commonplace in healthcare to measure the quality and impact of healthcare interventions. The phrase "patient-reported outcome" is loosely defined as the report of a health outcome made directly by the patient (rather than an assessment by the healthcare team) [1]. PROs include measures of quality of life (QOL), aspects of mental health, or assessment of physical function and symptoms, such as pain.

The value of measuring and reporting PROs and experience can be seen through nationally collected metrics in several countries [2]. In England, PROs for patients undergoing five surgical procedures have been collected since 2010 [3] with the aim on informing changes to the delivery of care to improve outcome, although there is some debate on how well this has been achieved [4, 5]. Similar benefits have been shown by measuring experience through the National Cancer Patient Experience Survey (NCPES). This has been conducted annually since 2010 and has been invaluable for informing changes to improve care [6, 7].
The survey includes patients with all cancer types but consistently over the last 7 years, patients with sarcoma have generally reported poorer care experience than those with other diagnoses. To further understand the reason for this, a sarcoma-specific experience survey was administered to participants of the 2014/15 NCPES [8]. Patients with sarcoma had a prolonged period to diagnosis, most were treated in multiple hospitals, and many reported experiencing side-effects of treatment, predominantly fatigue [8]. Furthermore, the results indicated that having a written treatment plan was more significant to a better experience than having a clinical nurse specialist (shown to be the most important factor for a good experience of patients with other cancers in the main NCPES).

While this survey elicited greater understanding of the experience of processes of care, it did not tell us about the outcomes. There have been a number of studies exploring QOL after a diagnosis of sarcoma, and the results of many of which have been presented in previous reviews [9–15]. These focus on specific populations, such as bone/extremity sarcoma to compare different surgical techniques [9–11, 13, 14], soft tissue sarcoma [15], and gastrointestinal stromal tumours (GIST) [12]. In most of these reviews, there is a predominant focus on physical function and its objective measurement rather than QOL or psychosocial outcome. Furthermore, despite reviews having similar target populations [10, 14] or inclusion criteria [9, 11, 13], there is a disparity in the studies included in these reviews, with none seeming to include all potentially relevant studies. These reviews consistently indicate that patients with sarcoma have poorer physical function than the general population and other types of cancer, probably associated with a high degree of disability. It is interesting to note that, despite poor physical function and disability, these reviews suggest no negative influence on emotional or social function. This is in contrast to what has been reported in the few qualitative studies that provide an in-depth description of the experience of living with a sarcoma diagnosis, that show the impact and challenges that treatment has on body image, self-esteem, mental health [16, 17], ability to work, and participation in social activities [16, 18–20].

To gain a greater understanding of the impact of sarcoma on patients’ psychosocial wellbeing, a more detailed review is therefore indicated. The aim of this review was to describe the impact of the diagnosis and treatment of all types of sarcoma on psychosocial wellbeing, in patients of all ages, undergoing all types of treatment. Psychosocial wellbeing was defined broadly as “the way a person thinks and feels about themselves and others, including being able to adapt and deal with daily challenges while leading a fulfilling life (e.g. this included measurements of quality of life, anxiety, coping, social support but excluded clinical/medical outcomes, such as toxicity, and adherence)” [21]. Specific objectives were to

1. Identify published research on patients’ psychosocial wellbeing using validated PRO measures
2. Describe psychosocial wellbeing
3. Identify psychosocial interventions that have been developed and evaluated to improve psychosocial wellbeing
4. Determine which factors influence or predict psychosocial wellbeing
5. Make recommendations for future research and clinical practice

2. Methods

2.1. Data Sources and Search Strategy. The literature review was guided by search terms used previously in reviews of patient-reported and psychosocial outcomes [10, 21, 22]. The search was conducted on the following electronic databases up until December 2017: BNI (British Nursing Index), Medline, PsycINFO, CINAHL (Cumulative Index to Nursing and Allied Health Literature), AMED (Allied and Complementary Medicine), and ASSIA (Applied Social Sciences Index and Abstracts). Selected journals were hand searched to ensure relevant references were not missed in the electronic search.

The search terms included population (sarcoma, bone tumour, and gastrointestinal stromal tumour) and terms reflecting psychosocial outcomes (quality of life, psychological wellbeing, and social function). The search used both text words and Medical Subject Headings (MeSH) terms (Supplementary Materials, Table A1).

2.2. Eligibility Criteria and Study Selection. Studies were eligible for inclusion in the review if they

(i) Reported a primary or secondary PRO related to psychosocial wellbeing, evaluated through reporting results from a validated measure
(ii) Used a quantitative study design
(iii) Published in English, Spanish, or Portuguese in a peer-reviewed publication

Studies were excluded if they

(i) Did not have a validated patient-reported outcome measure
(ii) Included groups other than sarcoma patients (e.g., partners, parents, friends, healthcare professionals, etc.) unless the results of sarcoma patients were reported independently
(iii) Included patients with a diagnosis other than sarcoma, unless the results for the sarcoma population were reported independently
(iv) Focused solely on Kaposi Sarcoma

An initial screening of the search results based on titles and abstracts was conducted by one reviewer, and a second reviewer independently screened 10%. The full texts of potentially eligible studies were obtained and information from each study was extracted directly by four reviewers (15–30 papers each) into a data extraction file on Microsoft Excel to ensure consistent information was recorded from all
studies. Where a study was suspected of not being eligible, the full text was independently reviewed by another team member before exclusion.

2.3. Methodological Quality. There is no critical appraisal tool specific for survey studies, only for the use of patient-reported outcome measures in randomised controlled trials [23], so review-specific criteria were established, based on the CONSORT PRO guidance [24] and recommendations for good practice in survey methods [25] (Table 1). The percentage of criteria that were fulfilled was calculated for each study and independently checked by a separate member of the review team. Studies were classified as Q1 (achieved >75% of quality criteria), Q2 (fulfilled 50–74% of quality criteria), or Q3 (<50% of quality criteria achieved) [26, 27].

2.4. Method of Synthesis. Two reviewers independently reviewed the results of the included studies. Due to the heterogeneity of participants, measures, and methods, it was not possible to conduct any meta-analysis, so results were summarised descriptively, and where a comparator was used (either reference group, healthy control, or other cancer population), this was tabulated to show whether it was better (+), worse (−), or no different (=). Factors influencing PRO were identified and tabulated according to the frequency with which each factor was reported.

3. Results

3.1. Objective 1: Identify Published Research on Patients’ Psychosocial Wellbeing Using Validated PRO Measures. The search identified 5,461 papers, of which 141 were reviewed in full and 81 were eligible for inclusion [9, 28–107] (Figure 1). Research on psychosocial outcomes had been conducted for over 35 years. Most studies had been conducted in Europe (n = 37) or North America (n = 35). The majority of studies were single centre (n = 52) and focused on investigating outcomes when active treatment had ended (n = 59; Table 2). The majority (n = 65; 80%) were observational studies although one paper reported QOL as part of a clinical trial of an investigational medicinal product. Data from this paper were included as they were presented as observational [94]. Most studies were good/reasonable quality (rated Q1 and Q2, n = 53), but 28 were of poor quality (rated Q2/3 and Q3) (Supplemental file, Table A2). The most common omissions were as follows: not reporting how missing data were handled (n = 74); not presenting a comparison of the demographic characteristics of non-participants (n = 59); not stating how the measure was administered (n = 36); and not giving details of how the scores were interpreted (n = 28; Table A2).

