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OBJECTIVE CLINICAL MEASUREMENT OF PHYSICAL FUNCTIONING AFTER TREATMENT FOR LOWER EXTREMITY SARCOMA–A SYSTEMATIC REVIEW

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Short title/Running title: Objective functional outcomes in sarcoma

Ethical Review Committee Statement and Statement of Location: Not Applicable.
Abstract

Background: Physical impairments and activity restrictions cause significant morbidity after surgery for sarcoma. Yet objective assessments of key components of balance, gait and physical activity (PA), using valid and reliable outcome measures, is lacking in routine clinical practice.

Purpose of Review: We therefore performed a systematic review to identify studies quantifying balance, gait and PA in clinically useful ways, after lower extremity sarcoma.

Patients and Methods: Relevant articles quantifying balance, gait and PA in patients who underwent surgery for lower extremity bone or soft tissue sarcoma were identified from Medline, Embase, Scopus, and Web of Science up to February 2016. Results were compiled by principal research findings, objective measures used, their ability to detect differences between important clinical groups, change over time and reliability.

Results: Eighteen articles were included. Surgery had a significant impact on outcomes (p<0.05). A wide range of measures and concerns about accuracy of measurement were noted, as gait and PA measures did not discriminate between distinct clinical groups such as limb sparing surgery and amputation, and did not detect changes over time. Few studies investigated reliability (n=1) and sensitivity to change (n=4).

Conclusion: There is a deficit of studies quantifying balance, gait and PA in patients with lower extremity sarcoma. Studies did not use consistent, valid and reliable instruments. There is an urgent need to develop novel objective measures of physical functioning in this patient group to encourage evidence-based clinical care.

Key words: balance, gait, physical activity, activity restrictions, functional outcomes, musculoskeletal cancer.
Introduction

Sarcomas are a heterogeneous group of rare cancers arising in bone and soft tissues, in almost any anatomical location, and with an estimated incidence of 27,908 new cases per year in Europe (1). About 84% are soft tissue sarcomas (STS), the incidence of which increases with age, and 14% are bone sarcomas (BS), which occur more frequently in children and adolescents (1). Multi-modality treatment for lower extremity sarcomas includes chemotherapy, radiotherapy and major surgery (2, 3). Although 85% of patients undergo limb sparing surgery (LSS), many face complications such as implant failure, limb shortening, wound healing, and infection (4), sometimes demanding multiple revision surgeries. In some cases amputation (AMP) is necessary.

Survivors of childhood cancer (also referred to as childhood cancer survivors, CS) face significant long term activity restrictions, education and employment problems due to extensive surgery (5, 6). On the other hand, older survivors of adult cancer (also referred to as adult cancer survivors, AS) commonly develop impaired balance and gait due to the combined effect of pre-existing comorbidities and surgery on the locomotor system (7). Poor balance and gait renders patients inactive, thereby further increasing health risks; for example: risk of falls, exposing them to serious consequences of fractures, disability and loss of independence (8-10), ultimately jeopardising their overall quality of life (QoL) (11, 12). Therefore quantifying balance, gait and physical activity (PA) levels in the pre-operative, early post-operative and rehabilitation period, can present clinicians with important information about the severity and nature of physical limitations. This can help identify “at risk” patients, suitable for targeted interventions and early rehabilitation referrals, which is key to enhanced recovery (13). Furthermore, as new techniques develop for the surgical treatment of extremity sarcomas, better measures of physical functioning are needed for their objective evaluation.
Although traditional measures of physical functioning (functional outcomes) in sarcoma survivors, the Toronto Extremity Salvage Score (TESS) (14), and the Musculoskeletal Tumour Society Scoring system (MSTS) (15) measure disability and impairments like joint range of movement, muscle strength, joint stability, pain, deformity, functional activity and emotional acceptance, respectively, they do not capture any objective information on balance, gait and PA. Moreover, TESS relies on subjective recall and does not relate to objective data about gait and PA (16), posing a difficulty in understanding underlying interactions. In spite of increasing research into balance, gait and PA in recent years (17-19), common barriers to clinical translation are high costs or that devices are cumbersome and inaccurate.

Cost-effective clinically useful accurate, valid and reliable outcome measures are urgently needed to ensure effective clinical management. (20). Useful measures would accurately detect differences between distinct treatment groups (LSS vs AMP), shed light on interactions with important clinical factors (for example: joint range, muscle strength), measure the impact of treatments (chemotherapy, surgery, rehabilitation strategies) over time and show reliability in repeat measurements (21, 22). Therefore, the aim of this paper was to systematically review the literature to identify studies quantifying balance, gait and PA in patients treated for lower extremity sarcoma, using methods which are likely to be easily translated into routine clinical practice.

Specific objectives are:

1. To identify methods used to quantify balance, gait or PA in patients after treatment for sarcoma, with the potential for translation into busy clinic settings.

2. To investigate whether these measures have been tested for validity, reliability and sensitivity to change.
Methods

Search Strategy:

We identified relevant studies by searching four electronic databases, Medline, Embase, Scopus, and Web of Science up to February 2016. An initial search combined four main search terms using the Boolean “AND” operator: 1) Bone neoplasms OR Soft tissue neoplasms 2) Physical functioning 3) Extremities 4) Measurement (Appendix A). After reviewing eligible articles, additional search terms covering the three physical functioning domains of balance, gait and PA were identified, and a second search implementing these terms was undertaken to ensure no relevant articles were missed. (Appendix B).

Selection of studies:

Search results from each database were imported into EndNote bibliographic management software (Thomson Reuters, Endnote version X7). The titles and abstracts of these references were screened by two independent reviewers (SF and CG) and appropriate articles selected. Differences in opinion were resolved by consensus. Additional hand searching of reference lists of included articles and excluded reviews identified further studies for inclusion (Figure 1). Studies were selected using the eligibility criteria outlined.

Inclusion Criteria:

1. Primary research investigating objective measures of postural balance, gait and physical activity in patients treated for lower extremity bone or soft tissue tumours.

2. Devices which have the potential to be used in routine busy clinical settings (advantages such as rapid to measure, portable depending on outcome measured)
Exclusion Criteria:

1. Conference proceedings or non-journal articles such as commentaries whose methodology is not clear.
2. Non-English articles
3. Including purely upper extremity tumours.
4. Case report/case reports
5. Full text not available after considerable search.
6. Cumbersome laboratory systems such as a Gait laboratory, EMG systems etc.
7. Review articles (secondary research)

Data Extraction:

The data extraction tool was prepared by the 2 independent reviewers, based on clinical information, and the psychometric properties of outcome measures. The tool consisted of 2 main tables. The first table comprised the patient population, demographics, treatments, instruments used to capture outcomes, objective measures used and main results/conclusions of the study (Table 2). The second table comprised psychometric properties, including validity, reliability and sensitivity of change of balance, gait and PA measures in these studies (Table 3). Data were extracted by the first independent reviewer (SF) using the tool and were reviewed, by a second independent reviewer (CG), to ensure accuracy and rigour.

Quality assessment tool:

As no standardised quality assessment tool is available for this topic (23), a checklist (Table 4, Section 1) was developed, including both methodological and patient criteria. This comprised a comprehensive list of criteria from the Critical Appraisals Skills Programme (CASP) (CASP, 2014) and Strengthening The Reporting of Observational Studies in Epidemiology (STROBE)
(24) for methodological issues; criteria related to patient specific issues were selected from a checklist developed in a previous study (25),[which was adapted from (26-28)]. The maximum score achievable was 18 (100%): studies achieving a score of greater than 70% were defined as “high quality”, 50-70% were “moderate quality” and less than 50% were “low quality” (29). A quality assessment of selected papers was conducted but was not used as a selection criterion.
Results:

A total of 2661 papers were identified, of which 18 were included (Figure 1, Table 1) published between 1998 and 2013. Of the 18 studies, 5 were case series (30-34), 7 cross-sectional studies (7, 16, 35-39), 2 prospective studies (40, 41), 2 prospective longitudinal studies (assessment at multiple time points) (6, 42), 1 retrospective cohort study (43) and 1 validity and reliability (44). 11 were high quality studies (>70% rating) and 7 moderate quality (50-70% rating) (Table 4, Section 2).

Of these 18 studies, 1 was about balance (31), 7 gait (30, 32-34, 36, 38, 39) and 10 PA (6, 7, 16, 35, 37, 40-44) (Table 2). The sample size in the studies ranged from 4 to 82.

15 were conducted in patients with bone tumours (BT) only and 3 in a mixed group of BT and STS. In 12 studies, patients had LSS and in 6 LSS+AMP. The age of patients ranged from 9 to 85 years and time since surgery from 6 weeks to 39 years. In longitudinal cohorts, patients were assessed pre-operatively and at several time points up to a maximum of 24 months. 7 were childhood Cancer survivors (CS), 5 adult cancer survivors (AS), 4 CS+AS and 2 not specified.

