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Title:
Outcomes of knee disarticulation and the influence of surgical techniques in dysvascular patients: a systematic review.

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Acknowledgments

The authors would like to thank Dr. Amar Jain (Consultant Orthopaedic Surgeon, Ninewells Hospital, Dundee UK) for his expert opinion in this review, together with Sarah Deans and Kim Gadsdon for their valuable contributions.
Title:

Outcomes of knee disarticulation and the influence of surgical techniques in dysvascular patients: a systematic review.
Abstract

Background: Dysvascularity is the main cause of lower limb amputations in Scotland and there is an insignificant proportion (1.7%) of knee disarticulations (KD), despite the benefits of the amputation.

Objectives: The outcomes of KD and its associated surgical techniques will be evaluated based on healing, reamputations, functional outcomes, prosthetic ambulation, and gait biomechanics, to determine if a greater rate of knee disarticulations can be justified among dysvascular patients.

Study Design: Systematic review.

Methods: Key electronic databases were searched for the relevant literature based on a pre-specified eligibility criteria.

Results: The 17 papers included in this review were appraised for their quality, and key findings extracted.

Conclusions: Healing rates are favourable, but there is a need for appropriate amputation level selection to prevent reamputations. KD patients have better maintenance of independent living status than trans-femoral patients, but overall prosthetic ambulation rates are inconsistent. In terms of gait biomechanics of KD, there are some positive indications but the evidence is insubstantial. A stronger body of evidence is required in this subject field, and recommendations are made for future research. SIGN Grade of Recommendation: C.

Word count: 182
Clinical relevance

This review aims to inform the multidisciplinary teams involved in the rehabilitation of dysvascular amputees about evidence-based outcomes following knee disarticulation. This knowledge will be beneficial when formulating treatment pathways for this vulnerable population group.

Word count: 35

Keywords

Knee disarticulation, through knee, Mazet, Gritti-Stokes, dysvascular, rehabilitation, prosthesis, amputee
Background

The rate of knee disarticulations (KDs) has frequently been disproportionally lower than transfemoral amputations (TFAs), even though they have greater functional outcomes. The dysvascular amputee population usually consists of elderly patients with comorbidities and minimal rehabilitation potential.\(^1\) They are ideal candidates to benefit from the additional functionality of KD but this is often avoided by the amputating surgeon due to wound healing complications. However, there are studies indicating positive results following KD, with some authors recommending different surgical techniques.

Demographics

Dysvascularity is the main cause (84\%) of lower limb amputations in Scotland, including diabetes and peripheral arterial disease without diabetes.\(^2\) KD consists of only 1.7\% of lower limb amputations, which is highly disproportional compared to trans-femoral (40.6\%) and transtibial (56.6\%) levels.\(^2\) These are depicted in Figure 1 and Table 1.
Figure 1. Aetiology of Lower Limb Amputations in 2011.

Figures adapted from the 19th Annual Report of the Scottish Physiotherapy Amputee Research Group

Table 1. Levels of Amputation for 2011.

<table>
<thead>
<tr>
<th>Amputation Type</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trans-pelvic</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Hip Disarticulation</td>
<td>8</td>
<td>1.1%</td>
</tr>
<tr>
<td>Trans-femoral</td>
<td>291</td>
<td>40.6%</td>
</tr>
<tr>
<td><strong>Knee Disarticulation</strong></td>
<td><strong>12</strong></td>
<td><strong>1.7%</strong></td>
</tr>
<tr>
<td>Trans-tibial</td>
<td>406</td>
<td>56.6%</td>
</tr>
<tr>
<td>Ankle Disarticulation</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>717</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Figures adapted from the 19th Annual Report of the Scottish Physiotherapy Amputee Research Group
Advantages and disadvantages

There are many known advantages and disadvantages of KD, listed in Table 2 and Table 3. For dysvascular patients, the tissue viability required for stump healing is similar to the trans-tibial (TT) level, but KD can be indicated for the reasons listed in Table 4. Trans-tibial amputations (TTA) often have risks of knee flexion contractures and stump necrosis for bedbound patients, as the contractures often cause pressure ulcers.

Surgical techniques

KD was unpopular due to poor prosthetic-fitting skills, poor healing, and poor flap interface consisting of only skin and subcutaneous tissue. The long anterior flap was a standard technique historically, usually leading to flap necrosis, reamputations, and was not recommended for dysvascular patients. Equal sagittal flaps were advocated by many, with better outcomes and a more reliable blood supply than anterior flaps. The minimised flap lengths are ideal for dysvascular patients. Suture lines lay posteriorly in the intercondylar region avoiding the weight-bearing area, with the use of gastrocnemius bellies to enhance end-bearing and preserve blood supply. Skin tension can be avoided with circular incisions, and trimming to sagittal flaps before suturing. When the long posterior myofasciocutaneous flap incorporating the gastrocnemius bellies was introduced, it provided excellent padding and blood supply. It was ideal for prosthetic rehabilitation, prevents flap necrosis, and was claimed to have better outcomes than sagittal flaps.
Table 2. Advantages of Knee Disarticulation.

- Stable sitting platform\textsuperscript{3, 15-17}
- Greater trunk stability with stable sitting platform \textsuperscript{3}
- Efficient transfers\textsuperscript{16-18}
- Less energy consumption than trans-femoral levels (with/without prosthesis) \textsuperscript{3, 19, 20}
- Less traumatic amputation (ideal for feeble patients)\textsuperscript{5}
- Reduced risk of infection with cartilage barrier maintained\textsuperscript{3, 14}
- Preservation of femur growth plates (paediatrics)\textsuperscript{15}
- Avoidance of painful bone spurs\textsuperscript{3, 15}

Prosthetics
- End bearing stump\textsuperscript{3, 5, 15, 17, 21}
- Good suspension and rotational control\textsuperscript{5, 15, 17}
- Long mechanical lever arm\textsuperscript{5, 15, 17}
- Better exertion of control forces by hip muscles\textsuperscript{21}
- Less tendency of developing hip flexion contractures\textsuperscript{14, 17}
- Muscles intact (greater strength)\textsuperscript{5, 15, 21}
- Anatomical positioning of femur due to intact muscle balance\textsuperscript{22}
- Greater abduction control\textsuperscript{21}
- Comfortable trimlines, less constricting on proximal tissues\textsuperscript{15}
- Lower stump socket pressures due to greater surface area\textsuperscript{3, 21}
- Reduced biomechanical forces of gait due to end bearing\textsuperscript{3}
- Greater ambulatory stability than trans-femoral levels in geriatric population\textsuperscript{3}
Mazet and Hennessy introduced another technique to reduce bulkiness of the KD stump by trimming medial, lateral, and posterior condyles, and patellectomy.\(^{24}\) Burgess modified the technique to remove 1.5cm of the distal end additionally, raising the prosthetic knee joint centre.\(^{25}\) The shorter flaps required allows improved healing,\(^{24, 26}\) while still retaining an end-bearing stump.\(^{26, 27}\) However, there were authors that condemned this technique due to the
reduced weight-bearing area,\textsuperscript{5, 8} impaired suspension,\textsuperscript{3, 8} risk of stump breakdown,\textsuperscript{5, 6, 10} and potential haematoma and infection from the bleeding bone.\textsuperscript{5}