Studies included between 1 and 6 measures with 34 reporting use of a single measure (Supplemental file, Table A3). The most commonly measured psychosocial outcomes were QOL (n = 65) and aspects of mental health (n = 28), but other outcomes included self-worth (n = 8); social support (n = 5); adjustment to normal life (n = 4); coping, body image, fatigue, and satisfaction with life (n = 3 each); sexual function (n = 2); and resilience, fear of recurrence, optimism, social wellbeing, family function, expectations for the future, and benefit finding (n = 1 each). While there were 64 different patient-reported outcome measures (with most studies using multiple measures), the most common were SF-36 (n = 31) and QLQ-C30 (n = 16). Ten studies used a QOL measure that could give a total and/or broad domain summary scores (such as physical or mental component score), but these results were not reported [41, 43, 44, 49, 53, 64, 74, 91, 99, 101].

Participant characteristics are presented in Table 3. In summary, psychosocial outcomes have been measured in 8,823 patients, with a sample size ranging from 10 to 1094 per study (response rate median 76%, range 13–100%). It was not possible to calculate the response rate in 12 studies due to a lack of reported information. The majority of studies included patients with bone tumours (n = 51) and lower limb/extremity tumours (n = 47). Thirty-five studies included adults only, four focused solely on children (participants aged less than 18 years), and 39 included children and adults. The age of participants was not reported in three studies.

3.2. Objective 2: Describe Psychosocial Wellbeing. A summary of all the results is presented in the supplemental file (Table A4). A number of papers reported findings which were unsurprising, including that patients who experienced higher pain also had lower psychological outcomes [104], patients with higher anxiety and depression had greater fear of recurrence [37], those who were distressed had lower QOL and had more shame and stigma than those without distress [97], and those with severe fatigue had

| Table 1: Quality assessment criteria. |
|--------------------------------------|
| Category | Description |
|----------|-------------|
| C1. Sample | Are details provided about the total population who are eligible to take part during the study period in enough detail that a response rate can be calculated? |
| C2. Valid measure | Is the measure valid for the included population, i.e., has been validated for the age and there is a valid translation available if used outside of the language it was originally developed? |
| C3. Purpose | Is it clear what the PROM measures? |
| C4. Domains | If the PROM is known to have domain scores, have these been accurately reported? |
| C5. Scoring | Have details of how the total and/or domain score are interpreted? |
| C6. Administration | Are details of the administration of the PROM included; as a minimum this needs to state the mode (interview, postal, or online)? |
| C7. Missing data | Have statistical approaches for dealing with missing data been explicitly stated? |
| C8. Nonparticipants | Has a comparison been made between those who participated and those who refused? |
lower QOL and self-efficacy compared to those with nonsevere fatigue [79].

Thirteen studies used a longitudinal design to compare between different phases of the cancer timeline (Table 4). Results suggest that there is an improvement in the physical aspects of QOL over time but not psychosocial function or mental health. There was no change in mental health scores [73, 75], but patients reported an improvement in adjusting to normal life [38] (Table 4). Twenty-three studies reported outcomes of a comparison of different types of treatment, e.g., limb-salvage surgery versus amputation (Table 5). While there were some reports of amputations being associated with a poor outcome [41], the majority showed no difference. Similarly, there were no differences in the comparison of outcome in patients who had limb-sparing surgery, amputation, and rotationplasty, although there was one report of better role function for patients with rotationplasty compared to those with limb-sparing surgery [56]. Other psychosocial outcomes that were measured mostly showed no difference according to type of surgery, although patients who had amputations were shown to have poorer mental health [30, 36] but better feelings of self-worth [30] (Table 5).

Twenty-six studies compared QOL scores to reference values, either general population data provided with the measure or noncancer control data collected as part of the study (Table 6). Six studies found no differences in QOL [51, 59, 62, 78, 85, 103] and 15 reported that patients with sarcoma had poorer QOL, mostly in the physical domains only [29, 43, 44, 47–49, 61, 63, 64, 74, 81, 99–101], but three studies found patients with sarcoma had better QOL in the psychosocial domains [34, 49, 53]. One study was not able to make any conclusions because it used three measures of QOL, which all gave different results [31] (Table 6). In comparison to patients with other types of cancer, those with sarcoma reported similar levels of fatigue [29] but poorer mental health [71, 72, 78]. Aksnes et al. [29] and Hind et al. [57] reported QOL being poorer in those with sarcoma in contrast to Ostacoli et al. [72] and Podleska et al. [78] who found better QOL (Table 7).