A. Methods used to quantify balance, gait and PA outcomes (Table 2):

A wide range of outcome measures were used to quantify balance, gait and PA. These included amplitude of the center of pressure (ACP), velocity of the center of pressure (VCP), step velocity, walking speed, stride length, step cycle duration, gait symmetry, double support time, swing time, stride time, steps/day, time spent walking, gait cycles (gcs)/day, strides/day, and movement intensity. 10 instruments were used to capture outcomes included force platforms, foot switches such as VA Rancho - Footswitch Stride Analyser ®, gaitmats such as GaitMatTMII and GaitRite ®, pedometer and activity monitors such as Dynaport ® ADL,
StepWatch™ Activity Monitor, Step Activity Monitor ® (SAM), Uptimer device ® and Actilog ® V3.0

Validity, Reliability and Responsiveness to change over time. (Table 3):

I. Indicators of validity including outcomes in different clinical groups and the impact of clinical factors:

Patients presented with significantly diminished balance, gait and ambulatory (walking) PA compared to healthy controls in the short and long term (6, 31, 34), where patients spent most of their time sitting (54+-18% of the time) (7, 16). LSS and AMP are distinct clinical groups, and most studies demonstrated no significant differences in ambulatory PA between LSS and AMP (35, 43, 44). However, one study showed that patients with above knee AMP, resection alone cases (simple LSS) and autoclaved bone reconstructions achieved a higher number of steps than patients who underwent complex LSS such as the Kotz modular reconstruction system, including total knee replacement (TKR) or semiconstrained total hip replacement (THR), (7). BT patients (6001 ± 2684 gcs) demonstrated lower average daily step counts than STS patients (7758 ± 3835 gcs ) (p < 0.05) (7). Patients with complications such as wound-healing problems, superficial or deep infection demonstrated significantly lower intensity of PA at 18 months, than those without complications (6). In terms of correlations with existing measures, contrasting results were seen, for example: in one study the number of step cycles or percentage of ambulatory time were not correlated with TESS or MSTS (16) but in others, MSTS correlated with “time spent walking” (44), and with steps/day (number of steps = 0.001 X MSTS score ± 14.499) (7). In addition, although instruments assessing similar outcomes (for example: Various walking activities (VWA) and Timed Up and Down Stairs (TUDS)), detected differences between LSS and AMP, the general physical activity (GPA) from the Actilog
activity monitor did not detect differences between these groups (35). Interestingly, age did not relate to PA, but body mass index (BMI) was negatively correlated with duration of data collection (p<0.01) (16). In addition, although time since surgery, length of bone resected and ROM did not correlate with PA, muscle strength was significantly positively correlated with PA (Sugiura et al, 2001).

II. Sensitivity or responsiveness to change:

Only 4 studies investigated change in outcomes over time. Of these, step-cycle duration, walking speed, and gait symmetry recorded by footswitches were sensitive to change over time, as at the end of rehabilitation gait improved compared to baseline (p<0.05) (34). Similarly PA captured by StepWatch™ Activity Monitor was sensitive to change from 6 weeks to 18 months post-surgery (6). However, contrasting results in another study revealed GPA from the Actilog monitor was not sensitive to change over time from 3 to 12 months post-surgery, although there was a change in PA detected by the Baecke questionnaire. (42).

III. Reliability:

Only 1 reliability study was undertaken, with good intraclass correlation coefficient (ICC) from 0.65 to 0.91. ICC values for PA volume in walking time were 0.65, standing time were 0.83, sitting time were 0.75. ICC values for movement intensity (m/s2) was 0.91 in walking, 0.69 in standing, 0.79 in sitting and a total of 0.91 in walking, standing or sitting (Van Dam et al, 2001).
Discussion

We have reviewed the literature and identified 18 relevant articles quantifying balance, gait and PA. Studies were highly variable, as they used a wide range of outcome measures, investigated different age groups, clinical sub-groups, ranged from case series to longitudinal studies, publication year from 1996 to 2013, and 11 were high quality and 7 moderate quality, posing a difficulty in synthesizing results.

Very few studies investigated aspects of validity of outcome measures raising questions on accuracy of measures and trustworthiness of results obtained. For example: Only one study investigated reliability and four sensitivity to change over time. Furthermore, overall results were perhaps surprising that some gait and PA measures were unable to distinguish between distinct clinical groups, such as LSS and AMP (35, 43, 44). In contrast, in another study, patients who had above knee AMP achieved a higher number of steps than complex LSS patients (Kotz TKR and Semiconstrained THR), and complex LSS were significantly different from simple LSS groups (resection alone) (7). The inability to distinguish between LSS and AMP groups might therefore be due to the wide variation in the level and complexity of surgery in each group, as well as the inaccuracy or inapplicability of measures to the clinical scenario.

It was interesting that GPA from Actilog could not detect differences between LSS and AMP, whilst TUDS and VWA did. (35). Although it could be argued that this is because GPA, TUDS, VWA measure different attributes of physical functioning it is of note that in another study, Baecke questionnaire measuring PA, was sensitive to changes in PA from 3 to 12 months ($p < 0.01$), but the GPA was not. (42). Therefore clearly GPA is not sensitive to change of PA over time. This could be attributed to non-linear methods of data analysis being more sensitive than linear methods, for PA data from activity monitors (45). For example: Pattern of PA (Distribution of activity also referred to as alpha ($\alpha$)) was found to be more sensitive than volume (percentage of time spent in an activity) in other clinical groups (46).
Although few studies demonstrated that established measures such as TESS/MSTS were related to total steps/day (16, 44), these measures alone do not provide a complete clinical picture of a patient’s impairment, disability and activity restrictions. This hampers clinicians from planning holistic management strategies often triggering poorer outcomes. It is clear that balance, gait and PA measures identified in this review provide new objective clinical information, completely different from TESS/MSTS, re-emphasizing the need to collect novel measures in conjunction with established measures in routine clinical practice. This is useful in planning clinical and cost-effective management strategies and significantly improving outcomes. However, a significant barrier to clinical use is the lack of validity and reliability testing of measures. This could present clinicians with potentially inaccurate information and may increase the risk that clinically important information is missed. In addition, costly or heavy devices pose added difficulties to clinical translation.

The ideal device for use in a clinical setting would be valid and reliable (47), cost-effective (7), portable and light-weight and able to be used for self-monitoring. Mounting such a device on the lower back using a belt (44), seems to be a suitable and pragmatic approach and avoids problems with limb mounting, such as the effects of major surgery, scars and amputation. Modern accelerometers have been used to improve balance and gait rehabilitation, by providing immediate biofeedback (48-50). For example: audio biofeedback from an accelerometer has been used to improve balance (51). Similarly simple inexpensive activity monitors have been used to monitor and guide PA rehabilitation strategies in home settings. (52, 53).

The studies identified showed that balance, gait and PA were significantly poorer in patients than healthy controls in both the short and long term, (6, 31-33). This clearly has clinical implications, emphasizing the importance of rehabilitation in both acute and chronic phases. Furthermore, the long-term rehabilitation of patients with complications requires a focus on intensity training, as intensity of PA continued to remain affected at 18 months post-surgery.
Other approaches which need to become a part of rehabilitation include reducing dependency on visual cues during progressive balance training (31). In addition, clinical factors such as proximal muscle strength and BMI significantly correlated with gait and PA (p<0.05), but not length of the bone resected or ROM (36) (7), stressing the importance of prioritising proximal muscle strengthening and weight reduction during physiotherapy. Rehabilitation of the unaffected extremity is also important as there may be bilateral hip muscle weakness (30), possibly because of over-compensation for the affected extremity.

This is the first systematic review investigating the measurement of balance, gait and PA in patients treated for lower extremity sarcoma. The main strengths of the review are a robust search strategy and a quality assessment tool specifically developed for this heterogenous patient group. Weaknesses of the review include sample size was low in some studies, presenting difficulty in generalizability of results. Some papers were older, and patients were treated at a time when primary amputation rates were higher, leading to a higher number of patients presenting with poorer physical function and is a potential source of bias. Although one paper showed contrasting results (47), the real reason could be that this sample is from an older study and may be significantly different to that seen in the clinic in the modern era. Other findings which would be important to account for in future studies are that balance and gait were significantly affected in unbalanced tasks (31, 34), arguing for the collection of outcomes in real life challenging situations. It is also important to account for differences in ambulatory PA at weekends, as a study demonstrated that LSS patients walked only 95% of the steps achieved during weekdays (16).
Conclusion:

There is a deficit in studies quantifying balance, gait and PA in patients treated for lower extremity sarcoma. Of the studies that exist, the majority did not use consistent, valid and reliable instruments developed specifically for sarcoma. Novel cost-effective, portable, valid and reliable instruments specific to assessing balance, gait and PA are important to develop, to gain accurate information, in patients treated for lower extremity sarcoma. Better measures of physical functioning are important when considering the impact of treatment and are essential if clinical management is to be improved. Wearable, portable and cost-effective tools such as activity monitors could be possible solutions, as are easy to apply and have a good potential for clinical translation.