The Gritti-Stokes technique involves using the patella and surrounding tissues as an osteoplastic flap for end-bearing\textsuperscript{28} by fixing the patella to the distal end of femur after a transcondylar amputation.\textsuperscript{28} The femur is beveled posteriorly, to prevent the patella from slipping.\textsuperscript{6, 30} Published reports indicated better healing rates\textsuperscript{6, 30-34} and an end-bearing stump,\textsuperscript{30, 32} while other authors disputed that it created high peak pressures\textsuperscript{3, 5, 6} and had risks of failure at the condylar-patella union.\textsuperscript{3, 5}

Objectives

The proportion of KDs does not correspond with the apparent advantages of KD and the claimed benefits of different surgical techniques. This review will aim to evaluate the outcomes of KD, based on healing, reamputations, functional outcomes, prosthetic ambulation, and gait biomechanics to determine if a higher rate of KD can be justified among dysvascular patients.
Methods

Protocol

The methodology of the review was pre-specified and documented, adapting the structure of the PRISMA statement. Studies were graded according to the Scottish Intercollegiate Guidelines Network (SIGN50) guidelines.

Eligibility criteria

Studies were picked based on the criteria listed in Table 5. Mortality was excluded from the outcome measures as it was mainly influenced by age, physical status and comorbidities, and not directly influenced by amputation surgeries. Higher mortality rates of patients with proximal amputations are generally due to poorer health conditions than patients with distal amputations.
Table 5. Eligibility Criteria.

<table>
<thead>
<tr>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Randomised controlled trials, controlled clinical trials, observational studies, and non-analytical studies.</td>
</tr>
<tr>
<td>2. English publications in peer-reviewed journals in the last 25 years.</td>
</tr>
<tr>
<td>3. Reviews, expert opinions and studies with abstracts only are excluded.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysvascular patients of all ages.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee disarticulation amputations (with or without indication of surgical technique)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one of the following outcomes measured:</td>
</tr>
<tr>
<td>1. Quality of stump (healing, revision, reamputation)</td>
</tr>
<tr>
<td>2. Quality of life</td>
</tr>
<tr>
<td>3. Functional outcomes</td>
</tr>
<tr>
<td>4. Prosthetic ambulation</td>
</tr>
<tr>
<td>5. Gait biomechanics</td>
</tr>
</tbody>
</table>

Information sources

Studies were identified by searching electronic databases and scanning the reference lists of included studies. Journals with the most relevant results were handsearched additionally to ensure a thorough search process, but this was only done for the recent publications. These are listed in Table 6. The last search was conducted on 3 April 2014, and the full search strategy including search terms is shown in Appendix A.
Table 6. Information Sources.

<table>
<thead>
<tr>
<th>Databases/ platforms</th>
<th>Journals (2014 publications)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Embase (OvidSP)</td>
<td>2. Archives of Physical Medicine and Rehabilitation</td>
</tr>
<tr>
<td>3. Cochrane Library (Wiley Online Library)</td>
<td>3. European Journal of Vascular and Endovascular Surgery</td>
</tr>
<tr>
<td></td>
<td>5. Journal of Vascular Surgery</td>
</tr>
</tbody>
</table>

Study selection

The author (Murakami) performed the eligibility assessment independently and studies that require difficult judgments of selection/rejection were discussed with the project supervisor (Murray). Due to the nature of the project, there was a lack of multiple expert reviewers and arbitration in the study selection; hence there cannot be a complete avoidance of biasness.

Data collection process

A data extraction template was developed and pilot-tested on three randomly selected included studies, and refined with the project supervisor. The data extraction was then conducted by the
first author and reviewed by the project supervisor. Any disagreements were resolved by discussion. The completed data extraction is found in Table 7.

Risk of bias

Risk of bias was evaluated using a self-developed checklist (Appendix B), modified from the SIGN50 Methodology checklist,\textsuperscript{36} to account for factors pertinent to this review. The checklist helps to determine the level of bias present in a study, and a methodological quality grading is given (++ very low risk, + low risk, - high risk). The study design and quality grading given will determine the level of evidence provided by the study, according to the SIGN50 guidelines.\textsuperscript{36}

Results

Study selection

A total of 17 studies were identified for inclusion in this review. The selection process is depicted in Figure 2, and key characteristics of the selected studies are listed in Table 7. No studies were found that measured quality of life among knee disarticulation amputees and hence this outcome measure was removed.
Quality Appraisal

The proportion of studies according to study designs and risk of bias are depicted in Figures 3 and 4 respectively. Specific quality appraisal of each study is shown in Appendix C. The study designs and the risk of bias will together determine the level of evidence of the studies, which were listed in Table 7. There were no controlled trials found (level 1), with 11 observational studies (level 2) \(^\text{10, 34, 38, 42-49}\) and six non-analytical studies (level 3) \(^\text{4, 16, 26, 50-52}\). Seven studies had a high risk of bias (\(-\)) \(^\text{16, 19, 34, 42, 48, 50, 52}\), eight studies had a low risk of bias (\(+\)) \(^\text{4, 26, 38, 43, 45-47, 49, 51}\), and only one study had a very low risk of bias (\(++\)) \(^\text{44}\). Most of the studies were retrospective with only four prospective studies \(^\text{19, 44, 47, 49}\), and it was due to the retrospective nature that a higher quality grading (\(++\)) could not be given in four other studies \(^\text{38, 43, 45, 46}\).
Relevant studies identified through database searching (based on title):
  Medline (n = 286)
  Embase (n = 193)
  Cochrane Library (n = 5)
  ScienceDirect (n = 142)

n = 442 (after duplicates removed)

Additional studies identified through hand searching journals: n = 0

Excluded (n = 319)
  Inappropriate/ Irrelevant research question (n = 213)
  Inappropriate subject groups (n = 66)
  Educational/ Informative articles (n = 30)
  Abstracts (and full text) not available (n = 7)
  Letters (n = 3)