Focusing on the most commonly used measures, results produced by the SF-36 (Table 8) indicated that there was no difference in QOL between amputation, limb-sparing surgery, and rotationplasty [28, 31, 44, 45, 52, 60], and QOL was poorer than reference values [29, 34, 44, 47–49, 63, 64, 81, 99, 101]; patients with sarcoma had poorer physical function in comparison to patients with other cancer types [29] and an improvement in QOL over time [33, 55, 83] (Table 8). QOL measured by the QLQ-C30 (Table 9) indicated no difference between amputation and limb-sparing surgery [31, 107], but patients
| First author | Year | Country of origin | Study aims | Study design | Setting | Time focus | Quality score |
|--------------|------|-------------------|------------|--------------|---------|-----------|---------------|
| Sugarbaker et al. [94] | 1982 | USA | To compare assessment of QOL between AMP versus LSS | Interventional | Single | During treatment | Q2/3 |
| Weddington et al. [102] | 1985 | USA | To determine if LSS had better psychological outcomes than AMP in extremity sarcoma | Observational | Single | Follow-up | Q1 |
| Postma et al. [80] | 1992 | Netherlands | To compare QOL in lower limb BT for LSS versus AMP | Observational | Single | Follow-up | Q2 |
| Rougraff et al. [86] | 1994 | USA | To compare long-term outcomes for survivors of OS between LSS, AMP, and disarticulation at the hip | Observational | Multicentre | Long-term survivor | Q3 |
| Sammallahti et al. [88] | 1995 | Finland | To describe the defences AYA OS survivors use | Observational | Single | Follow-up | Q2 |
| Christ et al. [36] | 1996 | USA | To explore patterns of adjustment of long-term survivors of lower limb BT | Observational | Single | Long-term survivor | Q2 |
| Felder-Puig et al. [46] | 1998 | Austria | To evaluate psychosocial adjustment, assess age-appropriate achievements, and identify problems in AYA with BT | Observational | Single | Follow-up | Q2/3 |
| Davis et al. [41] | 1999 | Canada | To compare levels of disability between patients treated with LSS versus AMP | Observational | Single | Follow-up | Q2/3 |
| Hillmann et al. [56] | 1999 | Germany | To evaluate the effect of rotationplasty, AMP, and LSS on QOL | Observational | Single | Follow-up | Q2/3 |
| Davis et al. [40] | 2000 | Canada | To identify predictors of functional outcomes after LSS for STS | Observational | Single | Follow-up | Q2 |
| Veenstra et al. [101] | 2000 | Netherlands | To assess the medium and long-term effects on QOL after rotationplasty | Observational | Multicentre | Follow-up | Q2 |
| Eiser et al. [44] | 2001 | UK | To compare QOL to population norms and the differences between AMP versus LSS | Observational | Single | Follow-up | Q2/3 |
| Malo et al. [64] | 2001 | Canada | To understand the impact of successful LSS for BT on patients’ function | Observational | Multicentre | Follow-up | Q2/3 |
| Rodl et al. [85] | 2002 | Germany | To evaluate QOL in patients at least 10 years after rotationplasty | Observational | Single | Long-term survivor | Q3 |
| Servaes et al. [90] | 2003 | Netherlands | To investigate the prevalence and predictors of fatigue in patients with BT and STS | Longitudinal | Single | Follow-up | Q1 |
| Marchese et al. [65] | 2004 | USA | To conduct a pilot study to examine the relationship between physical function and QOL in AYA survivors of OS | Pilot study | Single | Follow-up | Q2 |
| Nagarajan et al. [69] | 2004 | USA | To assess function and QOL in long-term childhood survivors of lower limb BT | Observational | Multicentre | Long-term survivor | Q2 |
| Zahlten-Hinguranage et al. [107] | 2004 | Germany | To determine the predictors of whether QOL is high for patients with AMP or LSS | Observational | Single | Follow-up | Q2 |
| Koopman et al. [61] | 2005 | Netherlands | To investigate QOL and coping strategies in children at 3 and 8 years after the end of treatment | Longitudinal | Single | Follow-up | Q1 |
| Tabone et al. [96] | 2005 | France | To assess the factors that impact on QOL in patients who had childhood BT | Observational | Multicentre | Follow-up | Q2 |
| Gerber et al. [51] | 2006 | USA | To evaluate function and performance in adult survivors of child and adolescent sarcoma | Observational | Single | Follow-up | Q2 |
| Hoffmann et al. [59] | 2006 | Germany | To determine the impact of surgery on QOL and function in long-term survivors after acetabulum resection | Observational | Single | Long-term survivor | Q2/3 |
| Hopyan et al. [60] | 2006 | Australia | To determine whether children with AMP or rotationplasty were more physically active, functionally satisfied, and less psychosocial cost than those with LSS | Observational | Single | Long-term survivor | Q1 |
| Marchese et al. [66] | 2006 | USA | Hypothesised that limited range of movement in children and adolescents who had LSS would have impaired functional mobility affecting QOL | Observational | Multicentre | Follow-up | Q3 |
| Schreiber et al. [89] | 2006 | Canada | To evaluate how functional disability impacts on QOL of patients with extremity STS 1 year after surgery | Observational | Multicentre | Follow-up | Q2/3 |
| First author          | Year | Country of origin | Study aims                                                                                                                                                                                                 | Study design | Setting                    | Time focus | Quality score |
|----------------------|------|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|----------------------------|------------|---------------|
| Thijsens et al. [99] | 2006 | Netherlands       | To investigate whether STS survivors had different QOL than a reference group and identify predictors of QOL and stress response                                                                         | Observational| Single                     | Follow-up  | Q2/3          |
| Wiener et al. [104]  | 2006 | USA               | To determine the prevalence of psychological distress and posttraumatic stress symptoms in childhood sarcoma survivors                                                                                | Observational| Single                     | Long-term survivor | Q1            |
| Akahane et al. [28]  | 2007 | Japan             | To compare QOL for patients with OS around the knee between rotationplasty, LSS, and AMP                                                                                                                 | Observational| Multicentre                | Follow-up  | Q2/3          |
| Aksnes et al. [29]   | 2007 | Norway            | To compare QOL, fatigue and mental distress in childhood survivors of BT to those with Hodgkin’s disease, testicular cancer, and normative data                                                          | Observational| Multicentre                | Long-term survivor | Q1            |
| Ginsberg et al. [52] | 2007 | USA               | To compare QOL and functional outcomes of AYA survivors of lower limb BT after AMP, LSS, and rotationplasty                                                                                              | Observational| Multicentre                | Follow-up  | Q2/3          |
| Beck et al. [32]     | 2008 | USA               | To compare functional outcomes and QOL following internal or external hemipelvectomy                                                                                                                     | Observational| Single                     | Follow-up  | Q2/3          |
| Davidge et al. [38]  | 2009 | Canada            | To examine the impact of preoperative outcome expectations with postoperative function and QOL                                                                                                           | Observational| Single                     | Follow-up  | Q2/3          |
| Hinds et al. [57]    | 2009 | USA               | To evaluate the ability of adolescents at the time of diagnosis to self-report their QOL                                                                                                               | Observational| Single                     | Diagnosis  | Q1            |
| Hinds et al. [58]    | 2009 | USA               | To assess the effect of treatment on children and adolescents QOL at the time of diagnosis, during and after treatment, and assess for differences in sex and age                                               | Longitudinal | Multicentre                | From diagnosis to follow-up | Q1            |
| Nagarajan et al. [70]| 2009 | USA               | To describe global function in childhood BT survivors, evaluate variables that may predict global function, and explore associations with QOL                                                             | Observational| Multicentre                | Long-term survivor | Q2            |
| Yonemoto et al. [106]| 2009 | Japan             | To describe psychosocial outcomes of long-term child and adolescent survivors of OS                                                                                                                     | Observational| Single                     | Long-term survivor | Q2            |
| Barrera et al. [30]  | 2010 | Canada            | To examine the impact of surgery and gender on sexual function in AYA survivors of lower limb BT                                                                                                            | Observational| Single                     | Long-term survivor | Q1            |
| Bekkering et al. [34]| 2010 | Netherlands       | To compare QOL in children and AYA following surgery for BT around the knee joint of the leg with healthy controls                                                                                         | Observational| Multicentre                | Follow-up  | Q2            |
| Robert et al. [84]   | 2010 | USA               | To compare psychosocial and functional outcomes of LSS and AMP in OS survivors                                                                                                                            | Observational| Single                     | Follow-up  | Q2            |
| Granda-Cameron et al. [54] | 2011 | USA               | To examine symptom distress and QOL in newly diagnosed patients with sarcoma                                                                                                                             | Observational| Single                     | Diagnosis  | Q2            |
| Nagarajan et al. [71]| 2011 | USA               | To evaluate survival, medical, and psychosocial outcomes and health status of survivors of childhood OS                                                                                                     | Observational| Multicentre                | Long-term survivor | Q2/3          |
| Paredes et al. [74]  | 2011 | Portugal          | To examine change in QOL through diagnosis to treatment, and analyse predictors of QOL                                                                                                                   | Longitudinal | Single                     | Diagnosis and during treatment | Q1            |
| Paredes et al. [73]  | 2011 | Portugal          | To understand how patients adjust to a sarcoma diagnosis at difference phases of the disease experience                                                                                            | Observational| Multicentre                | Diagnosis, treatment, and follow-up | Q3            |
| Exposito Tirado et al. [45] | 2011 | Spain             | To compare QOL and physical function in young people with LSS versus AMP                                                                                                                               | Observational| Single                     | Long-term survivor | Q1            |