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Declaration of Interest: CG and SF report securing grants from Children with Cancer UK Charity, Sarcoma UK Charity and Shear’s Foundation to the institution during the conduct of the study.

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References

17. Carty CP, Bennett MB, Dickinson IC, Steadman P. Electromyographic assessment of Gait function following limb salvage procedures for bone sarcoma. Journal of
16


Figure Legends:

Figure 1: Selection of Papers for this review.

**Figure 1: Selection of Papers for this review**

- 2644 articles identified in the initial + updated search (additional search terms) up to Feb 2016.
- 2661 potentially eligible articles before review of title and abstract of papers.
- 2555 articles rejected after review of title and abstract.
- 17 potentially eligible papers identified by reviewing reference lists of related reviews and eligible articles.
- 2661 potentially eligible articles before review of title and abstract of papers.
- 89 remaining before review of full texts.
- 71 articles rejected after review of full text.
- 18 papers included in the systematic review.
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<th>References found following automated de-duplication May 2014-Dec 2015</th>
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<tr>
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<td>1983</td>
<td>406</td>
<td>255</td>
</tr>
<tr>
<td>GRAND TOTAL</td>
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<td></td>
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### Table 2: Objective Measures of Balance, Gait and PA.

<table>
<thead>
<tr>
<th>No.</th>
<th>Author, Year and Type of study</th>
<th>Number of patients</th>
<th>Age (in years)</th>
<th>Childhood cancer survivors (CS)/Adult cancer survivors (AS)</th>
<th>Type of tumour</th>
<th>Procedure [Limb Sparing Surgery (LSS)/Amputation (AMP)]</th>
<th>Follow Up</th>
<th>Control group</th>
<th>Device/Instrument used</th>
<th>Parameters measured</th>
<th>Main Results/Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>De Visser et al, 2001 – A case series.</td>
<td>N= 11</td>
<td>Mean age (+/- SD) 41.45</td>
<td>10 patients with a PMBT in the lower</td>
<td>LSS (Resection with or without)</td>
<td>N/A</td>
<td>10 healthy controls.</td>
<td>Force Platform: wooden plate on four force</td>
<td>Balance measures: Measure of ACP (in millimetre)</td>
<td>After LSS for lower extremity sarcoma, patients demonstrated no significant differences in balance (ACP and VCP) compared to healthy controls, in upright standing.</td>
<td></td>
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</tbody>
</table>
extremity (ilium, proximal and distal femur) and one with a STS in the gluteal region. reconstruc tion)

transducers and recorded vertical ground reaction forces. (mm) and the VCP (millimetre/second (mm/sec) in normal standing and standing on balance board, with eyes open, eyes closed and a task demanding attention. However, upright standing in more challenging conditions such as visual and cognitive loads is associated with significantly higher ACP and VCP compared to normal standing. This suggests that postural automatism is affected in patients treated for lower extremity sarcoma.

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**Impairment – Balance**

**Patient group – LSS+AMP or AMP – No articles**
### Impairment – Gait

**Patient group: LSS**

| 2. | De Visser et al., 1998 | N =12 | Mean age 38 years | PMBT or locally aggressive primary BT of lower extremity (osteosarcoma (n=3), chondrosarcoma (n=6), ewing’s sarcoma (n=2) and aggressive locally aggressive primary BT of lower extremity) | LSS (Excision + reconstrucion or arthrodesis +) | Mean time since surgery (+/- SD) 34 +/- 21.63 (range, 13 to 59) months. | 10 age-matched healthy controls, mean age 37.5 years | **Foot switches:** Treadmill walking - At patient preferred speed. Footswitches in shoe insoles to record heel strike and heel off. | **Gait measures:** Spatio-temporal parameters of gait including walking speed, stride time and co-efficient of variation. | Restoration of walking after LSS is good in normal walking conditions, but patients exhibit lower preferred walking speed and higher coefficient of variation during normal walking. Complex walking with visual and cognitive load demonstrated a significant decrease in stride time in patients, but not in controls. Therefore, suggesting gait reautomatisation is not complete 2 to 5 years post-surgery. |
| 3. | De Visser et al, 2000 | N=19 | Mean age 45 (range 21 to 80) years | osteoblastoma (n=1)) | 12 to 24 months post surgery | LSS Group 1: Knee surgery: (n=9). | Group 2: Hip surgery. (n=10) | 10 healthy controls, mean age 37 (range, 22 to 61) years. | Foot switches: Treadmill walking, with footswitches in insole of shoes. Electrogoniometers to measure knee flexion angles. | Gait measures: Spatio-temporal parameters of gait including preferred walking speed, stride time, stance time, swing time, double-limb support time, and joint angles. | Mean preferred walking speed lower in patients compared to controls (0.7 m/s vs 1.1 m/s). Mean stride duration longer in patients compared to controls (1.5s vs 1.1s). Stance phase shorter in the affected leg (57% of cycle compared to 62%). No difference between hip and knee groups in these parameters. Range of motion is lower in the knee in patients compared with controls in the stance phase. Therefore, patient’s gait is significantly affected compared to healthy control demonstrating an incomplete re-organisation of gait. |
| 4. | Kawai et al, 2000 | N=15 | Median age 24 | PMBT of the LSS - Patients | Median time | Foot switches: | Gait measures: | Patients had significantly lower free walking velocity and cadence than |
A cross-sectional study.

Tumours included osteosarcoma (n=6), ewing’s sarcoma, (n=4), chondrosarcoma (n=4) and malignant fibrous histiocytoma (n=1). Patients underwent an intra-articular resection of the hip. The median length of femoral resection was 21 (8-28) centimetres (cms).

Reconstruction consisted of 1 THR and 14 controls (n=20) and 6 patients after hip disarticulation (n=6).

VA Rancho - Footswitch Stride Analyser ® (Rancho Los Amigos Medical Centre, California)

Gait stride characteristics including Free-walking velocity, stride length, cadence, gait cycle time, double-limb support time, and single-limb support time.

Controls, but higher than after hip disarticulation (walking velocity 63.9 m/min vs 80.6 and 50.6 respectively; cadence 101 steps/min vs 111 and 81.6 respectively). Asymmetry of single-limb support time significantly correlated negatively with gait velocity and positively with net energy cost. Use of a walking aid led to less asymmetry but did not change velocity because cadence was reduced and stride length increased.

Asymmetry of single-limb support time negatively correlated with the strength of hip abductors. Walking performance of LSS patients was better than those who had hip disarticulation.

<table>
<thead>
<tr>
<th>N=11</th>
<th>Mean age at time of surgery 43 (range 19 to 66) years.</th>
</tr>
</thead>
</table>

- **AS**
- **PMBT of the lower extremity.**
- **Tumours included osteosarcoma, ewing’s sarcoma, or chondrosarcoma.**
- **LSS** (Distal femoral knee prostheses n=4, proximal femoral hip prostheses n=4, and a saddle prostheses n=3)
- **Gait analysis at 5 months postoperatively.**
- **No control group.**

**Foot switches:**
- Treadmill walking - at patient preferred speed.
- Footswitches in the insoles of the shoes were used to record heel strike and heel off.

**Gait measures:**
- Preferred walking velocity, stance duration, swing duration, step-cycle duration, stride time.

**Improvement in walking speed and asymmetry is seen during recovery up to 15 months post operatively.** However even after the recovery period gait control is not optimal, which could be attributed to the sensory motor losses as a result of treatment of the cancer. Patients with knee prosthesis had a preferred walking speed of 3.9 km/hr and a stride time of 1.15 s, those with a hip prosthesis with 3.4 km/hr and 1.21 s and those with a saddle prosthesis 2.2 km/hr and 1.50 s respectively.
<table>
<thead>
<tr>
<th>No.</th>
<th>Authors (Year)</th>
<th>N =</th>
<th>Mean age (+/- SD)</th>
<th>CS + AS</th>
<th>PMBT</th>
<th>LSS – PMBT</th>
<th>Mean+/ -SD of follow-up</th>
<th>20 age sex-matched healthy control, mean age</th>
<th>Gaitmat:</th>
<th>Gait measures:</th>
<th>Gaitmat:</th>
<th>Gait measures:</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.</td>
<td>Tsauo et al, 2006 - A</td>
<td>20</td>
<td>21.7 +/- 7.3 (range 13 to 40 years)</td>
<td>PMBT (Osteosarcoma) around knee, located in the distal femur (n=13) and proximal tibia (n=7).</td>
<td>CS+AS</td>
<td>LSS – Wide resection and endoprosthetic knee reconstruction (TKR)</td>
<td>3.0 +/- 1.6 (range, 1 – 5) years post-operatively.</td>
<td>21.8 +/- 7.3 years.</td>
<td>GaitMatTMII; (Gait MatII E.Q. Inc., Philadelphia, USA), 3.6m in length.</td>
<td>Walking velocity of patients was significantly lower than controls’ (54 +/- 12m/min vs 72 +/- 6m/min, p&lt;0.05). The step length of the unaffected side was significantly shorter than that of controls and the affected side (p&lt;0.05). The stance phase of the affected leg was significantly shorter than that of controls and the unaffected side (p&lt;0.05). Conversely, swing phase of the affected leg, was significantly longer than that of the unaffected sides. Patients have achieved an acceptable recovery in gait outcomes, with some functional limitations.</td>
<td></td>
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<tr>
<td>7.</td>
<td>Beebe et al, 2009 – A</td>
<td>4</td>
<td>Skeletally immaturation</td>
<td>PMBT in the distal femur and</td>
<td>CS</td>
<td>4 LSS - Wide resection</td>
<td>Mean time since surgery with a non-invasive expandable endoprosthesis produces acceptable functional outcomes in</td>
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<p>| |</p>
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<td></td>
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<tr>
<td>Report of 4 cases.</td>
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<tr>
<td>Zohman et al, 1997 – A cross-sectional study.</td>
</tr>
</tbody>
</table>
musculoskeletal cancer (n=1). Mean age of controls were 43.6 years and time since surgery 24.1 years worn inside shoes, containing foot switches.