Included studies based on abstract: n = 123

Excluded (n = 319)
  No KD subjects (n = 30)
  Full text not available (n = 20)
  Participants not entirely dysvascular (n = 21)
  Outcomes not compared among amputation levels (n = 13)
  Inappropriate outcome measure (n = 11)
  KD grouped with other amputation levels (n = 5)
  Reviews (n = 3)
  Sample size of KD group is too insignificant compared to other groups (n = 2)
  Results not fully reported (n = 1)

Included studies based on eligibility criteria n = 17

Additional studies identified through scanning of reference lists (n = 0)

Additional studies identified from updated search done on 03/04/14 (n = 0)

Final number of studies reviewed n = 17

---

Figure 2. Study Selection Process.
<table>
<thead>
<tr>
<th>Bibliographic Citation</th>
<th>Evidence Level</th>
<th>Research Design</th>
<th>Amputation Technique</th>
<th>Sample Size Age Follow-up</th>
<th>Subject Characteristics</th>
<th>Outcome Measure Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayoub et al. (1993)</td>
<td>3(-)</td>
<td>Retrospective Case Series</td>
<td>Anterior Flap</td>
<td>Patients n=32, amputations n=35; 12 males; Mean age: 73yrs (59-96yrs)</td>
<td>Ischemia, all KD subjects. All patients were not prosthetic candidates.</td>
<td>Quality of stump</td>
</tr>
<tr>
<td>Campbell et al. (1994)</td>
<td>2-</td>
<td>Retrospective Cohort Study</td>
<td>Gritti-Stokes</td>
<td>Patients n=210, amputations n=228; 125 males; Median age: 76yrs (43-96yrs); 6mths follow-up (minimum)</td>
<td>PAD, Bilateral (n=18), Gritti-Stokes (n=8), TF (n=72), TT (n=148).</td>
<td>Quality of stump</td>
</tr>
<tr>
<td>Cull et al. (2001)</td>
<td>3(-)</td>
<td>Retrospective Case Series</td>
<td>Mazet and Hennessy</td>
<td>n=10; 1 male; Mean age: 63yrs (40-86yrs); Mean follow-up: 25mths (6-41mths)</td>
<td>Severe PVD. All KD subjects. Criteria for KD: Ambulatory potential and not TT candidate. Prosthetic prescription: total contact end-bearing suction socket with 4bar polycentric knee.</td>
<td>Quality of stump, Prosthetic ambulation</td>
</tr>
<tr>
<td>Jackson et al. (2012)</td>
<td>3(+)</td>
<td>Retrospective Case Series</td>
<td>Gritti-Stokes with trimmed lateral condyles</td>
<td>n=14; 86% male; Mean age: 72yrs; Median follow-up: 14.6mths</td>
<td>PVD, all KD subjects.</td>
<td>Quality of stump, Functional outcomes, Prosthetic ambulation</td>
</tr>
<tr>
<td>Kock et al. (2004)</td>
<td>3(+)</td>
<td>Retrospective Case Series</td>
<td>Posterior Flap</td>
<td>Patients n=66, amputations n=69; 50% male; Mean age: 66.7yrs (42-83yrs); Mean follow-up: 26mths (3-71mths) and 105mths (96-120mths)</td>
<td>Gangrene due to PVD, stage III PAOD n=3, stage IV PAOD n=63, all KD subjects.</td>
<td>Quality of stump, Prosthetic ambulation</td>
</tr>
<tr>
<td>Met et al. (2008)</td>
<td>2+</td>
<td>Retrospective Cohort Study</td>
<td>Sagittal Flaps</td>
<td>n=73; 67% male; Mean age: KD- 71.5 (SD=11.0), TF- 71.0 (SD=9.7); Mean follow-up: 250days (median 80days)</td>
<td>End-stage PAD KD indication: Patent iliac inflow, absence of skin ulcerations and sensory deficits around knee. KD (n=39), TF (n=34)</td>
<td>Quality of stump, Prosthetic ambulation</td>
</tr>
</tbody>
</table>
Table 7. (Continued)