| Barrera et al. [31]  | 2012 | Canada            | To investigate QOL in AYA survivors of lower limb BT as function of type of surgery, age, and gender                                                                                                | Observational| Single                     | Long-term survivor | Q1            |
| First author                | Year | Country of origin | Study aims                                                                 | Study design     | Setting  | Time focus | Quality score |
|----------------------------|------|-------------------|-----------------------------------------------------------------------------|------------------|----------|------------|---------------|
| Bekkering et al. [33]      | 2012 | Netherlands       | To evaluate QOL, functional ability, and physical activity during the first 2-years following surgery | Longitudinal     | Multicentre | Treatment and follow-up | Q2            |
|                            |      |                   | To gain more knowledge on the QOL and experience of patients treated by rotationplasty and identify factors related to disability |                 |          |            |               |
| Forni et al. [49]          | 2012 | Italy             | To investigate the QOL of patients with BT after surgery                     | Observational    | Single    | Follow-up  | Q2            |
| Han et al. [55]            | 2012 | China             | To investigate the QOL of patients with BT after surgery                     | Longitudinal     | Single    | Treatment and follow-up | Q1            |
|                            |      |                   | To gain more knowledge on the QOL and experience of patients treated by rotationplasty and identify factors related to disability |                 |          |            |               |
| Paredes et al. [76]        | 2012 | Portugal          | To determine if greater perceived social support is related to lower anxiety and depressions and better QOL, and explore differences at different phases of disease | Observational    | Multicentre | Diagnosis, treatment, and follow-up | Q1            |
|                            |      |                   | To assess the emotional adjustment to diagnosis and treatment, and identify demographic and clinical variables predictive of adjustment |                 |          |            |               |
| Paredes et al. [75]        | 2012 | Portugal          | To describe utility weights in metastatic sarcoma and explore QOL according to predefined health states | Observational    | Multicentre | Metastatic disease | Q3            |
|                            |      |                   | To assess adolescents’ expectations of the future after bone cancer treatment and to investigate the relationship between expectations of the future, resilience and coping strategies |                 |          |            |               |
| Reichardt et al. [82]      | 2012 | Germany, France, | To describe utility weights in metastatic sarcoma and explore QOL according to predefined health states | Observational    | Multicentre | Metastatic disease | Q3            |
|                            |      | Italy, Netherlands, Spain, UK, Sweden | To assess adolescents’ expectations of the future after bone cancer treatment and to investigate the relationship between expectations of the future, resilience and coping strategies |                 |          |            |               |
| Smorti [92]                | 2012 | Italy             | To assess QOL after surgical treatment for BT and assess risk factors for improving physical and mental QOL | Longitudinal     | Single    | Follow-up  | Q1            |
| Sun et al. [95]            | 2012 | China             | To examine perceived social support and benefit finding with respect to surgical intervention, gender, and age; to compare these to normative values; and to examine the relationship between social and psychological outcomes and sexual functioning | Longitudinal     | Single    | Treatment and follow-up | Q2/3          |
| Teall et al. [98]          | 2012 | Canada            | To describe utility weights in metastatic sarcoma and explore QOL according to predefined health states | Observational    | Multicentre | Long-term survivor | Q1            |
| Marina et al. [67]         | 2013 | USA               | To assess adolescents’ expectations of the future after bone cancer treatment and to investigate the relationship between expectations of the future, resilience and coping strategies | Longitudinal     | Multicentre | Follow-up  | Q3            |
| Mason et al. [68]          | 2013 | USA               | To assess QOL after surgical treatment for BT and assess risk factors for improving physical and mental QOL | Longitudinal     | Single    | Follow-up  | Q2            |
| Liu et al. [63]            | 2014 | China             | To examine perceived social support and benefit finding with respect to surgical intervention, gender, and age; to compare these to normative values; and to examine the relationship between social and psychological outcomes and sexual functioning | Observational    | Multicentre | Follow-up  | Q2/3          |
| Ostacoli et al. [72]       | 2014 | Italy             | To assess QOL after surgical treatment for BT and assess risk factors for improving physical and mental QOL | Observational    | Multicentre | Follow-up  | Q2            |
| van Riel et al. [100]      | 2014 | Netherlands       | To assess self-perception and QOL of adolescents during or up to 3 months after adjuvant treatment for BT | Observational    | Single    | Follow-up  | Q2            |
| Chan et al. [35]           | 2015 | Singapore         | To assess QOL, symptom burden, and medication use in adult sarcoma patients | Observational    | Single    | Follow-up  | Q1            |
| Custers et al. [37]        | 2015 | Netherlands       | To assess QOL, symptom burden, and medication use in adult sarcoma patients | Observational    | Single    | Follow-up  | Q1            |
| Furtado et al. [50]        | 2015 | UK                | To describe QOL and anxiety and depression in the early stages of treatment compared to those with common types of cancer | Observational    | Multicentre | Follow-up  | Q2            |
|                            |      |                   | To assess self-perception and QOL of adolescents during or up to 3 months after adjuvant treatment for BT |                 |          |            |               |
|                            |      |                   | To describe QOL, symptom burden, and medication use in adult sarcoma patients |                 |          |            |               |
|                            |      |                   | To assess QOL, distress, and fear of cancer recurrence or progression in patients with GIST |                 |          |            |               |
|                            |      |                   | To describe physical function, QOL, and pain after AMP |                 |          |            |               |
| First author            | Year | Country of origin | Study aims                                                                 | Study design | Setting          | Time focus                          | Quality score |
|------------------------|------|-------------------|----------------------------------------------------------------------------|--------------|------------------|-------------------------------------|---------------|
| Gradl et al. [53]      | 2015 | Germany           | To assess long-term QOL, functional performance, and psychosocial aspects after rotationplasty | Observational | Single           | Long-term survivor                  | Q2            |
| Rivard et al. [83]     | 2015 | Canada            | To document functional outcome and QOL in relation to wound complication rates | Observational | Single           | During treatment and follow-up      | Q2            |
| Shchelkova and Usmanova [91] | 2015 | Russia            | To investigate QOL and the relation to disease in patients with malignant BT | Observational | Single           | ns                                  | Q3            |
| Sish et al. [93]       | 2015 | USA               | To assess patient-reported functional and QOL outcomes in survivors of ES    | Observational | Single           | Long-term survivor                  | Q1            |
| Tang et al. [97]       | 2015 | Australia         | To investigate QOL and the relation to disease in patients with malignant BT | Observational | Single           | During treatment                    | Q2            |
| Fidler et al. [48]     | 2015 | UK                | To investigate the long-term risks of adverse outcomes in 5-year survivors of childhood bone sarcoma | Observational | National         | Long-term survivor                  | Q2/3          |
| Davidson et al. [39]   | 2016 | Canada            | To estimate the change in QOL between diagnosis and 1-year after surgery     | Longitudinal | Single           | Diagnosis and during treatment      | Q1            |
| Dressler et al. [42]   | 2016 | USA               | To analyse long-term QOL outcomes for patients with GIST                     | Observational | Single           | Follow-up                           | Q1            |
| Edelmann et al. [43]   | 2016 | USA               | To analyse long-term QOL outcomes for patients with GIST                     | Observational | Single           | Follow-up                           | Q2            |
| Leiser et al. [62]     | 2016 | Switzerland, Germany | To evaluate clinical outcomes for children with RMS treated with pencil beam scanning, assess QOL, and identify prognostic factors for tumour control | Longitudinal | Multicentre      | During treatment and follow-up      | Q2            |
| Phukan et al. [77]     | 2016 | USA               | To report QOL and functional outcomes after sacrectomy for malignant BT      | Observational | Single           | Follow-up                           | Q1            |
| Poort et al. [79]      | 2016 | Netherlands       | To determine the prevalence of severe fatigue in patients with GIST, the impact on QOL, psychosocial and physical function, and the association with tyrosine kinase inhibitor use | Observational | Single           | Follow-up                           | Q2            |
| Weiner et al. [103]    | 2016 | UK                | To explore the extent of which child, adolescents, and their family engaged with psychological screening and whether they report concerns during the follow-up appointments | Feasibility  | Single           | ns                                  | Q2/3          |
| Bekkering et al. [108] | 2017 | Netherlands       | To assess the course of QOL over time between 2 and 5 years or more after surgery | Longitudinal | Multicentre      | Long-term survivor                  | Q2            |
| Fernandez-Pineda et al. [47] | 2017 | USA               | To compare QOL and social role attainment between extremity sarcoma and healthy control | Observational | Single           | Long-term survivor                  | Q2            |
| Podleska et al. [78]   | 2017 | Germany           | To gain insight into patients’ QOL after isolated limb perfusion and long-term survival | Observational | Single           | Follow-up                           | Q2/3          |
| Ranft et al. [81]      | 2017 | Germany, Netherlands, Austria | To gather information on long-term outcome of ES, and look for prognostic factors for these outcomes | Observational | Multicentre      | Follow-up                           | Q1            |
| Saebye et al. [87]     | 2017 | Denmark           | To identify tumour- and patient-related factors associated with QOL after LSS for STS | Observational | Multicentre      | Follow-up                           | Q2            |
| Wong et al. [105]      | 2017 | Canada            | To examine how treatment-related toxicities affect QOL of patients with retroperitoneal sarcoma | Observational | Single           | Follow-up                           | Q3            |