7.6 m/minute) and control group of AMP (71.4 +/- 5.4 m/minute) (p=0.06). No significant differences were seen between length of stride (1.41 +/- 0.13 m vs 1.43 +/- 0.12 m) and the symmetry of stance time (0.90 +/- 0.07 vs 0.87 +/- 0.11) for proximal tibial replacement vs control group of AMP. The results suggest that LSS for proximal tibia leads to a gait comparable with that after above knee AMP with a prosthesis.

Impairment – Gait

Patient group – LSS+AMP or AMP – No articles

Participation Restrictions – Physical Activity (PA)
## Patient group – LSS

### Study Details

<table>
<thead>
<tr>
<th>Rosenbaum et al.</th>
<th>Year</th>
<th>N</th>
<th>Mean age (SD)</th>
<th>CS + AS</th>
<th>PMBT</th>
<th>LSS - Intraarticular resection of tumour + reconstruction</th>
<th>Mean (SD) of follow-up</th>
<th>No control data for Dynaport.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008 – A cross-sectional study.</td>
<td></td>
<td>22</td>
<td>26.2 +/- 18.4</td>
<td>(n=18) and proximal tibia (n=4).</td>
<td>Tumours included osteosarcoma (n=14) and chondrosarcoma (n=4), ewing’s sarcoma (mutars), (n=3), and malignant fibrous</td>
<td>7.9 (range, 2 to 39 years)</td>
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</tbody>
</table>

### Tumours

- Osteosarcoma (n=14)
- Chondrosarcoma (n=4)
- Ewing's Sarcoma (n=3)
- Malignant Fibrous

### Intraarticular resection of tumour + reconstruction

- Knee replacement: (rotating hinge (mutars), n=20; or fixed hinge)

### Follow-up

- Mean of follow-up: 7.8 +/- 7.9 years

### Activity monitors:

- The DynaPort® ADL monitor: (Mc Roberts, Den Haag, The Netherlands) worn for 24 hours
- The Sam® Step Activity Monitor: (Cyma Inc., Seattle, OR): SAM

### Ambulatory PA

- **Activity (walking) and sedentary PA in 24 hours**
  - a. Time spent in different activities
  - b. Movement intensity.

### Ambulatory PA in Patients

- **Ambulatory PA in patients:** The highest percentage of PA was sitting (54 +/- 18%) of the total time recorded, followed by standing as second highest (27 +/- 16%), walking (10 +/- 6%), and lying position (8 +/- 6%). During walking, the average ambulatory daily PA accumulated to 4,786 +/- 1,770 (range 2,045 – 8,135) step cycles, which corresponds to a yearly 1.75 million steps. No significant correlation was seen in between clinical scores and ambulatory PA measures.

### Activity (walking) and sedentary PA

- **Ambulatory PA Volume:**
  - Daily number of gcs.
- **Intensity as step**
| 10. | Sheiko et al, 2012 – A cross sectional study | N=20 | Mean age 15.8 (range, 11.7 to 20.8) years | CS | PMBT in distal tibia (n=1), proximal tibia(n=8), distal femur (n=9) and proximal femur (n=2). Tumours | LSS – Implants (n=12) and Allografts (n=8) | Mean time since surgery 1.79 (range, 0.39 to 3.82) years. | 20 age- and sex-matched healthy controls | Activity monitor: StepWatch™ activity monitor (2-dimensional accelerometer). Monitored for 7 consecutive days. | Ambulatory PA: a. Volume: Total stride/day, average walking minutes/day b. Intensity: Time spent/day at high activity levels (20 minutes vs 47 minutes; p = 0.001). | Patients who had undergone LSS had significantly poorer PA sub-scores compared to controls. Significant differences were seen between LSS patients and healthy controls in total PA/day (43% vs 48% of total time active; P = 0.03), median number of total strides/day (4487 vs 7671 strides; p = 0.001), and time spent/day at high activity levels (20 minutes vs 47 minutes; p = 0.001). This demonstrates patients...
### Table 1

<table>
<thead>
<tr>
<th>Study</th>
<th>Author(s)</th>
<th>Year</th>
<th>Study Design</th>
<th>Tumour Type</th>
<th>Age (Mean)</th>
<th>Activity Monitor</th>
<th>Activity Score</th>
<th>PA</th>
<th>Notes</th>
</tr>
</thead>
</table>
| 11.   | Van der Geest et al, 2013 | – A prospective study | N=43 (range, 19 to 41.5) | Benign or low-grade malignant bone and soft tissue tumours | LSS - Local excision or curettage and | Patients were assessed before surgery | Controls were Knee arthroscopy | Activity Monitor: GPA score defined as the average number of accelerations in a 5 minute | PA: In tumour patients, 35% of patients were severely fatigued before their surgery and 33% post-surgery. Significantly higher levels of anxiety were reported by tumour patients. No significant differences between |}

In a prospective study, Van der Geest et al., 2013, included osteosarcoma (n=13), Ewing’s (n=5), and other malignancy not specified (n=2). Patients were assessed before surgery and controls were Knee arthroscopy. Activity Monitor: GPA score defined as the average number of accelerations in a 5 minute. In tumour patients, 35% of patients were severely fatigued before their surgery and 33% post-surgery. Significantly higher levels of anxiety were reported by tumour patients. No significant differences between.
Mean age of control group was 43.1 (range, 23-68) years. Patients (n=24) and at 6 months after surgery. Device which senses motion and attached at the ankle for 12 consecutive days duration through the day. Higher GPA scores mean a high PA. Tumour patients and controls were seen in pain, physical limitations, self-efficacy or PA scored captured by actometer. Higher pain scores, higher anxiety and lower self-efficacy were significantly associated with fatigue severity. In controls the percentage of severely fatigued patients decreased from 38% before surgery to 29% 6 months post-surgery. A high numbers of patients were severely fatigued in both the tumour and the knee arthroscopy groups. Pain, anxiety and self-efficacy were seen to be the most important factors linked to fatigue severity in tumour patients prior to surgery.
| 12. | Winter et al, 2012 – A longitudinal study | N=20 | Mean age (+/- SD) | CS | PMBT in the lower extremity. | Tumours included osteosarcoma (n=15) and ewing’s sarcoma (n=5). | LSS - Endoprosthetic replacement of the affected bone (proximal femur 3, distal femur 12, proximal tibia 5) | 6 weeks, 3, 6 months, 12 months, and 18 months after surgery. | 20 healthy age- and gender-matched controls. | Activity monitor: StepWatch™ Activity Monitor SAM (OrthoCare Innovations) attached to ankle and worn for seven days. | Ambulatory PA: a. **Volume** in the form of the number of gcs (one gait cycle is two steps) b. **Intensity** measured as gcs/minute. | Patients with a PMBT in the lower limb demonstrated significantly lower ambulatory PA during the course of active treatments. However these patients recover markedly after cessation of treatments; reaching 71.9% of control group volume of gcs at 18 months. Patients with complications were slower to recover with some limitations seeming to persist at 18 months post operatively. |
Participation Restrictions - Physical activity (PA)

Patient group – LSS+AMP

<table>
<thead>
<tr>
<th>13.</th>
<th>Sugiura et al, 2001 – A cross-sectional study</th>
<th>Tumours included: PMB (n=20) and malignant soft-tissue tumours (n=36).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean age</td>
<td>45.3 (range, 14 to 85) years.</td>
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<tr>
<td></td>
<td>Mean period of follow-up was</td>
<td>4.3 ± 2.1 years.</td>
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<td></td>
<td>All cases of BS were widely resected (n=20)</td>
<td>In PMBT in the distal femur (n=9), proximal tibia (n=5), proximal femur (n=3), proximal fibula (n=2).</td>
</tr>
<tr>
<td></td>
<td>Mean period of follow-up was</td>
<td>4.3 ± 2.1 years.</td>
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<tr>
<td></td>
<td>20 healthy controls of mean age 30.4 years</td>
<td></td>
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<tr>
<td></td>
<td>Pedometer: Omron Health Counter HJ-5 pedometer®;</td>
<td>(Accuracy was 95%): Pedometer worn for 2 weeks.</td>
</tr>
</tbody>
</table>
|     | Ambulatory PA: Volume in the form of number of steps/day. | Patients achieved an average daily count of 7119 ± 3563 steps (69.8% of controls 10,206 ± 1388). BT group achieved lesser number of steps/day than soft-tissue tumours. Average daily step count scores were not correlated with ROM. However they were correlated with MSTS scores (coefficient 0.52). Kotz TKR and semiconstrained THR groups had lower numbers of steps than other groups. Proximal BT nearer to the trunk tended to be lower than those with tumours in other locations.
|     | ADL score | The daily number of steps obtained by a pedometer and ADL score appear to be clinically as useful as the
|     |           |
femoral shaft (n=1) and STS were located in thigh (n=16), hip (n=8), knee (n=5), calf (n=5), pelvis (n=1), foot (n=1).

