

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Biomechanical risk factors for knee osteoarthritis and lower back pain in lower limb amputees: protocol for a systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-066959
Article Type:	Protocol
Date Submitted by the Author:	28-Jul-2022
Complete List of Authors:	Wade, Logan; University of Bath, Department for Health McGuigan, M. Polly; University of Bath, Department for Health McKay, Carly; University of Bath, Department for Health Bilzon, James; University of Bath, Department for Health Seminati, Elena; University of Bath, Department for Health
Keywords:	Diabetic nephropathy & vascular disease < DIABETES & ENDOCRINOLOGY, REHABILITATION MEDICINE, SPORTS MEDICINE

SCHOLARONE™
Manuscripts

BIOMECHANICAL RISK FACTORS FOR KNEE OSTEOARTHRITIS AND LOWER BACK PAIN IN LOWER LIMB AMPUTEES: PROTOCOL FOR A SYSTEMATIC REVIEW

Logan Wade^{a,b}, M. Polly McGuigan^{a,b}, Carly McKay^{a,c,d}, James Bilzon^{a,b,d}, Elena Seminati^{a,b}

a) Department for Health, University of Bath, Bath UK

b) Centre for Analysis of Motion, Entertainment Research and Applications, University of Bath, United Kingdom

c) Centre for Health and Illness and Injury Prevention in Sport, University of Bath, Bath UK

d) Centre for Sport Exercise and Osteoarthritis Research Versus Arthritis, University of Bath, Bath UK

Corresponding Author:

Logan Wade

lw2175@bath.ac.uk

University of Bath

1 West, Office 5.111, Bath, BA2 7AY, United Kingdom

Email:

Logan Wade - lw2175@bath.ac.uk, M. Polly McGuigan - mpm21@bath.ac.uk, Carly McKay - cdm47@bath.ac.uk, James Bilzon - jb438@bath.ac.uk, Elena Seminati - es685@bath.ac.uk

Registration

In accordance with guidelines, this protocol was submitted and approved with the International Prospective Register of Systematic reviews (PROSPERO) on 03/02/2020 and was last updated 21/01/2022 (ID: CRD42020158247).

1
2
3 28
4
5 29
6
7
8 30
9
10 31
11
12
13 32
14
15 33
16
17 34
18
19 35
20
21 36
22
23 37
24
25 38
26
27 39
28
29
30 40
31
32 41
33
34 42
35
36 43
37
38 44
39
40 45
41
42 46
43
44 47
45
46 48
47
48 49
49
50 50
51
52 51
53
54 52
55
56 53
57
58 54
59
60 55

Abstract

Introduction: There is limited research exploring biomechanical risk factors for the development of knee osteoarthritis (KOA) and lower back pain (LBP) between lower limb amputee sub-groups, [e.g., transtibial amputees (TTA) vs transfemoral amputees (TFA) or TTA dysvascular vs TTA traumatic]. Previous reviews have focussed primarily on studies where symptoms of KOA or LBP are present, however, due to limited study numbers, this hinders their scope and ability to compare between amputee sub-groups. Therefore, the aim of this systematic review is to descriptively compare biomechanical risk factors for developing KOA and LBP between lower limb amputee sub-groups, irrespective of whether KOA or LBP was present.

Methods and analysis: This review is currently in progress and screening results are presented alongside the protocol to highlight challenges encountered during data extraction. Five electronic databases were searched (Medline – Web of Science, PubMed, CINAHL, Embase and Scopus). Eligible studies were observational or interventional, reporting biomechanical gait outcomes for individual legs in adult lower limb amputees during flat walking, incline/decline walking or stair ascent/descent. Two reviewers screened for eligibility and level of agreement was assessed using Cohen’s Kappa. Data extraction is ongoing. Risk of bias will be assessed using a modified Downs and Black method, and outcome measures will be descriptively synthesised.

Ethics and dissemination: There are no ethical considerations for this systematic review. Due to its scope, results are expected to be published in three separate manuscripts: 1) Biomechanical risk factors of KOA between TTA and TFA, relative to non-amputees, 2) Biomechanical risk factors of LBP between TTA and TFA, relative to non-amputees, and 3) Biomechanical risk factors of KOA and LBP between transtibial amputees with traumatic or dysvascular causes, relative to non-amputees.

PROSPERO registration number: CRD42020158247).