AMP: amputation; AYA: adolescents and young adults; BT: bone tumour; ES: Ewing sarcoma; GIST: gastrointestinal stromal tumour; LSS: limb-sparing surgery; ns: not stated; OS: osteosarcoma; QOL: quality of life; RMS: rhabdomyosarcoma; STS: soft tissue sarcoma. 1Patient reported outcome measured as part of a clinical trial but reported independent to the trial results as it was an observational study. 2Described by the authors as a “qualitative study.” 3Quality rating includes 50% in both Q2 and Q3, so these were classified as both and rated as borderline poor.
Table 3: Participant characteristics.

| First author               | Participants (response %) | Type of sarcoma | Site     | Age at study (years) | Gender male (%) |
|----------------------------|---------------------------|-----------------|----------|----------------------|-----------------|
| Sugarbaker et al. [94]     | 21 (91)                   | STS             | Extremity | ns                   | ns              |
| Weddington et al. [102]    | 33 (67)                   | BT, STS         | Extremity | Range 15–71          | 45              |
| Postma et al. [80]         | 33 (92)                   | BT              | LL       | Range 13–56          | 55              |
| Rougraff et al. [86]       | 29 (13)                   | OS              | LL       | ns                   | 66              |
| Sammallahti et al. [88]    | 16 (100)                  | OS              | All      | Range 21–31          | 50              |
| Christ et al. [36]         | 45 (69)                   | BT              | LL       | Range 17–34          | 58              |
| Felder-Puig et al. [46]    | 60 (55)                   | BT              | Extremity | M 23.5 (sd 4.3)      | 57              |
| Davis et al. [41]          | 12 (92)                   | BT, STS         | LL       | M 34.4 (sd 11.6)     | 67              |
| Hillmann et al. [56]       | 65 (97)                   | BT              | LL       | Range 11–24          | 62              |
| Davis et al. [40]          | 172 (76)                  | STS             | LL       | M 51 (sd 15.2)       | 51              |
| Veenstra et al. [101]      | 33 (97)                   | BT              | LL       | Range 16–50          | 55              |
| Eiser et al. [44]          | 37 (93)                   | BT              | LL       | Range 12–47          | 57              |
| Malo et al. [64]           | 53 (95)                   | BT              | LL       | M 36.7 (sd 18.3)     | 53              |
| Rodl et al. [85]           | 22 (89)                   | BT              | LL       | Range 18–49          | ns              |
| Servaes et al. [90]        | 170 (75)                  | BT, STS         | ns       | Range 18–65          | 53              |
| Marchese et al. [65]       | 18 (64)                   | OS              | LL       | Range 10–27          | 44              |
| Nagarajan et al. [69]      | 528 (84)                  | BT              | LL/pelvis| M 34.8 (sd 19.5)     | 49              |
| Zahltten-Hinguranage et al. [107] | 124 (66)                  | BT              | LL       | Range 14–76          | 63              |
| Kooiman et al. [61]        | 18 (90)                   | BT              | Extremity | Range 12–23          | 72              |
| Tabone et al. [96]         | 37 (82)                   | BT              | All      | Range 10–18          | 68              |
| Gerber et al. [51]         | 32 (40)                   | BT              | ns       | M 35.4 (sd 10.6)     | 53              |
| Hoffmann et al. [59]       | 45 (71)                   | BT              | Pelvis   | Range 16.1–83.2      | 64              |
| Hopyan et al. [60]         | 45 (83)                   | BT              | LL       | Range 10–39          | 49              |
| Marchese et al. [66]       | 68 (80)                   | BT              | LL       | Range 10–26          | 56              |
| Schreiber et al. [89]      | 100 (90)                  | STS             | Extremity | Range 18–86          | 56              |
| Thijssens et al. [99]      | 39 (95)                   | STS             | Extremity | Range 15–78          | 41              |
| Wiener et al. [104]        | 34 (41)                   | BT, STS         | ns       | M 17 (sd 5)          | 53              |
| Akahane et al. [28]        | 21 (72)                   | OS              | LL       | Range 8–69           | 81              |
| Aksnes et al. [29]         | 57 (76)                   | BT              | Extremity | Male M 34 (sd 9.4)   | 54              |
| Ginsberg et al. [52]       | 91 (2)                    | BT              | LL       | Female M 27 (sd 4.8) | 54              |
| Beck et al. [32]           | 97 (94)                   | BT              | Pelvis/femur | IQR 33.3–66.5        | 68              |
| Davidge et al. [38]        | 157 (100)                 | STS             | Extremity | Range 16.1–87        | 62              |
| Hinds et al. [57]          | 39 (93)                   | OS              | All      | Range 13–23          | 54              |
| Hinds et al. [58]          | 66 (93)                   | OS              | All      | Range 5–23.5         | 55              |
| Nagarajan et al. [70]      | 528 (84)                  | BT              | LL       | M 34.8 (sd 5.8)      | 49              |
| Yonemoto et al. [106]      | 30 (55)                   | OS              | All      | Range 7–17          | 37              |
| Barrera et al. [30]        | 28 (39)                   | BT              | LL       | M 25.1 (sd 4.5)      | 50              |
| Bekkering et al. [34]      | 81 (92)                   | BT              | Knee     | M 16.9 (sd 4.2)      | 49              |
| Robert et al. [84]         | 57 (57)                   | OS              | Extremity | Range 16.1–52        | 35              |
| Granda-Cameron et al. [54] | 11 (65)                   | BT, STS         | ns       | M 44.5 (sd 13.7)     | 36              |
| Nagarajan et al. [71]      | 733 (68)                  | OS              | All      | Range 13–51          | 52              |
| Paredes et al. [74]        | 36 (88)                   | BT, STS         | All      | Range 18–72          | 53              |
| Paredes et al. [73]        | 142 (2)                   | BT, STS         | All      | M 48.3 (sd 16.4)     | M 48.1 (sd 17.7), M 48.3 (sd 18.5) | 56              |
| Exposito Tirado et al. [45] | 17 (44)                   | OS, ES          | Extremity | Range 20–25          | 41              |
| Barrera et al. [31]        | 28 (40)                   | BT              | LL       | M 25.1 (sd 4.5)      | 50              |
| Bekkering et al. [33]      | 44 (90)                   | BT              | Knee     | M 14.9 (sd 4.8)      | 61              |
| Forni et al. [49]          | 20 (67)                   | BT              | Femur    | Range 17–38          | 60              |
| Han et al. [55]            | 120 (100)                 | BT              | LL       | M 14.1 (sd 4.6)      | 66              |
| Paredes et al. [76]        | 151 (2)                   | BT, STS         | All      | M 47.5 (sd 17)       | M 44.9 (sd 16.9), M 46.9 (sd 18.1) | 56              |
| Paredes et al. [75]        | 36 (88)                   | BT, STS         | All      | M 40.5 (sd 16)       | 53              |
| Reichardt et al. [82]      | 116 (2)                   | BT, STS         | All      | Range 18.5–83.4      | 41              |
| Smorti [92]                | 32 (80)                   | BT              | ns       | Range 11–20          | 56              |
| Sun et al. [95]            | 344 (97)                  | BT              | LL       | M 18.7 (sd 4.9)      | 57              |
| Teall et al. [98]          | 28 (40)                   | BT              | LL       | Range 18–32          | 50              |
| Marina et al. [67]         | 1094 (2)                  | BT, STS         | Extremity | Range 10–53         | Unclear         |
| Mason et al. [68]          | 82 (82)                   | BT              | LL       | 14–19.9             | 52              |
Table 3: Continued.