<table>
<thead>
<tr>
<th>Bibliographic Citation</th>
<th>Evidence Level</th>
<th>Research Design</th>
<th>Amputation Technique</th>
<th>Sample Size Age Follow-up</th>
<th>Subject Characteristics</th>
<th>Outcome Measure Classification</th>
</tr>
</thead>
</table>
| Moran et al. (1990)     | 3(-)           | Retrospective Case Series | Sagittal Flaps       | Patients n=104, amputations n=106; 66 men; Mean age: 72yrs (51-92yrs) | Vascular disease, all KD subjects. KD criteria: high-risk patients requiring urgent amputation, unsuitable for prosthetic rehabilitation. | • Quality of stump  
• Prosthetic ambulation |
| England, UK             |                |                 |                      |                          |                        |                                |
| Morse et al. (2008)     | 3(+)           | Retrospective Case Series | Mazet and Hennessy   | n=50; 50% male; Mean age: 63yrs (37-87yrs); Mean follow-up: 33mths (39days-99mths) | PVD, all KD subjects. Prosthetic prescription: total contact end-bearing suction socket with 4bar polycentric knee. Exclusion: trauma and malignancy | • Quality of stump  
• Functional outcomes  
• Prosthetic ambulation |
<p>| USA                     |                |                 |                      |                          |                        |                                |
| Nellis and Van De Water (2002) | 2-            | Retrospective Cohort Study | &quot;Gritti-Stokes&quot; without bevel. | n=185; males only; Mean age: 72yrs (63-85yrs); No follow-up | Atherosclerotic, KD modified (n=61), KD standard (n=2), TF (n=24), TT (n=68), TM (n=29) | • Quality of stump |
| USA                     |                |                 |                      |                          |                        |                                |
| Pinzur et al. (1992)    | 2-             | Case-control Study | NA                   | n=25; Mean age: Experimental- 57.8yrs Control- 54.5yrs | Peripheral vascular insufficiency, no residual limb pain, swelling, or pressure ulcers, at least 6mth prosthetic wear, prosthetic prescriptions described. Midfoot n=5, Syme’s n=5, TT n=5, KD n=5, TF n=5, Control n=5 | • Gait Biomechanics |
| USA                     |                |                 |                      |                          |                        |                                |
| Pinzur et al. (1993)    | 2+             | Within Subject Comparison Study | NA                   | n=4; Mean age: 58yrs (43-67yrs) | Unilateral TT amputees undergoing contralateral KD amputation, all PVD. Inclusion: Community amputators before contralateral amputation, adequate potential of TTA wound healing for contralateral amputation, primary healing of contralateral KD amputation. | • Gait Biomechanics |
| USA                     |                |                 |                      |                          |                        |                                |</p>
<table>
<thead>
<tr>
<th>Bibliographic Citation</th>
<th>Country</th>
<th>Evidence Level</th>
<th>Research Design</th>
<th>Amputation Technique</th>
<th>Sample Size</th>
<th>Age Follow-up</th>
<th>Subject Characteristics</th>
<th>Outcome Measure Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schoppen et al. (2003)</td>
<td>Netherlands</td>
<td>2++</td>
<td>Prospective Cohort Study</td>
<td>NA</td>
<td>n=46; 70% male; Mean age: 73.9 (SD 7.9); Follow-up: 2weeks, 6weeks, 6months, 1year</td>
<td>Inclusion: Unilateral TT/KD/TF vascular amputees of age &gt;60yrs. Exclusion: Cannot understand test instructions, or severely disabled with no walking ability for non-dysvascular reasons. TT 72% (n=72), KD 17% (n=8), TF 11% (n=5)</td>
<td>Functional outcomes</td>
<td></td>
</tr>
<tr>
<td>Siriwardena and Bertrand (1991)</td>
<td>England, UK</td>
<td>2+</td>
<td>Retrospective Cohort Study</td>
<td>Gritti-Stokes</td>
<td>n=598; 61% male; Follow-up: 3, 6, 9, 12 months after prosthetic fitting.</td>
<td>Arteriosclerotic amputees. Exclusion: hip disarticulation and Syme’s amputation. TT (n=267), Gritti-stokes (n=81), TF (n=195), Bilateral (n=55)</td>
<td>Prosthetic ambulation</td>
<td></td>
</tr>
<tr>
<td>Taylor et al. (2005)</td>
<td>USA</td>
<td>2+</td>
<td>Retrospective Cohort Study</td>
<td>NA</td>
<td>Patients n=553, amputations n=627; 55% male; Mean age: 63.7yrs; Follow-up: 1 year</td>
<td>PAD, TT 37.6% (n=236), KD 4.3% (n=27), TF 34.5% (n=216), Bilateral 23.6% (n=148)</td>
<td>Functional outcomes Prosthetic ambulation</td>
<td></td>
</tr>
<tr>
<td>Ten Duis et al. (2009)</td>
<td>Netherlands</td>
<td>2+</td>
<td>Retrospective Cohort Study</td>
<td>Sagittal Flaps</td>
<td>Patients n=80, amputations n=89; 56% male; Mean age: 76.9yrs (SD 9.6); Median follow-up: 9.9yrs (IQR: 4.1; 14.3)</td>
<td>PAD, all KD subjects. Exclusion: incomplete records</td>
<td>Quality of stump</td>
<td></td>
</tr>
<tr>
<td>Witsø et al. (2010)</td>
<td>Norway</td>
<td>2+</td>
<td>Prospective Cohort Study</td>
<td>NA</td>
<td>KD and TT amputation n=137</td>
<td>PVD, KD (n=84), TT (n=53)</td>
<td>Quality of stump</td>
<td></td>
</tr>
<tr>
<td>Yusuf et al. (1997)</td>
<td>England, UK</td>
<td>2-</td>
<td>Retrospective Cohort Study</td>
<td>Gritti-Stokes</td>
<td>n=434; Male:female (Gritti-Stokes, TF, TT): 1.1, 1.6, 1.7; Median age: 76, 75, 70; Median follow-up: 23mths</td>
<td>PVD Gritti-Stokes (n=144), TF (n=117), TT (n=173)</td>
<td>Quality of stump Prosthetic ambulation</td>
<td></td>
</tr>
</tbody>
</table>

KD: knee disarticulation; NA: not applicable; PAD: peripheral arterial disease; PAOD: peripheral arterial occlusive disease; PVD: peripheral vascular disease; TF: transfemoral; TM: transmetatarsal; TT: transtibial; TTA: transtibial amputation; SD: standard deviation; IQR: inter-quartile range
Figure 3. Distribution of studies by study design.

Figure 4. Distribution of studies according to the risk of bias.
Quality of Stump

A summary of results for the quality of stump is listed in Table 8. 12 studies reported on the quality of stump, with a total of 709 KD amputations, however data pooling was not possible due to heterogeneous samples. Primary healing ranged between 60-100%, delayed healing/revision was between 0-26%, and reamputation was between 0-21%. Gritti-Stokes had lower reamputation rates ranging between 0-13%; no other distinct observations can be made between techniques or countries.

Nine studies used clinical judgments to determine the appropriate amputation level, none of the studies utilised physiological tests, and three studies did not indicate the method of assessment. The number of identified variables/confounders that affect wound healing ranged from 0-5 among the studies, but only one study analysed how the variables influenced the results.
Table 8. Summary of results for quality of stump in KD.

<table>
<thead>
<tr>
<th>Bibliographic Citation</th>
<th>Technique</th>
<th>No. of KD Amputations</th>
<th>Primary Healing</th>
<th>Delayed Healing / Revision</th>
<th>Reamputation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayoub et al. (1993)</td>
<td>Anterior Flap</td>
<td>35</td>
<td>88%</td>
<td>9%</td>
<td>3%</td>
</tr>
<tr>
<td>Met et al. (2008)</td>
<td>Sagittal Flaps</td>
<td>39</td>
<td>-</td>
<td>26%</td>
<td>21%</td>
</tr>
<tr>
<td>Moran et al. (1990)</td>
<td>Sagittal Flaps</td>
<td>106</td>
<td>71%</td>
<td>8%</td>
<td>13%</td>
</tr>
<tr>
<td>Ten Duis et al. (2009)</td>
<td>Sagittal Flaps</td>
<td>89</td>
<td>71%</td>
<td>13%</td>
<td>12%</td>
</tr>
<tr>
<td>Kock et al. (2004)</td>
<td>Posterior Flap</td>
<td>69</td>
<td>80%</td>
<td>8%</td>
<td>12%</td>
</tr>
<tr>
<td>Cull et al. (2001)</td>
<td>Mazet Hennessy</td>
<td>10</td>
<td>60%</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>Morse et al. (2008)</td>
<td>Mazet Hennessy</td>
<td>50</td>
<td>81%</td>
<td>0%</td>
<td>19%</td>
</tr>
<tr>
<td>Campbell et al. (1994)</td>
<td>Gritti-Stokes</td>
<td>8</td>
<td>-</td>
<td>13%</td>
<td>13%</td>
</tr>
<tr>
<td>Jackson et al. (2012)</td>
<td>Gritti-Stokes</td>
<td>14</td>
<td>79%</td>
<td>21%</td>
<td>0%</td>
</tr>
<tr>
<td>Nellis and Van De Water(2002)</td>
<td></td>
<td>61</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Yusuf et al. (1997)</td>
<td>Gritti-Stokes</td>
<td>144</td>
<td>-</td>
<td>6.3%</td>
<td>-</td>
</tr>
<tr>
<td>Witsø et al. (2010)</td>
<td>-</td>
<td>84</td>
<td>-</td>
<td>18%</td>
<td>-</td>
</tr>
</tbody>
</table>