1
2
3 54
4
5
6
7 55
8
9 56
10
11 57
12
13 58
14
15 59
16
17 60
18
19 61
20
21 62
22
23
24 63
25
26 64
27
28 65
29
30
31 66
32
33
34
35 67
36
37 68
38
39 69
40
41 70
42
43 71
44
45 72
46
47 73
48
49 74
50
51 75
52
53 76
54
55 77
56
57
58 78
59
60

Strength and Limitations

- This systematic review protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines.
- This will be the first review to compare biomechanical gait between amputee sub-groups such as transtibial and transfemoral amputees, as well as transtibial dysvascular and transtibial traumatic amputees.
- Studies must include at least one temporospatial, joint kinematic or joint kinetic outcome measure for individual legs to ensure valid and thorough biomechanical technique and analysis.
- Unexpected variations in measurement methodologies have required papers without non-amputee controls to be removed from the study, to ensure rigorous comparison between amputee sub-groups.

Introduction

Lower limb amputations of the hip, knee and ankle considerably alter walking gait and function, with over 42 000 major lower limb amputations performed over a ten year period (2003-2013) in the UK ¹. In 2005, major lower limb amputations in the USA and UK accounted for over 90% of all major limb amputations ², ³ and compared to healthy populations, lower-limb amputees have significantly higher rates of secondary disorders such as knee osteoarthritis ^{4,5} and lower back pain ⁶⁻¹¹. These higher rates are likely due to altered gait mechanics that are experienced as a result of missing limbs and joints ¹², requiring the intact leg to support greater load and produce increased force to maintain stable gait. Furthermore, differences between amputation levels (below ankle, below knee and above knee) and amputation causes (traumatic, vascular disease, cancer, congenital) likely produce different functional impairments, which may increase risk of developing knee osteoarthritis (KOA) and lower back pain (LBP).

1
2
3 79 Considering the prevalence of lower limb amputations, transfemoral (above the level of the knee)
4
5 80 amputees (TFA) and through knee (at the level of the knee joint) amputees account for 17-23% of all
6
7 81 amputations^{13,14}. Transtibial (below the level of the knee) amputees (TTA) and through ankle (at the level
8
9 82 of the ankle joint) amputees account for 12-32%, while partial foot amputees account for 15-26% of all
10
11 83 amputations^{13,14}. Minor amputations of the foot make up the remaining percentages, however these
12
13 84 generally do not substantially alter gait and are therefore not a focus of this review. As amputation level
14
15 85 moves up the leg, functional mobility and quality of life is reduced¹⁵, requiring greater altered gait
16
17 86 mechanics to accommodate the limited power output and instability of the prosthetic limb during stance
18
19 87¹². Thus, above knee amputees are at an increased risk of developing knee pain⁴ and KOA in the intact limb
20
21 88 compared to below knee amputees, with OA of the intact knee occurring in roughly 60% of TFAs and 40%
22
23 89 of TTAs, compared to just 20% of non-amputees¹⁶. Similarly, prevalence of LBP is found in roughly 50-76%
24
25 90 of lower limb amputees, compared to 35% of non-amputees¹⁰⁻¹². Evidence suggests that there may not be
26
27 91 a difference in prevalence or intensity of LBP between TTA and TFA¹⁷, although a previous systematic
28
29 92 review of LBP in lower limb amputees was unable to draw comparisons between TTA and TFA due to limited
30
31 93 studies in TTA¹⁸. Thus, there is a need to explore biomechanical gait differences between TTAs and TFAs,
32
33 94 to understand how biomechanical risk factors associated with the development of and potential
34
35 95 predisposition to KOA and LBP differ between groups.
36
37
38
39
40
41
42

43 97 While amputation level plays a crucial role in altered gait mechanics, cause of amputation likely also
44
45 98 contributes significantly to the development of secondary musculoskeletal symptoms. The two primary
46
47 99 causes of amputation are vascular diseases and traumatic accidents, with cancer and congenital causes
48
49 100 only making up 1-3% of all amputations^{3,14}. Prevalence of amputation cause varies worldwide, with
50
51 101 traumatic amputations making up 6 - 45% of all amputations^{3,14} and patients primarily characterised as
52
53 102 being young and fit³. Alternatively, dysvascular amputations have increased significantly in recent decades
54
55 103 due to the increasing prevalence of diabetes and dysvascular disease, making up 65%-91% of all
56
57 104 amputations^{3,14}. This population is generally older than other amputee cause types³ and commonly have
58
59 105 a higher body mass index¹⁹, which additionally puts individuals at a greater risk of KOA²⁰. Dysvascular