| First author | Participants (response %) | Type of sarcoma | Site | Age at study (years) | Gender male (%) |
|---------------|---------------------------|-----------------|------|---------------------|-----------------|
| Liu et al. [63] | 94 (88) | BT | LL | M 22.8 (sd 9.7) | 45 |
| Ostacioli et al. [72] | 56 | STS | All | M 53.5 (sd 14.1) | 50 |
| van Riel et al. [100] | 10 | BT | All | Range 12–17 | 60 |
| Chan et al. [35] | 79 (98) | BT, STS, GIST | ns | M 57.3 (sd 15.2) | 58 |
| Custers et al. [37] | 54 (63) | GIST | GI | Range 21–84 | 54 |
| Furtado et al. [50] | 100 (40) | BT, STS | LL | Range 9–91 | 60 |
| Gradl et al. [53] | 12 (86) | BT | LL | M 33 (sd 11) | 58 |
| Rivard et al. [83] | 45 (87) | STS | All | Range 24–83 | 78 |
| Shchelkova and Usmanova [91] | 82 | BT | ns | Range 12.2–83.8 | 62 |
| Tang et al. [97] | 76 (75) | BT, STS | Extremity | Range 16–86 | 59 |
| Fidler et al. [48] | 411 (81) | BT | All | Range 7.5–76.8 | 84 |
| Davidson et al. [39] | 220 (38) | STS | Extremity | M 54.4 (sd 16.6) | 59 |
| Dressler et al. [42] | 36 (52) | GIST | GI | Range 42–89 | 56 |
| Edelmann et al. [43] | 80 (67) | OS | ns | M 38.9 (sd 7.1) | 58 |
| Leiser et al. [62] | 83 (91) | Rhabdomyosarcoma | ns | Range 0.8–15.5 | 55 |
| Phukan et al. [77] | 33 (73) | BT | Sacrum | Range 23–77 | 58 |
| Poort et al. [79] | 89 (75) | GIST | GI | Range 21–86 | 58 |
| Weiner et al. [103] | 21 (91) | BT | ns | Range 9–18 | 52 |
| Bekkering et al. [108] | 20 (43) | BT | Knee | M 22.3 (sd 4.0) | 50 |
| Fernandez-Pineda et al. [47] | 206 (63) | BT, STS | Extremity | Range 19.4–65.1 | 52 |
| Podleska et al. [78] | 26 (96) | STS | LL | Range 12–73 | 54 |
| Ranft et al. [81] | 614 (47) | ES | All | ns | 56 |
| Saebye et al. [87] | 128 (67) | STS | LL | IQR 47–70 | 45 |
| Wong et al. [105] | 48 | STS | Retropertioneal | Range 38–82 | 54 |

BT: bone tumour; ES: Ewing sarcoma; GIST: gastrointestinal stromal tumour; IQR: interquartile range; LL: lower limb; M: mean; ns: not stated; OS: osteosarcoma; sd: standard deviation; STS: soft tissue sarcoma. 1Calculated from interpreting the information reported in the paper not necessarily what the authors report. 2Not enough detail reported to be able to calculate a response rate. 3Age at diagnosis; age at study not reported. 4Age reported for each group: diagnosis, treatment, and follow-up. 5The age reported in the text is different to the age reported in the table (range 33–77). 6Reported for the whole cohort (n = 664) not just the 411 respondents of the patient-reported outcome.

Table 4: Longitudinal outcomes.

| First author | Comparator | Quality of life | Domains | Mental health | Others |
|--------------|------------|-----------------|----------|---------------|--------|
| Davidge et al. [38] | Time: before surgery vs. after surgery | + | | + adjustment to normal life |
| Hinds et al. [58] | Time: diagnosis to end of treatment | + | PF, EF |
| Granda-Cameron et al. [54] | Time: cycles 1–8 of chemotherapy | ns |
| Paredes et al. [74] | Time: diagnosis to treatment | + | GH |
| Paredes et al. [73] | Time: diagnosis to follow-up | = |
| Bekkering et al. [33] | Time: 3 to 12 months after surgery | + | BT specific, PCS |
| Han et al. [55] | Time: before surgery to 6 months after surgery | + |
| Paredes et al. [75] | Time: diagnosis to treatment | = |
| Sun et al. [95] | Time: treatment to 1 year after treatment | ns |
| Rivard et al. [83] | Time: before surgery vs. 12 months after surgery | + |
| Leiser et al. [62] | Time: treatment to 2 years after surgery | + |
| Bekkering et al. [108] | Time: 3 to >60 months after surgery | + | PCS |
| Wong et al. [105] | Time: before treatment to 5 years after treatment | ns |

BT: bone tumour; EF: emotional function; GH: global health; ns: significance not specified; OS: osteosarcoma; PCS: physical component score; PF: physical function. 1Minus (−): poorer in comparison; plus (+): better; equals (=): no difference. 2Direction of significance, i.e., better or worse, based on the first comparator, or the last time point if a longitudinal comparison. 3Result based on overall or summary scores; if these were not provided, result at domain score level was provided (QLQ-C30 functional scale only). 4Based on SF-36 and bone tumour-specific measure results reflecting the comparison across the whole sample.
with rotationplasty had better role function [56]. A greater number of studies showed no difference to reference values [59, 78, 85] and poorer QOL in patients with sarcoma [74, 101] (Table 9). Four studies used both the SF-36 and the QLQ-C30; results were comparable in two [79, 91], whereas Veenstra et al. [101] noted no difference in comparison to the general population with the QLQ-C30 but significant difference in SF-36 scores. Likewise, Barrera et al. [31] found significantly poorer SF-36 Physical Component Scores but similar Mental Component Scores in comparison to the reference value. However, results using the QLQ-C30 indicated patients with sarcoma had significantly better Global Health Status, Role Function, Emotional Function, and Social Function than the reference value and similar physical function.