*With trimmed lateral condyles; **Without bevel

Functional Outcomes

Four studies reported on results relating to the functional outcomes. One prospective study used the Sickness impact profile (SIP-68), Groningen Activity Restriction Scale (GARS), Timed
up and go (TUG) test.\textsuperscript{44} Another study measured the maintenance of preoperative independent status based on clinical records.\textsuperscript{38} Both studies made comparisons to TT and TF levels.\textsuperscript{38, 44} The last two studies used custom surveys to measure independent living with no comparison to other amputation levels.\textsuperscript{26, 51}

\textit{Prosthetic Ambulation}

A summary of results for prosthetic ambulation is listed in Table 9. Prosthetic ambulation rates do not include therapeutic and cosmetic limb wearers. Nine studies reported on results relating to prosthetic ambulation, and data pooling was not possible due to heterogeneous studies. The prosthetic ambulation rate for KD amputees ranged from 13-75%. No distinct observations can be made between the countries undertaking these studies. Moran et al.’s results excluded reamputated TF ambulant patients,\textsuperscript{52} and the follow-up results from Kock et al.’s study were based on surviving patients only, hence the rates increased at nine years when a greater proportion of ambulant patients survived.\textsuperscript{4}

Three studies used mobility scales,\textsuperscript{43, 45, 48} and six studies did not do so,\textsuperscript{4, 26, 38, 50-52} out of which two were surveys.\textsuperscript{26, 51} Three studies involved a prosthetist in the research team,\textsuperscript{38, 50, 51} while others did not.\textsuperscript{4, 26, 43, 45, 48, 52} The number of identified variables/confounders that affect prosthetic ambulation ranged from 0-5 among the studies, however only two studies analysed how these variables influenced the results.\textsuperscript{38, 45}
Table 9. Summary of results for prosthetic ambulation in KD.

<table>
<thead>
<tr>
<th>Bibliographic Citation</th>
<th>Technique</th>
<th>Outcome Measure</th>
<th>Mean Follow-up</th>
<th>Prosthetic Ambulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Met et al. (2008)</td>
<td>Sagittal Flap</td>
<td>SIGAM* mobility grades</td>
<td>≤1 year</td>
<td>31%</td>
</tr>
<tr>
<td>Moran et al. (1990)</td>
<td>Sagittal Flap</td>
<td>None (descriptive)</td>
<td>≤1 year</td>
<td>53%</td>
</tr>
<tr>
<td>Kock et al. (2004)</td>
<td>Posterior Flap</td>
<td>None (descriptive)</td>
<td>≤1 year</td>
<td>58%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 years</td>
<td>53%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9 years</td>
<td>75%</td>
</tr>
<tr>
<td>Cull et al. (2001)</td>
<td>Mazet Hennessy</td>
<td>None (descriptive)</td>
<td>2 years</td>
<td>70%</td>
</tr>
<tr>
<td>Morse et al. (2008)</td>
<td>Mazet Hennessy</td>
<td>Survey</td>
<td>3 years</td>
<td>56%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 years</td>
<td>41%</td>
</tr>
<tr>
<td>Jackson et al. (2012)</td>
<td>Gritti-Stokes**</td>
<td>Survey</td>
<td>“Long-term”</td>
<td>36%</td>
</tr>
<tr>
<td>Siriwardena and Bertrand (1991)</td>
<td>Gritti-Stokes</td>
<td>Walking Ability Index (WAI)</td>
<td>≤1 year</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Yusuf et al. (1997)</td>
<td>Gritti-Stokes</td>
<td>Stanmore mobility grades</td>
<td>≤1 year</td>
<td>21%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 years</td>
<td>13%</td>
</tr>
<tr>
<td>Taylor et al. (2005)</td>
<td>-</td>
<td>None (descriptive)</td>
<td>≤1 year</td>
<td>62%</td>
</tr>
</tbody>
</table>

*SIGAM: Special Interest Group in Amputee Medicine; **with trimmed lateral condyles

Gait Biomechanics
Two studies reported on results relating to gait biomechanics. One study compared the walking capacity and metabolic costs of amputees. The walking capacity, measured by speed, cadence and stride length, decreased with proximal amputations. Some of the results involving the metabolic costs (net oxygen cost, max capacity, and functional energy cost) were unclear and did not relate to their derivations in the reported table legends in the study, hence they are excluded from this review. The other study analysed the gait of 4 bilateral patients with TT and contralateral KD amputations, comparing forefoot propulsion, vertical ground reaction forces (GRF), and centre of pressure (CoP) progression within the foot.

Discussion

Quality of Stump

Due to a small number of studies, the effects between surgical techniques were not obvious, and no patterns were observed between countries where the studies were conducted. As only four studies made comparisons to other amputation levels, the comparisons were not conclusive too. There was also a lack of statistical analyses in most studies, hence it was hard to determine if results were significant especially for studies with small sample sizes.

With regards to primary healing, low rates in Cull et al.’s study could be attributed to subjects having severe peripheral vascular disease, secondary amputations (40% had failed TTA) and high rates of previous unsuccessful revascularisation (90%). Furthermore, the study had a
small sample size (n=10), and would not be statistically significant. Excluding this study, the primary healing rates would range between 71-100%, which is similar to 70% primary healing rates of TFAs.\textsuperscript{53} However healing rates were subjective due to a lack of full reporting of confounders, and multivariate analyses of reported confounders. Factors affecting wound healing are manifold, such as smoking, malnutrition, absence of demarcation, method of amputation level selection, use of prophylactic antibiotics, surgeon experience, drain usage, and type of dressing.\textsuperscript{54} Other controversial factors include hemorheology, previous revascularisation, and presence of diabetes mellitus.\textsuperscript{54} One study found that the type of dressing may not affect KDs as much as TTAs (p=0.447), but a high number of comorbidities may influence healing as well (p=0.009).\textsuperscript{46} These factors need to be addressed with multivariate analyses for conclusive comparisons of primary healing of KD against other amputation levels.