1
2
3 106 amputees also have poorer uptake of prosthetic devices, which further increases their risk of sedentary
4
5 107 lifestyle and weight gain after amputation ²¹. Counterintuitively, some research suggests that this lower
6
7 108 activity status and prosthetic use may result in TFAs having a reduced risk of developing LBP compared to
8
9 109 traumatic amputees ^{16, 18}. Unfortunately, despite a much higher prevalence of dysvascular amputations,
10
11 110 gait biomechanics research within this population is relatively limited, especially compared to the high
12
13 111 proportion of research surrounding traumatic amputations ^{4, 11, 18, 22-25}. We therefore need to determine
14
15 112 whether current research, investigating the development of secondary disorders primarily in traumatic
16
17 113 amputees, is generalisable to dysvascular amputees, and if there are any additional biomechanical factors
18
19 114 specific to dysvascular amputees that would increase or decrease their likelihood of developing KOA and
20
21 115 LBP.
22
23
24
25
26
27

28 117 Additional sub-groups include bi-lateral amputees, osseo-integrated amputees and adult amputees who
29
30 118 had an amputation as children or were born without a limb (i.e. congenital amputees). Bilateral amputees
31
32 119 have a high variation between individuals, often presenting with multiple amputation levels (e.g. one leg
33
34 120 with a trans-tibial amputation and the other with a trans-femoral amputation), which can dramatically alter
35
36 121 gait and may influence development of secondary disorders. Osseo-integrated amputees generally do not
37
38 122 suffer from skin problems, ill-fitting prosthesis issues or bone degeneration issues of their socket wearing
39
40 123 counterparts. Thus, this population may have greater prosthetic use and increased risk of KOA and LBP,
41
42 124 although they also have alternate complications such as recurring infections and risk of bone fractures ^{26, 27}.
43
44 125 Finally, adult amputees who experienced amputations during childhood, or were congenital amputees,
45
46 126 have spent the most time with their amputation. This group may have altered gait patterns as a function
47
48 127 of growing with their prosthesis, which may place them at an increased risk of developing secondary
49
50 128 symptoms much earlier in life. Across all amputee sub-groups, the primary barrier to understanding altered
51
52 129 biomechanical gait is in recruiting a sufficient sample from each population, especially in these latter
53
54 130 specialised sub-groups. Furthermore, longitudinal cohort studies, following patients throughout their life
55
56 131 are very rare, with most studies being performed cross-sectionally. Therefore, a large-scale systematic
57
58 132 review that examines biomechanical gait between amputee sub-groups is presently the best available
59
60

1
2
3 133 option for exploring which biomechanical gait factors may contribute to development of KOA or LBP
4
5 134 between lower limb amputee populations.
6
7

8 135
9

10
11 136 Several reviews have examined amputee biomechanical gait with a focus on KOA and LBP. However, the
12
13 137 majority of these reviews have not been performed using systematic methods ^{11, 22, 23, 28-30}, and generally
14
15 138 have not described differences between amputee sub-groups, often only including a single sub-group (e.g.
16
17 139 only traumatic or transtibial amputees). Moreover, those few systematic reviews on gait and secondary
18
19 140 disorders in amputees have generally only been performed on a single amputee subgroup, using studies
20
21 141 where symptoms of KOA or LBP are present, which severely limits their scope (11-17 studies per review)
22
23 142 and ability to compare between amputee groups ^{16, 18, 31, 32}. Due to such small study numbers included
24
25 143 within these systematic reviews, knowledge of the biomechanical gait characteristics associated with KOA
26
27 144 and LBP and their prevalence between amputee sub-groups is considerably limited. Sagawa, Turcot ³³ has
28
29 145 performed a large-scale systematic review (89 studies) of altered biomechanical gait factors across all lower
30
31 146 limb amputees, aiming to broadly characterise biomechanics and physiological parameters during gait.
32
33 147 They identified that TTA knee flexion during heel strike is limited to 9-12°, while TFA knee flexion was zero
34
35 148 or negative (extension). Additionally, TFAs had twice the pelvic ROM compared to healthy individuals which
36
37 149 may contribute to the development of LBP. Unfortunately, their review was very broad, was not targeted
38
39 150 at gait characteristics of KOA and LBP and generally did not make any comparisons or conclusions between
40
41 151 sub-groups (e.g., amputation level or amputation cause). To fill this gap in the literature, a large-scale
42
43 152 systematic review targeted at identifying how biomechanical risk factors of KOA and LBP differ between
44
45 153 amputee sub-groups is needed. Understanding what biomechanical factors influence gait will help facilitate
46
47 154 specific and personalised rehabilitation programmes and prosthetic designs.
48
49
50