Mostly there were no differences in other aspects of psychosocial outcome that were measured such as social support, body image, and self-worth. However, patients reported having better expectations for the future and greater satisfaction with leisure compared to the general population.

3.3. Objective 3: Identify Psychosocial Interventions That Have Been Developed and Evaluated to Improve Psychosocial Wellbeing. While psychosocial measures were identified as being secondary end points in a number of clinical trials (not included in this review), no psychosocial interventions specific to patients with sarcoma were identified to improve PRO.

3.4. Objective 4: Determine Which Factors Influence Psychosocial Wellbeing. Twenty-three studies conducted analysis to identify factors that could predict aspects of psychosocial wellbeing. Factors predicting QOL included disease-related variables, gender, age at the time of diagnosis/study, level of education, employment and marital status, body image, everyday competence, physical function, recurrence of disease, and symptom distress [29, 38, 40, 44, 47, 50, 57, 66, 69, 73, 81, 87, 89, 93, 96]. Severe fatigue was influenced by disease-related variables, optimism, physical function, and psychological distress [79, 90]. General psychosocial outcomes (including mental wellbeing and posttraumatic growth) were associated with age at the time of diagnosis/study, gender, marital status, disease-related variables, time since treatment ended, coping, and social support [36, 67, 73–76, 106]. While these factors were shown to predict PRO in some studies, this was not always the case. For example, age at diagnosis/study, gender, time since treatment, level of education, recurrence, and physical function were also shown not to be predictive of outcome [36, 40, 69, 89, 90, 93].

Due to the huge variation in outcomes, measures, population, and methods used, it was not possible to explore in any detail or make conclusion about what might influence or predict psychosocial wellbeing.
Interestingly, while there has been much work comparing between different types of surgery, there has been little exploration of differences according to type of sarcoma. A number of studies included patients with multiple cancer types [35, 41, 47, 50, 54, 67, 73–76, 90, 97, 102, 104], but the only direct comparisons were made by Chan et al. [35] who reported patients with GIST had better QOL and mental health compared to those without GIST, and patients with giant cell tumours had poorer quality of life compared to those with osteosarcoma and chondrosarcoma [91]. Similarly, Marina et al. [67] identified type of diagnosis as being an influencing factor for anxiety, showing patients with Ewing sarcoma had a relative risk of anxiety double that of patients with soft tissue sarcoma. However, other studies showed type of diagnosis was not found to influence psychosocial outcomes [73–76].

### Table 6: Comparison to a reference value

| First author          | Quality of life | Domains |
|-----------------------|-----------------|---------|
| Veenstra et al. [101] | −               | PF, RP  |
| Eiser et al. [44]     | −               | PF, RP, SF, vitality, pain, GH |
| Malo et al. [64]      | −               | PF, RP  |
| Rodl et al. [85]      | =               |         |
| Koopman et al. [61]   | −(1997)         | MF, autonomy |
|                       | + (2002)        | Cognition, SF, NE |
| Gerber et al. [51]    | =               |         |
| Hoffmann et al. [59]  | =               |         |
| Thijsens et al. [99]  | =               | PF, RP  |
| Aksnes et al. [29]    | =               |         |
| Bekkering et al. [34] | =               | PCS     |
| +                     |                 | PCS     |
| Paredes et al. [74]   | =               | PF, RP, SF, GH, SF |
| Barrera et al. [31]   | =               |         |
| Forni et al. [49]     | =               | PF      |
| Reichardt et al. [82] | =               | MH      |
| Sun et al. [95]       | =               |         |
| Liu et al. [63]       | =               |         |
| van Riel et al. [100] | −               | PWB, autonomy, SE, SS |
| Gradl et al. [53]     | +               | RS, MH, vitality |
| Fidler et al. [48]    | =               |         |
| Edelmann et al. [43]  | =               | PF, GH  |
| Leiser et al. [62]    | =               |         |
| Weiner et al. [103]   | =               |         |
| Fernandez-Pineda et al. [47] | = | PCS |
| Podleska et al. [78]  | =               | PCS     |
| Ranft et al. [81]     | =               | PCS     |

GH: global health; MCS: mental component score; MF: motor function; MH: mental health; NE: negative emotion; ns: significance not specified; PCS: physical component score; PF: physical function; PWB: physical wellbeing; RP: role-physical; RS: role-social; SE: school environment; SF: social function; SS: social support/peers. 1Minus (−): poorer in comparison; plus (+): better; equals (=): no difference. 2Reference values either supplied with the measure or collected from noncancer controls as part of the study. 3Result based on overall or summary scores; if these were not provided, result at domain score level was provided (QLQ-C30 functional scales only). 4Total and/or summary scores can be calculated with the measure used, but this was not reported. 5Three quality of life measures used, all giving different results.

### 4. Discussion

This review aimed to collate all studies reporting psychosocial wellbeing using a valid measure, in patients with sarcoma. Overall it seems there is an improvement in the physical aspects of QOL over time but not in psychosocial function or mental health. Psychosocial wellbeing is poorer than the general population, and there is no difference if patients have amputation, limb-sparing surgery, or rotationplasty. However, results are not conclusive and, due to a number of factors, must be viewed with caution. The methodological quality of many studies was poor, especially in the selection and administration of outcome measures; even those rated “high quality” using our prespecified criteria reported some significant limitations. For example, Hinds et al. [58] used the PedsQL, a well-established, validated measure of QOL for children and adults, but in their study of adolescent QOL they noted low internal consistency in the social function domain so were unable to report these results. This also limited their ability to report an aggregate psychosocial domain and overall QOL score.

Incomplete reporting of QOL data was noted in a number of papers where the authors did not present total, summary, and domain scores [40, 44, 64, 99, 101]. While the level of reporting depends on the aims of the study, if the aim, as in the majority of the included studies, was to report QOL, then domain as well as summary/total scores can help to identify which aspects of life are better/worse than the comparator. The lack of detail on how a measure was administered was also a considerable problem. Our minimum criteria of quality was the mode of administration; if we had included a criteria of the precise detail of administration (including who, where, and how), then more studies would have been judged as poor quality. Such information is likely to help the reader to judge the degree of bias and how the administration of questionnaires could have influenced the results [24]. Finally, if the item scores are combined to make an overall aggregated score without appropriate imputation, then the overall score could be erroneously low.

Another problem with assessing PRO in patients with sarcoma is the heterogeneity of the population, both in terms of age, disease type, and anatomic location. Sarcoma affects children, adolescents, and adults, and a number of studies used measures which had not been validated for that age group. This was especially an issue with studies using the SF-36 and QLQ-C30, which are only validated for patients aged 18 onwards but 43% included participants younger than 18 years old. Measures developed for adults may not be specific enough to detect QOL differences in children and adolescents. The lack of measures that can span the full age range of a sarcoma population is a well-recognised limitation of PRO research in adolescents and young adults with cancer, especially with the content of current generic measures not reflecting issues important to young people [1, 109–111].