Reamputation rates are also multifactorial, including non-physiological methods of determining amputation levels, surgeon experience, infection, circulatory failures and enfeebled patients.\textsuperscript{1} None of the studies used physiological methods (eg. systolic/perfusion pressure measurements\textsuperscript{54}) for determining amputation levels, hence higher reamputation rates of KD compared to TF levels may be due to the fact that many patients were unsuitable for KD in the first instance. 40-50% of reamputations in certain studies were also previously failed TTAs, indicating inappropriate amputation level selection.\textsuperscript{50, 52} Met et al. recognised that not using physiological methods might explain higher reamputation rates,\textsuperscript{43} and Witsø et al. highlighted the need for additional methods of assessment.\textsuperscript{47} Patients with absent ipsilateral femoral pulse should not be undergoing KD due to high risks of complications (Odds Ratio: 74.0).\textsuperscript{20} TF is naturally the safest level of amputation with lowest reamputation rates, however it does not
mean KD should not be considered. The key is having ancillary physiological tests to supplement clinical judgments in deciding the appropriate level of amputation. These would include testing of skin blood flow, perfusion, and nutritional status of the patient before amputation. Reamputations lead to increased risks to patient, prolonged hospitalisation and low morale.\textsuperscript{42} This warrants the need for continued research in valid and reliable assessment methods of amputation levels.

The amount of viable tissues required for KD is similar to a short TT stump,\textsuperscript{3} but none of the studies addressed when a KD is indicated over a short TTA. Witsø et al. highlighted the need for a well-circulated posterior flap in KD,\textsuperscript{47} which is advocated by Kock et al., as the blood supply to the knee region comes from the gastrocnemius heads.\textsuperscript{4} Gritti-Stokes had lower reamputation rates which coincides with findings from the ISPO consensus,\textsuperscript{1} but issues with long term pain and patella instability have been previously reported.\textsuperscript{55} These were however, not reported in the studies of this review. The follow-up period could be too short, or it could be a past issue. There were also many detriments reported against the Mazet technique,\textsuperscript{3, 5, 8, 16} but these were not present in the studies included in this review. The technique allows shorter flaps for wound closure, and hence improved healing.\textsuperscript{26} Mazet also recommended the technique for the dysvascular patient only if the patient has a palpable femoral pulse and good skin quality around the knee joint.\textsuperscript{56}

The belief that KD is prone to wound complications was based on dated studies in the 1970s, when anterior flaps were used.\textsuperscript{57-60} This is possibly no longer relevant, and there should be a
reconsideration of KDs since healing rates are similar to TFAs. However, the crucial point is to have accurate methods of assessing appropriate amputation levels. With regards to modified KD techniques like the Gritti-Stokes and Mazet, there needs to be further well-established research done to justify that these techniques are suitable for the dysvascular patient.

**Functional Outcomes**

There was no significant differences among the amputation levels in Schoppen et al.’s study with the outcome measures, however it might be due to a high proportion of TT patients and interaction of different variables.\(^{44}\) Patients with poor one leg standing balance did significantly poorly in all tests, and these patients were likely to have more proximal amputations.\(^{44}\) Hence proximal amputation levels are likely to be linked with poorer outcomes. Taylor et al. found that the TFA had the poorest maintenance of preoperative independent status (p<.001), whereas KD, like the TTA, did not have any significant influence.\(^{38}\) TFA was also the only level that was independently associated with the failure to maintain independence (Hazard ratio 1.8).\(^{38}\) Patients with the Mazet technique had almost identical maintenance of independence at a three year follow-up to Taylor et al.’s study, however no comparisons to other amputation levels were made and the survey results were subjective.\(^{26}\) Gritti-Stokes patients had poor rates of independence, but measurements were not related to maintenance of preoperative independence, and it was a survey (subjective) with no comparisons to other levels.\(^{51}\) Studies suggesting that KD gives a greater functional outcome than TFA in dysvascular patients were only from a one-year follow-up period,\(^{38,44}\) and further research is required to determine the long-term effects of KD.
Prosthetic Ambulation

Due to the small number of studies, the effects between surgical techniques were not conclusive, and no patterns could be seen between countries where the studies were conducted. Met et al. found no significant differences between KD and TF levels but the identification of variables/confounders to prosthetic ambulation was poor and hence the results cannot be directly attributed to amputation levels. Variables that influence prosthetic rehabilitation are advancing age, presence of comorbidities (including mental diseases), premorbid functional/ambulatory level, condition of contralateral limb, presence of oedema, and psychosocial factors. These factors will have to be part of a multivariate analysis together with the level of amputation, to determine if any amputation level has an independent influence on prosthetic ambulation. It will also be more accurate to indicate the maintenance of ambulatory status rather than actual ambulation rates, as many older dysvascular patients have limited preoperative mobility. The only study that fulfilled these criteria indicated that KD had better ambulatory rates than TF (p<0.001). The study also found that only the TFA had an independent factor in influencing non-prosthetic wear (Odds ratio 4.4). In terms of outcome measures used, there was a lack of reliable and validated mobility scales, and the use of surveys would be subjective. It will be difficult to have reliable results, since all of the studies were retrospective and mostly based on clinical records. There was also minimal involvement of prosthetists in the research teams; ideally both a prosthhetist and a physiotherapist should be present in assessing the ambulation of an amputee, to rule out any bias.
Yusuf et al. mentioned that prosthetic rehabilitation was difficult in their study due to old age and associated diseases. Met et al. stated that the reasons for diminished mobility in their study were serious comorbidities and mental diseases, and Jackson et al. stated that 50% of the subjects in their study were not ambulating due to comorbidities but 81% achieved expected preoperative functional status. These three studies accounted for the lowest ambulatory rates ranging between 13-36%, and hence higher rates may be achieved if maintenance of preoperative ambulatory status was reported.

Kock et al. used the posterior flap technique, and the rates of prosthetic ambulation increased at 9 years follow-up, excluding non-survivors. This is possibly indicating that ambulatory rates are high among the healthy surviving patients, and results from the initial years were influenced by patients with greater comorbidities. The posterior flap aids prosthetic rehabilitation as it allows a well-padded end bearing stump, and is particularly beneficial to the elderly. The study appeared to have better results than studies that used the sagittal flap technique, but a direct comparison is not possible due to the other variables that influence prosthetic ambulation.