51
52 155
53
54

55 156 OBJECTIVES

56 157 While previous systematic reviews have been limited by only including studies with amputees who are
57
58 158 diagnosed with KOA and LBP, there is a substantial amount of experimental literature that has examined
59
60

1
2
3 159 lower limb amputee gait and posture where no KOA or LBP has been recorded. Because of the high
4
5 160 prevalence of KOA and LBP, it is likely that biomechanical abnormalities leading to these secondary
6
7 161 disorders will be present across the majority of amputees. Therefore, the aim of this systematic review is
8
9 162 to descriptively compare biomechanical risk factors for developing KOA and LBP between amputee sub-
10
11 163 groups, irrespective of whether KOA or LBP was present. Amputee sub-groups will be categorised by level
12
13 164 of amputation (below ankle, below knee and above knee), cause of amputation (vascular disease, traumatic
14
15 165 injury, cancer, congenital) and special sub-groups (bilateral amputees, osseo-integrated amputees, adult
16
17 166 amputees who had an amputation or congenital missing limb as children. Individual sub-groups will only
18
19 167 be included for analysis if sufficient data is available to support comparisons (see data extraction section).
20
21
22
23 168

26 27 169 **Methods**

28 170 This systematic review is currently in progress and screening results are presented within this paper to
29
30 171 highlight challenges encountered during data extraction. This approach was chosen to ensure the
31
32 172 transparency of our methods and increase the replicability of the review.
33
34
35
36 173

38 39 174 **ELIGIBILITY CRITERIA**

40 175 In accordance with PRISMA-P guidelines³⁴, this protocol was submitted and approved by the International
41
42 176 Prospective Register of Systematic reviews (PROSPERO) on 03/02/2020 and was last updated 21/01/2022
43
44 177 (ID: CRD42020158247). This protocol has adhered to the PRISMA-P guide and checklist for publishing
45
46 178 systematic review protocols³⁴.
47
48
49
50 179

52 53 180 **STUDY CHARACTERISTICS**

54 181 Studies included in this review had to be observational studies such as cross-sectional/cohort studies and
55
56 182 longitudinal studies. Intervention and randomised control trial (RCT) studies were included in this review
57
58 183 but only the control amputee group or baseline measures were extracted (observational data). Review
59
60

1
2
3 184 papers, case studies, conference proceedings and animal studies were excluded. Studies that included
4
5 185 quantitative biomechanical measures of lower limb amputees were included if results were reported for
6
7 186 individual legs (intact leg and prosthetic leg presented separately). To ensure application of valid and
8
9 187 thorough biomechanical technique and analysis, data had to include at least one temporospatial, joint
10
11 188 kinematic or joint kinetic outcome measure for individual legs (see Appendix 2 for a full list of extracted
12
13 189 outcome measures). Outcome variables were determined from previous reviews that outlined
14
15 190 biomechanical differences between: amputees and non-amputee populations ^{12, 17, 22, 23, 28, 33, 35}; healthy
16
17 191 non-amputee populations and KOA and LBP non-amputee populations ³⁶⁻³⁸; and healthy amputees and
18
19 192 amputees with KOA and LBP ^{12, 16, 18, 31, 32}. While ground reaction force (GRF) outcome measures for
20
21 193 individual strides were extracted, studies that only reported GRF measures were not included in this
22
23 194 review, as GRF is a measure of full body force and is not specific to the knee joint or lower back region.
24
25 195 Observational studies had to be performed during walking on flat, incline or stair surfaces, at either
26
27 196 preferred or controlled walking speeds. Studies that only investigated running-specific prostheses or
28
29 197 running gaits were not included. Studies that examined powered ankles were included in this review, but
30
31 198 only if an unpowered condition was performed. All microprocessor-controlled ankles and knees (devices
32
33 199 that do not add energy to the system) were included in this review.
34
35
36
37
38
39
40

41 PARTICIPANTS

42 201 Lower limb amputees were included in this review, but only if results were separated by different
43
44 202 amputation levels (e.g., studies that combined results of transtibial and transfemoral amputees were not
45
46 203 included). Due to the differences between child and adult gait, and the focus on development of secondary
47
48 204 disorders which primarily occurs in adults, studies performed only on children (younger than 18 years)
49
50 205 were not included.
51
52 206
53
54
55
56
57

58 Patient and Public Involvement

59 208 None
60 209

210

211 INFORMATION SOURCES

212 Literature searches were performed across five databases: Medline – Web of Science, PubMed, CINAHL,
213 Embase and Scopus. Manual searches were conducted using the reference lists within previous reviews
214 and reference lists within papers obtained from database searches, to ensure all relevant literature was
215 identified (Figure 1).