MSTS outcome measure. Thus the pedometer is a cost-effective and useful objective assessment tool for measuring walking ability in sarcoma.

| 14. | Van Dam et al, 2001 – A reliability and | N=20 | Median age 49 (range, 18 to 76) | N/A | Malignant BT in the leg, including tumours located in LSS (n=12) included allograft (n=1), allograft | Median time since surgery 2 (range, N/A) | No control group. | Activity monitor: Dynaport monitor ®; (McRoberts BV, PA: Seven aspects were measured over a period of 24 hours which were time spent | The reliability of the monitor was satisfactory, with an Intraclass correlation coefficient (ICC) from 0.65 to 0.91 over the function measured. |
| validity study. | 69) years. | femur (n=12) and tibia (n=8). | + endoprosthesis (knee) (n=5), Kotz prostheses (n=5) and mutars prostheses (n=1) or AMP (n=8) which included Above knee | 1 to 13) years. | The Hague, The Netherlands – Uniaxial accelerometer. | walking, standing and sitting (as a percentage of 24 hours), the movement intensity, and also sum of the movement Intensities. | There was a significant correlation seen between ‘time spent walking’ and the MSTS scores and also the Rand-36 scores. A significant association was also seen between ‘movement intensity during walking’ and MSTS. Results demonstrate promising reliability and validity of the monitor to clinically measure PA objectively in patients treated for a lower extremity malignant BT. |
Hopyan et al, 2006 – A retrospective cohort study

| 15. | **N** = 54 (45 completed study and 9 lost to follow-up) | **Mean age of patients who completed the study (n=45)** | **Mean age of these patients at diagnosis** 11.9 +/- 4.2 | **PMBT of the lower extremity** | **Mean follow-up time of study patients (n =45)** | **No control group.** | **Activity monitor:** Uptimer device ®; (National Aging Research Unit, Victoria, PA) **PA:** PA was measured using the uptime device **SF-36** (36-Item Short Form Survey) and uptime measured by the activity monitor, were similar between groups. Uptime had higher values in patients with rotationplasty, although statistical comparisons were not feasible. |
| 16. | Winter et al, 2009 – A prospective study. | N=23 | Median age (+/- SD) of all BT patients (n=29) | 15.1 +/- 3.2 years. | 80 patients including BT (n=29), leukaemia (n=20), lymphoma (n=15), brain tumours (n=12), germ cell tumours (n=3), and Prosthetic AMP (n=1). | LSS+AM P | 2 | 45 | Activity monitor: StepWatch™ (OrthoCare Innovations, Seattle, WA) - A uniaxial accelerometer. | Ambulatory PA: | a. Volume measured as gcs/day. Patients were more physically activity at home (3,185 gcs, 40% of controls) rather than inpatient stays (1,830 gcs, 23% of controls). | b. Intensity measured as gcs/minute. Patients with BT exhibited lower PA scores than those with leukemia with respect to the volume (1,849 gcs vs. 2,992 gcs) and also the intensity of PA. | Pediatric cancer patients (2,787 gcs/day) scored significantly lower than healthy controls (8,096 gcs). |
and lower extremity (n=23)

neuroblastoma (n=1), limb replacement (n=7), AMP (n=3), and excision (n=3) 13 patients on an average of 12 weeks post-operatively. (BMI), height and weight comparable to patients. worn on ankle

13 patients on an average of 12 weeks post-operatively. (BMI), height and weight comparable to patients. worn on ankle

17. Bekkerinck et al, 2011 – A cross-N = 82 Mean age (+/- SD) at time of surgery CS PMBT around knee, located in the LSS (n=39) consisting of surgery was No control group Activity monitor: Actilog ® V3.0; Radboud PA: a. GPA score defined as the average number of accelerations significantly better scores were seen in the LSS group for the timed up and down stairs (TUDS) and various walking activities test (VWA) as compared to the AMP group. No

during inpatient stay and 27% of the PA compared to controls during their home stay. Patients with leukaemia achieved higher percentage of PA in both inpatients and home when compared to BT, however this difference was not significant. Patients with BT seem to be at a substantially high risk of reduced PA. This indicates individualised rehabilitation interventions need to be delivered during treatment to improve outcomes.
| section study | 14.2 +/- 4.1 years. | proximal femur (n=54) and distal tibia (n=28). | allograft (n=24), endoprosthesis (n=15) | 2.8 +/- 1.6 years. | University Nijmegen Medical Centre, Nijmegen, The Netherlands | in a 5 minute duration through the day, and b. Average peak amplitude and duration (average peaks is the number of high peak accelerations in a 5 mins duration, during the day and is a reflection of intensity of PA) of accelerations significant differences were seen between LSS and AMP for any of the Actilog PA measures. In long term (from 1 to 5 years), post-surgery due to a bone cancer in paediatric population and adolescents, there is no significant difference seen between patients having a LSS and AMP with respect to overall physical functioning and PA, apart from going up and down stairs and few walking activities.

| Mean age (+/- SD) at assessment | 16.9 +/- 4.2 years. | Tumours included osteosarcoma (n=43) and ewing’s sarcoma. | Ablative surgery (n=43) | Consisting of AMP (n=27) and Rotationplasty (n=16) | University Nijmegen Medical Centre, Nijmegen, The Netherlands | – Placed on ankle of non-affected limb and worn for 7 consecutive days. | &nbsp;
| 18. | Bekkerinck et al, 2012 – A prospective longitudinal study | N=44 patients were recruited into study, out of which 24 patients completed study | Mean age (+/- SD) at time of surgery 14.9 +/- 4.8 years | CS | PMBT around knee, located in distal femur (n=32) and proximal tibia (n=12). | LSS including allografts (n=8), prostheses (n=19), Ablative surgery (n=17) | At 3, 6, 9, 12, 18, and 24 months post-surgery. | No control group. | Activity monitor: Actilog ® V3.0; Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands) – Placed on ankle of non-affected limb and worn for 7 consecutive days. | PA: a. GPA score defined as the average number of accelerations in a 5 minute duration through the day, and b. Average peak amplitude and duration of accelerations | Over the first year post-operatively, patients demonstrated significant improvements in quality of life (QoL), physical ability and activity levels as measured by Baecke questionnaire. Over the second year after surgery, the improvements were present but less pronounced. No difference in PA was detected by the Actilog activity monitor. |
Abbreviations:

CCS – Childhood cancer survivors
AS – Adult cancer survivors
LSS – Limb Sparing Surgery
AMP – Amputation
vs – Versus
PMBT – Primary malignant bone tumour
BT – Bone tumour
STS – Soft tissue sarcoma
TKR – Total knee replacement
THR – Total hip replacement
MSTS - Musculoskeletal Tumour Society Rating Scale
ACP - Displacement of amplitude of the centre of pressure
VCP - Velocity of the centre of pressure
PA – Physical Activity
gcs – Gait cycles
GPA – General physical activity
ADL - Activities of daily living
SAM - Step activity monitor
N/A – Not available
m/s = metre per second
m/min – metre per minute
km/hr – kilometre per hour
s = second
m = metre
SD – Standard deviation
/day – per day
/min per minute
Table 3: Validity and Reliability of measures in the literature: Reference Values for patients treated for Musculoskeletal Cancer

<table>
<thead>
<tr>
<th>Sr No.</th>
<th>Article</th>
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<tbody>
<tr>
<td></td>
<td>Comparison to controls (Form of construct validity – divergent validity)</td>
</tr>
<tr>
<td></td>
<td>Comparison between subgroups of patients (Divergent validity) or relations between demographics, clinical characteristics and outcome (Convergent validity)</td>
</tr>
<tr>
<td></td>
<td>Comparison between different testing conditions (Form of construct validity)</td>
</tr>
<tr>
<td></td>
<td>Association with established validated measures in Sarcoma (Form of construct validity)</td>
</tr>
<tr>
<td></td>
<td>Comparison with a gold standard (Criterion validity)</td>
</tr>
<tr>
<td></td>
<td>Reliability (Test-retest validity or intra-tester or inter-tester reliability)</td>
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<tr>
<td></td>
<td>Sensitivity /Responsiveness to change</td>
</tr>
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</table>
**Balance – LSS**