It was claimed that the Mazet technique allows effective use of KD suction sockets, distributing forces over the entire stump surface rather than over the condyles, while maintaining some end bearing characteristics. This is possible due to the conical stump shape from the shaved condyles, and the authors reported no late skin breakdown, no rotational instability, no
belts/straps required, and ease of donning. If the claims are true, that could potentially reduce the disadvantages of KD, with no prosthetic shear forces on the condyles, ease of fit, and better cosmesis. The weightbearing area is reduced, but the suction sockets would redistribute forces over a greater area. Compared to the TFA, the long lever arm is maintained with a reduced need for ischial bearing or auxiliary suspension. An excluded study, which consisted of both dysvascular and non-dysvascular patients, combined the posterior flap and the Mazet technique for patients who were likely to ambulate and achieved 81% maintenance of ambulation. Other authors condemned the technique due to the risk of haematoma and infection from the bleeding bone, however that may not be entirely relevant as TFAs also involve bone transection. Consequently there is a possibility of a greater level of trauma involved in using the osteotome for the Mazet technique, compared to the amputation saws used in TFA. There needs to be more detailed reporting of follow-up results, and direct comparisons with TF patients within the studies to justify the benefits of the Mazet technique.

The Gritti-Stokes amputation had a lower prosthetic ambulation rate ranging between 13-36%. It allows space for the prosthetic knee mechanism, and the posterior bevel prevents the patella from slipping forward. However, some authors have stated that high peak pressures are created during weight-bearing, with possible failure of patella union. These issues were not reported in the studies of this review, although many patients abandoned prosthetic use over a 23-month follow-up in one study. The reasons were not stated, but it could be possible that it was due to the stated detriments by other authors. Jackson et al. stated that long-term pain and patella instability were not apparent in their study, however they failed to mention the exact period of follow-up. Only 50% of Gritti-Stokes patients were satisfied with their prosthetic
cosmesis, compared to 84% of TF and 94% of TT patients in another study, and it took a longer
time for prosthetic fitting. However the study was conducted two decades ago and current
prosthetic advancements may have improved prosthetic fitting and cosmesis in Gritti-Stokes
amputations. Gritti-Stokes amputees were known to achieve poor prosthetic fitting and
ambulation compared to standard KD amputees, which is also apparent in this review. Overall,
Gritti-Stokes subjects did not perform significantly better than TF subjects in these studies
during follow-up.

Gait Biomechanics

Metabolic results from Pinzur et al.’s earlier study were excluded due to the reasons stated in
the results section. There were also no consistent patterns observed; the authors stated that
the metabolic cost of walking increased with proximal amputations but this was not apparent
from the tables and figures presented. The values fluctuated with higher amputation levels;
furthermore there was no statistical analysis to determine the significance of the results. Only
walking capacity decreased with proximal amputations, although there was also no proven
statistical significance, and the sample size of each group was small (n=5).

In the study that analysed the gait of bilateral dysvascular amputees with TT and contralateral
KD amputations, there was a greater transfer of body weight to the prosthesis in the KD limb
compared to the TT limb, based on the vertical GRF results. This was statistically significant in
both early (p<0.01) and late stance (p<0.005), and it is likely attributed to the end bearing nature
of KD stumps. In normal gait, a limb should experience peak vertical GRFs (approximately 110% of body weight) during loading response (weight acceptance) and push-off due to the deceleration and acceleration of body mass. There was also a smoother transition of GRF in the KD limb than the TT limb as measured in the CoP progression in the foot, although the recording was only provided from one patient. There was no significant difference between the forefoot propulsion of the KD and TT limb, indicating that there is no loss of propulsion with a polycentric prosthetic knee in KD when compared to an anatomical knee in TT. This may be attributed to the fact that dysvascular TT patients with limited ambulatory function do not maintain quadriceps and hamstrings muscle activity as effectively as active TT walkers, and hence not gaining the full benefits of the knee joint. The study indicated greater stability with the KD limb compared to the TT limb, however more proximal amputations could result in increased energy consumption and decreased walking capacity, this was not addressed in the study. This study was also limited by a small sample size (n=4), and further credible research is required.

Quality Appraisal

There were no controlled trials, a substantial amount of non-comparative studies, and only one study had a very low risk of bias. This led to an overall low strength of evidence in this topic of interest, although it is very difficult to conduct controlled trials in amputation surgeries. There was also a lack of detailed, reliable, and validated outcome measures along with a lack of relevant multidisciplinary teams. There was a substantial amount of studies that did not execute any statistical analyses, and the results can be deceiving especially with studies of small
sample sizes. Some of these studies only had a KD population group, but made claims in comparison to the other amputation levels. Many of these studies failed to recognise that rehabilitation outcomes are multifactorial, with many influencing variables. Even when some variables are identified, there was a lack of multivariate analyses to identify independent factors. There was also a lack of follow-up, or poor reporting of follow-up results.

SIGN Grade of Recommendation: C

Limitations

This review only considered English publications, and other research in foreign languages may be overlooked. There was also a lack of multiple expert reviewers with independent judgments during the conduct of this review. No other medical professions were involved, however key findings were discussed with an experienced orthopaedic consultant, in an effort to reduce the risk of bias judgments.

Conclusion

When dysvascular patients are considered for proximal lower limb amputation levels they are usually in their advanced ages, with poor preoperative functional status and associated comorbidities. It is difficult to determine the direct effects of KD on such a vulnerable population,
especially with the limitations of the available literature. Healing rates are similar to TFAs, but there is a need for valid and practical assessment methods for appropriate amputation level selection to prevent reamputations. It is also unclear when a KD is appropriate over a short TTA for ambulatory patients as they have similar requirements of tissue viability. This warrants the need for further research into formulating prescription guidelines for KD. KD patients have better maintenance of independent living status than TF patients, but prosthetic ambulation rates are inconsistent across studies. The prosthetic ambulation results would be more accurate if variables were accounted for and maintenance of preoperative ambulatory status measured.

There is no conclusive evidence regarding the gait biomechanics of dysvascular amputees due to the paucity of credible research in this subject area.

There is a consensus that the anterior flap is a dated technique and should be avoided in KD. Correspondingly, the only study that used this technique was conducted two decades ago. Theoretically, the posterior flap allows better vascularisation and padding for the end bearing stump than sagittal flaps, but there were no direct comparisons of the two techniques in current studies. The Mazet technique is potentially propitious in both the quality of stump and prosthetic ambulation, but the study designs need to be more robust in providing evidence that previously reported technical flaws are no longer relevant, and the technique is suitable for the dysvascular population. Gritti-Stokes amputations had low reamputation rates, but controversial ambulation rates. If it is proven to be unsuitable for prosthetic ambulation, it is still suitable for non-ambulatory patients to achieve the non-prosthetic benefits of KD, with less risk of revisions.
Recommendations

A stronger body of evidence is required to determine if a greater proportion of KD can be justified among dysvascular amputees. The authors recommend future research to be of prospective studies, with comparison to different amputation levels in the dysvascular population and with long-term follow-up. Variables have to be fully accounted for in a multivariate analysis as rehabilitation outcomes are multifactorial. There is a need for continued research and the use of valid and reliable assessment methods of amputation levels, and the formulation of prescription guidelines in the selection of a KD level of amputation. If prosthetic ambulation is measured, the involvement of prosthetists and physiotherapists with the use of validated mobility scales are necessary. The maintenance of preoperative ambulatory status should also be measured. No quality of life outcomes have been found during the conduct of this review, and it will be beneficial to analyse the perceptions of KD amputees with comparison to other amputation levels.