A further factor impacting the results in the current review has been the use of generic population or generic cancer measures of QOL. The need for disease-specific measures is well recognised as having the sensitivity to detect changes related to a particular condition [112]. Quality of life measures
### Table 8: QOL measured by the SF-36I.

| First author                  | Comparator | Quality of life | Domains |
|-------------------------------|------------|-----------------|---------|
| Davis et al. [41]             | AMP vs. LSS | −5 PF           |         |
| Veenstra et al. [101]         | Reference values | −5 PF, RP     |         |
| Eiser et al. [44]             | AMP vs. LSS | =5 PF, RP, SF, vitality, pain, GH |         |
| Malo et al. [64]              | Reference values | =5 PF, RP |         |
| Gerber et al. [51]            | Reference values | =         |         |
| Hopyan et al. [60]            | Rotationplasty, AMP vs. LSS | =         |         |
| Thiissens et al. [99]         | Reference values | =5 PF, RP |         |
| Akahane et al. [28]           | Reference values | =         |         |
| Aksnes et al. [29]            | Hodgkin’s disease | − PCS |         |
| Ginsberg et al. [52]          | Rotationplasty, AMP vs. LSS | =         |         |
| Bekkering et al. [34]         | Reference values | + MCS |         |
| Expósito Tirado et al. [45]   | AMP vs. LSS | =         |         |
| Barrera et al. [31]           | Reference values | =6         |         |
| Bekkering et al. [33]         | Time: 3 to 12 months after surgery | + BT specific, PCS |         |
| Forni et al. [49]             | Reference values | + MH |         |
| Han et al. [55]               | Time: before surgery to 6 months after surgery | + |         |
| Liu et al. [63]               | Reference values | = ns |         |
| Gradl et al. [53]             | Reference values | =5 RS, MH, vitality |         |
| Rivard et al. [83]            | Time: before surgery vs. 12 months after surgery | + |         |
| Shchelkova and Usmanova [91]  | GCT vs. OS | =5 PF, MH, GH, SF |         |
| Fidler et al. [48]            | Reference values | =         |         |
| Edelmann et al. [43]          | Reference values | =5 PF, GH |         |
| Poort et al. [79]             | Severe fatigue vs. none | =         |         |
| Bekkering et al. [108]        | AMP vs. LSS | − PCS |         |
| Fernandez-Pineda et al. [47]  | Reference values | = PCS |         |
| Ranft et al. [81]             | Reference values | = PCS |         |

AMP: amputation; BT: bone tumour; GCT: giant cell tumour; GH: global health; LSS: limb-sparing surgery; MH: mental health; ns: significance not specified; OS: osteosarcoma; PCS: physical component score; PF: physical function; RP: role-physical; RS: role-social; SF: social function. Minus (−): poorer in comparison; plus (+): better; equals (=): no difference. Direction of significance, i.e., better or worse, based on the first comparator, or the last time point if a longitudinal comparison. Result based on overall or summary scores; if these were not provided, result at domain score level was provided (QLQ-C30 functional scale only). Reference values either supplied with the measure or collected from noncancer controls as part of the study. Total and/or summary scores can be calculated with the measure used, but this was not reported. Three quality of life measures used, all giving different results. Based on SF-36 and bone tumour-specific measure results reflecting the comparison across the whole sample.
for various cancer types have been developed (for example, see http://qol.eortc.org/questionnaires/). The lack of difference between a sarcoma population and general population may not be detected because the content of the measure may not reflect the specific challenges related to having a sarcoma diagnosis. The fact that there are questionnaires specific for other cancer types supports the need for content reflecting tumour-specific experience. This was highlighted in a study by Skalicky et al. [113] who showed the uniqueness of sarcoma in the development of the Soft Tissue Sarcoma Symptom Inventory; clinicians and patients identified eight important symptoms not reflected in existing measures (including the SF-36 and QLQ-C30). If a measure does not reflect the experience of the population, then it is unlikely that it will detect important differences.

The size of the studies in this review also compromised our ability to conduct any statistical analysis of the results. Most of the identified studies had small samples, with less than a quarter including more than a hundred patients, and half including less than fifty patients. Sample size was also a particular issue for studies aiming to identify influencing or predictive factors that included large numbers of variables; these were potentially underpowered to be able to identify anything of significance.

5. Conclusion

Unfortunately, the results of the studies included in this review do not provide us with a clear understanding of the impact of sarcoma on psychosocial outcomes. Instead, the review demonstrates that there is a need for well-designed studies in this area and a more consistent approach to the measurement of patient-reported outcomes. It is clear that sarcoma has an impact on psychosocial wellbeing, but we do not know enough about what aspects are impacted, and at what point in the patients diagnostic trajectory.

We make a number of recommendations based on this review: first, more detailed understanding of patients’ experience of being diagnosed and living with sarcoma is needed, so similarities and differences between sarcoma-related variables (at a minimum, type of sarcoma) can be identified. Second, outcome measures which reflect the particular physical and psychosocial concerns and experiences of patients with sarcoma need to be developed. Third, in order to achieve the second recommendation, a large qualitative study is required including patients across ages, types and sites of sarcoma, and various times from diagnosis to ensure measures that are developed or existing validated measures reflect issues important to patients and will therefore be sensitive enough to detect change. The final recommendation is for clinicians and researchers to take a more standard approach in the administration of outcome measures and report this more thoroughly; the criteria described to assess quality in this review could act as a guide.

Disclosure

The views are of the authors and do not necessarily reflect those of Sarcoma UK, the NIHR/NHS, or Teenage Cancer

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**Table 9: QOL measured by the QLQ-C30**

| First author | Comparator | Quality of life | Domains |
|--------------|------------|----------------|---------|
| Hillmann et al. [56] | Rotationplasty vs. LSS | + | Role |
| Veenstra et al. [101] | Reference values | − | PF, RP |
| Rodl et al. [85] | Reference values | = | |
| Zahlten-Hinguranage et al. [107] | AMP vs. LSS | = | |
| Hoffmann et al. [59] | Hip disarticulation vs. AMP vs. LSS | = | |
| Paredes et al. [74] | Time: diagnosis to treatment | + | GH |
| Barrera et al. [31] | AMP vs. LSS | = | |
| Reichardt et al. [82] | Metastatic STS vs. metastatic BT | ns | |
| Custers et al. [37] | High vs. low fear of recurrence | = | |
| Schelkova and Usmanova [91] | GCT vs. OS | − | PF, MH, GH, SF |
| Tang et al. [97] | Distress vs. no distress | − | |
| Poort et al. [79] | Severe fatigue vs. none | − | |
| Podleska et al. [78] | Other cancer patients | + | |
| Wong et al. [105] | Time: before treatment to 5 years after treatment | ns | |

AMP: amputation; BT: bone tumour; GCT: giant cell tumour; GH: global health; LSS: limb-sparing surgery; MH: mental health; ns: significance not specified; OS: osteosarcoma; PF: physical function; RP: role-physical; SF: social function; STS: soft tissue sarcoma. Minus (−): poorer in comparison; plus (+): better; equals (=): no difference. Direction of significance, i.e., better or worse, based on the first comparator, or the last time point if a longitudinal comparison. Result based on overall or summary scores; if these were not provided, result at domain score level was provided (QLQ-C30 functional scale only). Reference values either supplied with the measure or collected from non-cancer controls as part of the study. Total and/or summary scores can be calculated with the measure used, but this was not reported. Text is unclear, and data presented in an appendix are no longer available. Three quality of life measures used, all giving different results.
Trust. None of the funders were involved in conducting the review or drafting the manuscript.

Conflicts of Interest

The authors have no conflicts of interest.

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Supplementary Materials

The supplemental files contain detailed tables of information referred to in the text of the manuscript. (Supplementary Materials)

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