<table>
<thead>
<tr>
<th>1. De Visser et al, 2001</th>
<th><strong>Upright Standing:</strong></th>
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</thead>
<tbody>
<tr>
<td></td>
<td><em>Eyes-open:</em></td>
</tr>
<tr>
<td></td>
<td>• No significant differences in ACP and VCP measures between patients and controls (p&gt;0.05).</td>
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<tr>
<td></td>
<td><em>Eye-closed:</em></td>
</tr>
<tr>
<td></td>
<td>• Both patients and controls have an increased VCP with eyes closed, in comparison to eyes open</td>
</tr>
<tr>
<td></td>
<td><strong>Upright Standing:</strong></td>
</tr>
<tr>
<td></td>
<td><em>Eyes-open:</em></td>
</tr>
<tr>
<td></td>
<td>• No significant differences in ACP and VCP measures between patients and controls (p&gt;0.05).</td>
</tr>
<tr>
<td></td>
<td><em>Eye-closed:</em></td>
</tr>
<tr>
<td></td>
<td>• Closing the eyes increases ACP and VCP in patients in</td>
</tr>
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</table>
However, displacement of CP in eyes closed condition, was smaller for patients than controls (p<0.05).

**Dual-Task:**
- Only patients showed a significantly higher ACP (4.5+/−0.8 mm) when compared to normal standing.

**Dual-Task:**
- When the auditory stroop task was performed, only patients showed a significantly higher ACP (4.5+/−0.8 mm)
and VCP (18.6 +/- 3.0 mm/sec) when compared to normal standing (11.9 +/- 1.0 mm/sec) when the auditory stroop task was performed, however patients and controls were not significantly different. When compared to eyes-open normal standing (2.9 +/- 0.4 mm) and VCP (18.6 +/- 3.0 mm/sec) when compared to eyes-open normal standing (11.9 +/- 1.0 mm/sec).
<table>
<thead>
<tr>
<th>Standing on balance board:</th>
<th>Standing on balance board:</th>
</tr>
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<tbody>
<tr>
<td><strong>Eyes open:</strong> No significant differences were seen between patients and controls.</td>
<td><strong>Eyes Closed and Dual-task:</strong></td>
</tr>
<tr>
<td><strong>Eyes-closed and Dual-task:</strong></td>
<td></td>
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<tr>
<td>• A significant difference in VCP was seen for both groups with eyes closed condition and also under dual-task</td>
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<tr>
<td>(patients, 80.1+/−12.9 and 23.6+/−3.4 mm/sec).</td>
<td></td>
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<tr>
<td>Conditions</td>
<td>Gait – LSS</td>
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<td>---------------------------------------------------------------------------</td>
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<tr>
<td>(controls, 23.2+/-.3.3 and 14.9+/-.2.9 mm/sec; patients, 80.1+/-.12.9 and 23.6+/-.3.4 mm/sec).</td>
<td>2. De Visser et al, 1998&lt;br&gt;• Patients walked with a lower preferred walking speed (2.4 km/hr) than controls (3.8 km/hr) and showed a higher&lt;br&gt;• There was no relation between sub-groups such as tumour type, surgery type&lt;br&gt;• In complex walking such as dual task or visual restrictions, patients showed a significant</td>
</tr>
<tr>
<td>co-efficient of variation of stride time than the normal subjects, in normal and complex walking.</td>
<td>and location of tumour with the level of visual and cognitive dependency.</td>
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- When walking with constraints, a significant reduction in stride time was seen in patients, but not in normal subjects, (p<0.05). Controls did not show any significant
differences in the three conditions.

3. De Visser et al, 2000

- The preferred speed of walking in LSS patients (0.7+/-0.3 m/s) was lower than that in controls (1.1+/-0.08 m/s).
- The mean stride duration in patients (1.5+/-0.6 s) was longer than controls (1.1+/-0.06 s)(p<0.05).

There were no significant differences between gait parameters in hip and knee group (p<0.05)
The stance phase of affected leg was shorter and of non-affected leg was longer. The stance phase of non-operated legs in patients was longer than controls. All patients treated for LSS showed a reduced knee flexion during stance phase in the operated leg.
| 4. | Kawai et al, 2000 | • The patients walked with a significantly less cadence and stride time compared to controls (p<0.05). | • Patients with proximal femoral replacement had a superior gait than patients with hip disarticulation in characteristics listed below. Patients with proximal femoral | • Patients who used a cane, walked with less cadence longer stride length, and with walking velocity not significantly changed. The single-limb support times were prolonged and asymmetry was | • Free-walking velocity was negatively correlated with the net energy cost (r = -0.55, p = 0.05). | • Free-walking velocity and asymmetry |
asymmetry difference was 0.09 seconds (0.01 to 0.22).

Replacement had a significantly higher walking velocity and asymmetry than patients with hip disarticulation (p < 0.05). In addition, energy cost and asymmetry of walking significantly decreased.

- Asymmetry of single-limb support time demonstrated a significant negative co-relation (r = -0.67, p = 0.006).
was higher in patients with hip disarticulation compared to those who had a proximal femoral replacement.

<table>
<thead>
<tr>
<th>strength of abductor muscles demonstrated a weak negative correlation ($r = -0.62$, $p = 0.05$).</th>
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<tbody>
<tr>
<td>No significant correlation was seen between gait outcomes</td>
</tr>
</tbody>
</table>
in patients and length of the proximal femur resected.


- Patients treated with a knee prosthesis walked at a speed of $3.9+/-0.15$ km/hr and stride time during the recovery period, patients step cycle duration were reduced by complex add-ons such as dual task and visual restriction while walking.

Patients have an improvement in the gait outcome such as step-cycle duration, walking speed, gait symmetry over time and with rehabilitation:
Patients with a hip prosthesis walked with a preferred speed of 3.4+/− 0.23 km/hr and a step-cycle duration of 1.21+/− 0.07 sec after 15 months.

Walking speed was seen to increase from 2.1+/− 0.9 km/hr to 3.5+/−0.3 km/hr during the end of rehabilitation.

Step-cycle duration 2+/− 1.04 sec was significantly decreased to 1.18+/− 0.106 sec.
- Patients with saddle prosthesis walked at a speed of 2.2 +/- 1.1 km/hr and a stride time of 1.50 +/- 0.33 sec.

- A slight improvement of gait symmetry was observed, with some gait asymmetry still persistent after 15 months.

| 6. Tsauo et al, 2006 | Patients walking velocity were 54 +/- 12 m/min, | The ratio of quadriceps strength of | sec at end of rehabilitation. |
and controls’ was 72 +/- 6m/min (p<0.05).
- The step length of patient’s unaffected side is significantly shorter than controls and affected side (Affected side was 115.8+22.2% of unaffected limbs’) (p<0.05).
- The stance phase of patients’ operated by normal knee, and isometric strength of hamstring by quadriceps ratio of operated knee was correlated significantly to the difference of stance-phase duration of both sides (p<0.05).
affected leg was significantly shorter than that of controls and unaffected side (88.2±5.9% of unaffected limbs')(p<0.05).

- Conversely, swing phase of patients’ affected leg, was significantly longer than that of their unaffected sides (127.3±22.1% of
<table>
<thead>
<tr>
<th>7. Beebe et al, 2009</th>
<th>Aspects of gait reduced were:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Gait velocity</td>
</tr>
<tr>
<td></td>
<td>(range, 86.8 – 108.4cm/s;</td>
</tr>
<tr>
<td></td>
<td>controls from literature</td>
</tr>
<tr>
<td></td>
<td>128cm/s),</td>
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<tr>
<td></td>
<td>• Stride length</td>
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<tr>
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<td>(range, 101.68–120.04cm in the</td>
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<td></td>
<td>affected limb; 102.07–114.19cm</td>
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<tr>
<td></td>
<td>in the unaffected</td>
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<tr>
<td></td>
<td>MSTS gait sub-component</td>
</tr>
<tr>
<td></td>
<td>were reported as 3/5</td>
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<tr>
<td></td>
<td>and total MSTS score as 23.5/30</td>
</tr>
<tr>
<td></td>
<td>Only scores were stated.</td>
</tr>
<tr>
<td></td>
<td>No formal comparisons have been</td>
</tr>
</tbody>
</table>
limb; controls from literature 128cm), and

- Cadence (range, 87.9 –113.5 steps/min; controls from literature is 117 steps/min).

- Double-limb support was higher in patients (range, 26.0–32.3% Gait Cycle (GC) in the affected limb, 26.8–32.4% GC compared to made therefore no testing of validity in this section.
unaffected limb; values for controls from literature is 20% GC).

- Stance phase was greater in all patients in the unaffected limb (range, 59.8–67.7% GC; values for controls from literature is 60% GC) but only in half of the patients in the affected limb (range, 58.1–
67.8% GC, values for controls from literature is 60% GC).