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Word count: 4556
References


Appendices

Appendix A: Database Search Strategy

Search Terms
#1A: "Knee disarticulation", "through knee", transgenicicular, transcondylar, supracondylar
#1B: "Gritti-stokes", Callander, Mazet, "posterior flap", "sagittal flap"
#2: Transfemoral, "trans femoral", "above knee", "through thigh"
#3: Amput*, surg*, technique
#4: Rehabilitation, success, complication, prosthe*, healing, ambulat*, "quality of life", mortality, morbidity
#5: Dysvascular, "peripheral vascular disease", "peripheral arterial disease", "peripheral arterial occlusive disease", ischaemi*, vascular*, diabet*, sclero*, atherosclero*
#6 (exclusion): Tumour, trauma, athroplasty, "total knee replacement", bypass, fracture*, osseointegrat*, humer*, "aortic valve", transradial, coronary

Transfemoral keywords were included to search for potentially relevant studies. Search strategies were adapted as the search progressed to eradicate irrelevant studies. Any changes and adaptations are recorded and listed below.

Medline (Proquest)
Limit to: Peer reviewed; Publication date: After December 31 1988; Language: English.
A. 05/02/2014
   (#1A) OR (#2) AND (#3) NOT (tumour or trauma)
   3029 results → title screen → 117 results
B. 05/02/2014
   Updated settings: Within abstract; Limited to: Humans
   (#1A OR #1B) AND (#4)
   192 results → title screen → 32 results
C. 06/02/2014
   Updated settings: removed 'within abstract' option
   (#2) AND (#4) NOT (tumour or trauma or fracture or "vascular surgery" or osseointegrat* or bypass)
   1282 results → title screen → 85 results
D. 06/02/2014
   (#4) AND (#5) AND ti(amput*) NOT (tumour or trauma or "vascular surgery" or bypass or coronary or aortic valve)
   947 results → title screen → 254 results
MEDLINE TOTAL: n = 286 (duplicates removed)

Embase (OvidSP)
Database: Embase 1980 to date; Limits: English language, human, 1989 to current.
A. 07/02/2014
   (#1A) OR (#2) AND (#3) NOT ti(#6)
   1321 results → title screen → 177 results
B. 07/02/2014
   (#1A OR #1B) AND (#4) NOT ti(#6)
   440 results → title screen → 40 results
C. 08/02/2014
   (#2) AND (#4) NOT ti(#6)
   1881 results → *exclude medline journals → 103 results → title screen → 7 results
D. 08/02/2014
   (#4) AND (#5) AND ti(amputation) NOT ti(#6)
   706 results → *exclude medline journals → 37 results → title screen → 16 results
EMBASE TOTAL: n = 193 (duplicates removed)
Cochrane Library (Wiley Online Library)
Limits: 1989-2014; word variations allowed
A. 08/02/2014
([#1A OR #2]titles,abstracts,keywords) AND ([#3]record title only) NOT ([#6]record title only)
Cochrane reviews: 3 results → title screen → 2 results
Trials: 21 results → title screen → 1 result
Technological assessments: 2 results → title screen → 0 results
B. 08/02/2014
(#1A OR #1B) AND (#4) NOT ([#6]record title only)
Cochrane reviews: 2 results → title screen → 1 result
Trials → 6 results → title screen → 0 result
C. 08/02/2014
(#2) AND (#4) NOT ([#6]record title only)
Cochrane reviews: 2 results → title screen → 1 result
Trials: 47 results → title screen → 1 result
Technological assessments: 1 result → title screen → 0 result
D. 08/02/2014
(#4) AND (#5) AND [(amputation)record title only] NOT ([#6]record title only)
Cochrane reviews: 2 results → title screen → 1 result
Trials: 24 results → title screen → 1 result
COCHRANE LIBRARY TOTAL: n = 5 (duplicates removed)

ScienceDirect (Elsevier)
Limit to: 1989 to present
A. 09/02/2014
tak(#1A OR #2) AND ttl(#3) NOT ttl(#6)
346 results → title screen → 49 results
B. 09/02/2014
tak(#1A OR #1B) AND tak(#4) NOT ttl(#6)
75 results → title screen → 11 results
C. 09/02/2014
tak(#2) AND #4 NOT ttl(#6)
512 results → title screen → 41 results
D. 09/02/2014
tak(#4 AND #5) AND ttl(amputation) NOT ttl(#6)
242 results → title screen → 96 results
SCIENCE DIRECT TOTAL: n = 142 (duplicates removed)

Combined databases search: n = 442 (duplicates removed)
### Appendix B. Risk of Bias Checklist

#### Study Construct
1. Appropriate and clearly focused question
2. Brief and appropriate literature review to place the study in context
3. Appropriate ethical approval sought
4. Indication of source of data (retrospective studies)

#### Study Population
5. Detailed reporting of information of study population, with comparison of population characteristics to similar studies
6. Appropriate and representative sample (eligibility criteria and sample size)
7. Variables and potential confounders accounted for, with comparison to similar studies
8. Univariate/ multivariate analyses of variables and potential confounders carried out.
9. Adequate follow-up
10. Attrition rate accounted for (prospective studies)

#### Outcome measures
11. Clearly defined outcome measures
12. Outcome measures carried out by the appropriate medical profession (eg. prosthetist assessing prosthetic mobility grades)
13. Double blinding, or recognition that outcomes may be influenced if these were not possible (prospective studies)
14. Reliability ensured: interrater, intra-rater, test-retest, evidence from other sources
15. Valid outcome measures: Sufficient evidence to demonstrate accuracy, from other sources or enough items/questions relating to the concept of characteristic being evaluated
16. Appropriate and in-depth discussion of results, with comparison to similar studies

#### Statistical Impact
17. Inclusion of power analysis (prospective studies), p-values/ odds ratios (or any relevant measure), and confidence intervals.
18. Well defined and executed statistical analysis
## Appendix C: Quality Appraisal of Studies According to the Risk of Bias Checklist

<table>
<thead>
<tr>
<th>Bibliographic Citation</th>
<th>1</th>
<th>2</th>
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= Adequately addressed; / = Partially addressed; x = Poorly not addressed; NA: Not applicable.