- Swing phase, step length, and step time were higher in the affected limb compared to unaffected limb.


- No statistical significance was seen between mean step velocity.
after intraarticular proximal tibial replacement (79.2 +/- 7.6 m/min) and control group of amputees (71.4 +/- 5.4 m/min) (p=0.06)

- Significant difference was seen
between cadence after intraarticular proximal tibial replacement (112.4 +/- 10.6 steps/minute) vs control group of amputees (100.1 +/- 2.4)
steps/minute) (p=0.03).

- No significant differences were seen between length of stride (1.41 +/- 0.13 m vs 1.43 +/- 0.12 m) and the symmetry of stance time (0.90 +/-
|   |   | 0.07 vs 0.87 +/- 0.11) for proximal tibial replacement vs control group of amputees. |   |   |   |   |

### Physical Activity – LSS

<table>
<thead>
<tr>
<th></th>
<th>Rosenbaum et al, 2008</th>
<th>Ambulatory (walking) and sedentary PA: Volume:</th>
<th>Volume:</th>
<th>Volume:</th>
<th>Volume:</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.</td>
<td></td>
<td>Patients performed the predominant</td>
<td>Data collection duration was negatively</td>
<td>On weekends, patients walked only 95% of the</td>
<td>A low correlation was observed between SAM</td>
</tr>
<tr>
<td>Activity</td>
<td>Daily Activity of Sitting (54+/−18%) of the Time Recorded</td>
<td>Compared to Control (42%), then Followed by Upright Standing (27+/−16%) Compared to Controls (41%), Followed by Ambulation (10+/−6%) Compared to Controls (11%), and Lying (8+/−)</td>
<td>Steps Achieved during Weekdays. Correlated with Body Mass Index (BMI) (p&lt;0.01). No Correlations Were Seen between PA and the Duration of Follow-up.</td>
<td>The GCS Did Not Correlate with Patient’s Age but</td>
<td>And MSTS (p=0.2).</td>
</tr>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>A Poor Correlation Coefficients for Locomotion vs MSTS or TESS, and Also Between SAM and TESS Score.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No Significant Relations Between Gait Analysis in Laboratory and Activities of Daily Living</td>
<td></td>
</tr>
</tbody>
</table>
6% compared to controls (4%).

- The ambulatory activity level in patients was significantly lower (4,786±1,770 cycles/day) than normal healthy adults (6,517±1,489 cycles/day) (p=0.01), however it was comparable to the level of activity for other patients. For

- The mean movement intensity during walking activity was 2.4±0.4 m/s². This did not demonstrate marked subject differences (range 2,045–8,135).

- (ADL) monitoring in a sub-group of patients.
example, with hip arthroplasty reported in literature.

**Intensity:**
- Healthy controls spent more time in higher intensity activities (absolute values). No significance testing performed.
- No significant differences were seen between location of tumour in proximal vs distal femur (p>0.05).

<table>
<thead>
<tr>
<th>10. Sheiko et al, 2012</th>
<th><strong>Ambulatory PA:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>correlate with the age, weight or BMI.</td>
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<tr>
<td></td>
<td><strong>Volume:</strong></td>
</tr>
</tbody>
</table>
Patients who underwent LSS had significant reduced PA levels when compared to healthy controls:

**Volume:**
- There were significant differences between patients who had undergone LSS and healthy controls in total PA/ day (43% vs...

| Self-reported PA questionnaire ASKp-38 summary score significantly correlated with step watch average strides/day (r=0.50, p<0.05), ASKp-38 locomotion sub-score correlated significantly with step watch average strides/day (r= 0.63, p<0.01) and StepWatch % time active r=0.56, |  |  |
the median value of total strides/day (4487 vs 7671 strides; p = 0.001).

- Average walking minutes/day in LSS patients were 370 (211 - 587) as compared to healthy controls as 438 (275-518) (p=0.05)

**Intensity:**
- Time spent/day at high activity levels

Correlations were tested using spearman’s correlation.
(20 minutes vs 47 minutes; p = 0.001).

Others:
- Significant differences were also seen between patients treated for LSS and healthy controls for endurance (18 vs 28, p<0.001), accumulated peak effort (22 vs 33, p<0.001), cardiovascular score (27
<table>
<thead>
<tr>
<th>No.</th>
<th>Author(s)</th>
<th>Study Details</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.</td>
<td>Van der Geest et al, 2013</td>
<td><strong>PA:</strong> No significant differences between change in PA scores between tumour patients and controls (arthroscopy patients). (No reference values mentioned)</td>
<td>No significant correlation between fatigue and PA scores.</td>
</tr>
</tbody>
</table>

Absolute values of actometer scores increased over time from pre-surgery to recovery. However, significance tests were not performed due to...
Winter et al., 2012

**Ambulatory PA:** Patients achieved significantly lesser volume (gcs/day) and time spent in moderate intensity (time spent in >50 gait cycles/min)) of PA than controls at all time points (p<0.001).

**Volume:**
- Controls achieved 7,100±1,918 gcs/day, whereas

**Volume and Intensity:**
- The lowest scores for volume and intensities for PA were seen at 6 weeks post-

**Volume and Intensity:**
- A continuous increase in absolute values of volume and intensity of PA was observed at each follow-up
- However significant
patients achieved 770±793 gcs/day at 6 weeks,
1,847±1,047 at 3 months,
2,351±1,842 at 6 months,
3,917±1,703 at 12 months,
5,107±1,600 at 18 month, which was significantly different from controls at each time point (p<0.001).

observed between sub-groups such as patients with and without complications 6 months post operatively.

- Significant increases in the volume of ambulatory activity were seen after cessation of therapy (chemotherapy) at 6 months.

increases were only seen when comparing the first measurement after surgery to the 12 month and 18-month follow-ups (p<0.003).

- No significant differences observed between other...
**Intensity:**

- Controls spent 27.6±14.5 minutes at moderate intensity (time >50 gait cycles/min), whereas patients spent 1.1±2.1 minutes at 6 weeks, 2.2±5.9 at 3 months, 3.1±7.0 at 6 months, 10.5±13.5 at 12 months and 15.2±16.1 at 18 months, which

<table>
<thead>
<tr>
<th>Time</th>
<th>Minutes</th>
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<tr>
<td>6 weeks</td>
<td>1.1±2.1</td>
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<tr>
<td>3 months</td>
<td>2.2±5.9</td>
</tr>
<tr>
<td>6 months</td>
<td>3.1±7.0</td>
</tr>
<tr>
<td>12 months</td>
<td>10.5±13.5</td>
</tr>
<tr>
<td>18 months</td>
<td>15.2±16.1</td>
</tr>
</tbody>
</table>

**Intensity:**

- With 3,279 vs. 3,826 gcs/day. At 18 months post-operatively, no significant differences were present with regards to volume of PA. 

**Intensity:**

- Postoperatively, however intensity showed minor and no significant changes.

Increase in intensity to higher levels was seen post-operatively.
was significantly different from controls at each time point (p<0.001).

Therefore patients did not reach level of healthy controls even at 18 months post-operatively.

- Patients with complications did not perform any moderate intensity activities at 12 months, whereas patients with complications achieved 4 minutes/day. At this moderate level in longer term follow-up.

- 12 months post-operatively patients significantly improved volume of activity compared to the
differences were more pronounced at 12 months (0.3 – 12.6 minutes), 18 months (3.7 vs 18.9 minutes) post-operatively.

treatment phase, with no major improvements in moderate intensity levels of PA.

<table>
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<th>Physical Activity – LSS + AMP</th>
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<tr>
<td><strong>13</strong> Sugiura et al, 2001</td>
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count of 7119 ± 3563
which as 69.8% of controls
(10,206 ± 1388)

- The BT group demonstrated a significantly lower average step count compared to controls, with averages of 6001 ± 2684 and 7758 ± 3835 steps (which was 58.8% and 76.0% of the controls, respectively).

Average daily step count was significantly correlated with MSTS (coefficient 0.52, P<0.001). A relation value was also determined as The number of steps = 0.001 X MSTS score ± 14.499

soft-tissue tumour clinical groups were 6001 ± 2684 and 7758 ± 3835 steps (which was not correlated with ROM. Average daily step count was significantly correlated with MSTS (coefficient 0.52, P<0.001). A relation value was also determined as The number of steps = 0.001 X MSTS score ± 14.499
daily step count compared to the soft-tissue tumour (p < 0.05)

- Kotz TKR and semiconstrained THR groups, achieved significantly lower number of steps than other groups

The hip abductors and hip flexors strength were more closely correlated (measured by correlation rate) with daily step count than with knee extensors and knee flexors strength.
such as resection without reconstruction of bone (n = 30), above-knee AMP (n = 4), total femur autoclaved bone (n = 5), autograft (n = 2), heat-treated bone (n = 5),
replacement (n = 1). (No values for each group, only represented graphically)

- For patients with a tumour more proximally (closer to the trunk) tended to achieve lower steps than those
with tumours in other locations, and this was mainly seen in BT group.


**PA:**

**Volume:**
- The LSS (n=12) and AMP (n=8) group were both similar on MSTS, TESS, Baecke, Euro-

**Volume:**
- There was a significant correlation seen between ‘time spent walking’ and the MSTS scores and

- The test-retest reliability (n=17) of the monitor was satisfactory, with an ICC
QOL and Rand-36 scores.
Percentage of time spent walking (in 24 hours) in whole group was 5.1(2.37)%. In LSS group was 5.6 (2.02) % and in AMP was 4.3 (2.78).

Intensity:

- A significant association was also seen between ‘movement intensity during walking’ and MSTS.

<table>
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<tr>
<th></th>
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<th>from 0.65 to 0.91 over the function measured.</th>
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<tbody>
<tr>
<td>Intensity:</td>
<td></td>
<td>ICC for individual aspects of function were as follows:</td>
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<td></td>
<td></td>
<td>Volume:</td>
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<tr>
<td></td>
<td></td>
<td>- Time spent in walking task ICC = 0.65,</td>
</tr>
</tbody>
</table>
- Walking intensities were 2.1 (0.39) m/s² in whole group. LSS patients scored 2.26(0.43) m/s² and AMP group scored 1.9 (0.15) m/s². However no significant differences were seen.

<table>
<thead>
<tr>
<th>Movement Intensity (m/s²)</th>
<th>Time in standing = 0.83,</th>
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<tbody>
<tr>
<td>Walking</td>
<td>Time in sitting = 0.75.</td>
</tr>
<tr>
<td>Standing</td>
<td></td>
</tr>
<tr>
<td>Sitting</td>
<td></td>
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</tbody>
</table>

*Intensity:*  
- Movement intensity (m/s²)  
  - Walking = 0.91  
  - Standing = 0.69  
  - Sitting = 0.79
between the LSS and AMP groups with respect to ‘time spent in certain activities’ and ‘movement intensities’ (p>0.05).

| 15 | Hopyan et al, 2006 | **PA:**  
**Volume:**  
- Uptime (expressed in percentage) in | **Volume:**  
Significant differences were seen between LSS and AMP |
<table>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Total (walking, standing or sitting) 0.91</td>
</tr>
</tbody>
</table>
LSS group (n=15) was 24.0+/−9.2 (range, 10-40), Above-knee AMP group (n=15) was 26.7+/−7.3 (range, 18-40), rotationpstå last y group (n=5) was 30.1+/−9.2 (18-43) and below groups, using TESS (p=0.06) and MSTS (p<0.0001). However no significant differences were seen between LSS and AMP in uptime (p=0.39)
knee AMP was 26 (n=1)

- Uptime measured by the activity monitor, were similar between groups. Uptime had higher values in patients with rotationplasty, although statistical
| 16. | Winter et al, 2009 | **Ambulatory PA:**

**Volume:**
- Patients with BT exhibited $1275+/-1105$, median $943$ gcs/day, which was $16\%$ of the PA when compared to controls ($8096+/-2951$, median $7438$ gcs/day) during inpatient stay.

**Volume:**
- Patients with BT exhibited lower volume of PA scores than those with leukemia ($1,849$ gcs vs. $2,992$ gcs).

**Volume:**
- However no statistical significant differences were observed.

Significant differences between inpatient ($1275+/-1105$, median $943$ gcs/day) and home stays ($2145+/-1422$, median $1490$ gcs/day) were seen in BT patients. During
stay and achieve 2145+/-1422 median 1490 gcs/day which is 27% of the PA compared to controls during their home stay (p<0.001).

**Intensity:**
- Patients in the BT group spent a lesser percentage of time at high intensity activities during in patient stay as seen in both settings.

- Percentage of time on high intensity activities were 6.1+/-3.7, median 5.7 compared to BT patients (3.5+/-4.7, median 2.1). However though clearly reduced in stay patients achieved 59% of the PA, they achieved at home (p<0.001).
stay (3.5+/−4.7, median 2.1) when compared to controls (14.7+/−7.2, median 12) (p<0.001) and 4.2+/−5.5, median 2.9 during home stay, which was significantly lower than controls (14.7+/−7.2, median 12) (p<0.05). Intensities of activities in bone cancer patients, there were no statistically significant differences seen between the leukaemia’s and BT patients.
PA:
- GPA values for LSS (n=30) group was 93.9 (25.4) and for AMP (n=36) group was 94.8 (29.7).
- No significant differences between groups.
- Average peaks were 142.3 (14.7).

Significantly better scores were seen in the LSS group for the timed up and down stairs (TUDS) and various walking activities (VWA) test as compared to the AMP group. However no significant differences were seen between
<p>| | for LSS and 143.8 (21.9) for AMP. No significant differences between groups. | LSS and AMP for any of the PA measures | | | |</p>
<table>
<thead>
<tr>
<th>18. Bekkerin g et al, 2012</th>
<th><strong>PA:</strong></th>
<th>GPA and average peak of accelerations measured with Actilog activity monitor did not show statistical significant differences at various time points.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PA was measured using Baecke questionnaire and Actilog activity monitor. A significant increase in activity levels between 3 to 12 months (p &lt; 0.01) was detected by the Baecke questionnaire.</td>
<td></td>
</tr>
</tbody>
</table>

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97
However the GPA and average peak of accelerations measured with Actilog activity monitor did not show statistical significant differences at various time points.

- Average peaks: 3 months 121 +/- 4.9, 6 months 125 +/- 5.0, 12 months 127 +/- 5.4, 18 months 126 +/- 5.7, and 24 months 92 +/- 7.3, 18 months 98 +/- 7.8, and 24 months was 93 +/- 8.2.
|   |   |   |   |   |   | months 127+/- 6.1. |   |   |   |
Abbreviations:

LSS – Limb Sparing Surgery

AMP – Amputation

vs - Versus

BT – Bone tumour

TKR – Total knee replacement

THR – Total hip replacement

TESS – Toronto Extremity Salvage Score

MSTS - Musculoskeletal Tumour Society Rating Scale

Rand 36 – Rand 36-Item Health Survey

QOL – Quality of life

ACP - Displacement of amplitude of the centre of pressure

VCP - Velocity of the centre of pressure

PA – Physical Activity

GC – Gait cycle

gcs – Gait cycles
GPA – General physical activity
ASKp-38 - Activity scale for kids
SAM - Step activity monitor
m/s² = Movement intensity
mm/sec = millimetre per second
m/s = metre per second
cm/s = centimetre per second
m/min = metre per minute
km/hr = kilometre per hour
s = second
m = metre
/day = per day
ICC - Intraclass correlation coefficient
Table 4: Quality Assessment of Articles

Section 1: Criteria for assessing quality of studies.

A. The study mentions a clear scientific background and rationale for conducting the investigation.
B. The study mentions clear aim/objectives and/or including hypothesis.
C. Use of an appropriate study design to address the aim/objectives - Prospective study design (also positive in studies where previously unknown outcomes are measured in a historical cohort, case series or cross-sectional patient group)
D. The study size calculation is explained – to ensure appropriately powered.
E. Study population was well defined and types of sarcoma described.
F. Socio-demographic data mentioned.
G. Time since diagnosis reported.
H. Participant eligibility criteria outlined and the methods and sources of selection/recruitment.
I. Data collection process has been described.
J. Type of sarcoma interventions has been reported.
K. Presence of a control group for relevant studies (no score if study data was compared to literature)
L. Participation rate (score given if rate of participation > 75%).
M. Use of a standardised and valid assessment tool (internal validity)
N. Precision of result reported.
O. Mention of efforts to reduce any potential sources of bias (example: selection bias, performance bias).
P. The impact of confounding factors on outcome was clearly mentioned (example: age, time since surgery, level of surgery, rehabilitation interventions etc).
Q. Use of an appropriate statistical analysis tests to answer meet the aim/objectives.
R. Generalisability (external validity) of the results to a local population (for example: results when patients are receiving treatments in hospitals or outpatient departments).
Adapted from following sources:

(Kwong, Furtado et al. 2014), CASP [Critical Appraisal Skills Programme (CASP) 2014], STROBE (Elm, Altman et al. 2007).

References:

CASP [Critical Appraisal Skills Programme (CASP) 2014], CASP Checklists [URL used], Oxford. CASP


### Section 2: Quality Scoring of Articles.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Article</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
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<th>P</th>
<th>Q</th>
<th>R</th>
<th>Score (%)</th>
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<td>De Visser et al, 2001</td>
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<td>15(83)</td>
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<td>(80% participation rate as 20 out of 25 participated)</td>
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<td>(34% as 10 out of 29 patients participated)</td>
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<td>(80% participation rate as 20 out of 25 participated)</td>
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<td>(90% 44 out of 49 recruited, participated in initial assessment) and 49%, 24 out of 49 completed the study at 2 years)</td>
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