216

217 SEARCH STRATEGY

218 Studies were only examined if they were published in English. Only peer-reviewed studies were included.
219 No publication date limit was imposed on the search criteria. Search terms included a combination of
220 amputation terms AND gait/biomechanics terms AND secondary disorders. While inclusion for this
221 systematic review did not require the presence of secondary disorders, this term helped to refine the
222 search and identify papers with outcome measures of relevance to the development of secondary
223 disorders in amputee populations. An example search strategy is presented below and a table of the full
224 search strategy, formatted for each database, can be found in Appendix 1.

- 225 1) Amputee: "transtibial amput*" OR "transfemoral amput*" OR amput* OR "Lower limb amput*" OR "Lower extremity amput*" OR "Leg prosthesis"
- 226 2) Activity: walking OR running OR gait OR locomotion OR biomechanics OR kinematics OR kinetics OR "biomechanical parameter*" OR *symmetr* OR forc* OR angle* OR moment* OR power EMG OR electromyogra*)
- 227 228 229 3) Secondary disorder: Osteoporosis OR Osteopenia OR "Back Pain" OR Backache OR Osteoarthritis OR "musculoskeletal diseas*" OR "musculoskeletal condition*" OR "secondary diseas*"

232

233 DATA MANAGEMENT AND SELECTION PROCESS

234 Records retained for abstract and full paper screening were compiled using an excel spreadsheet designed
235 for systematic reviews³⁹. Two reviewers individually applied the eligibility criteria to all records based on

1
2
3 236 the inclusion/exclusion criteria outlined in Figure 1. Where conflicts arose, reviewers met to discuss and if
4
5 237 agreement still could not be made, a third reviewer was consulted to make the final decision. Review stages
6
7 238 progressed from title and abstract review to full paper review (Figure 1). For the title and abstract stage,
8
9 239 there were four reviewers, with one person reviewing all papers and the remaining three people each
10
11 240 reviewing a third of the papers. For the full paper stage, there were three reviewers, with one person
12
13 241 reviewing all papers and the remaining two people reviewing half of the papers each. Level of agreement
14
15 242 was assessed using Cohens Kappa ⁴⁰. Agreement for the title and abstract review stage was 0.76, while
16
17 243 agreement for the full paper review stage was 0.64, where agreement between 0.61-0.80 represents
18
19 244 substantial agreement between reviewers. A minimum of five studies that evaluated a specific sub-group
20
21 245 were required to be included for evaluation of said sub-group within this systematic review. Due to a
22
23 246 limited number of papers included after full text review, studies that examined below ankle amputation (2
24
25 247 papers), rotationplasty amputation (1 paper), bi-lateral amputation (1 paper), osseo-integration (1
26
27 248 papers), and adult amputees who had an amputation or congenital missing limb as children (0 papers) were
28
29 249 ultimately excluded.
30
31
32
33
34 250
35
36 251
37
38
39

40 252 CURRENT STAGE

41 253 This systematic review is currently at the stage of performing data extraction.
42
43
44 254
45
46

47 255 DATA COLLECTION PROCESS

48 256 Data is currently being extracted from studies using a standardised excel spreadsheet. All data are being
49
50 257 extracted by a single reviewer to ensure consistency, though a random sample of 20% of the data are also
51
52 258 being extracted by a second reviewer to assess the risk of bias in the extraction process. Where necessary,
53
54 259 extraction from figures is being performed using the desktop version of WebPlotDigitizer ⁴¹, which is a
55
56 260 data extraction tool for plots, images and maps.
57
58
59
60

261

262 **DATA ITEMS**

263 Data items being extracted include manuscript title, authors, journal, year, country where data was
264 collected, study type, amputee population, number of participants, amputation level, age, biological sex,
265 body mass, height, time since amputation, cause of amputation, type of prosthetic, years of prosthetic use,
266 secondary symptoms, tasks performed in the study and outcome variables (temporospatial, joint
267 kinematics and joint kinetics). For a detailed list of all biomechanical outcome variables, see Appendix 2.
268 Mean/median values, along with standard deviation/ranges are being extracted. For intervention studies,
269 only the baseline measure will be extracted, thus all data included within this review will be observational
270 and cross-sectional in nature.

271

272

273 During data extraction, it has become evident that some outcome measures may appear very high or very
274 low for both amputee and non-amputee groups within the same study. For example, Hendershot and Wolf
275 ⁴² examined trunk angle during walking gait using inverse dynamics, identifying that maximum extension
276 for TTA was 4.89°, TFA was 0.48° and non-amputee controls were 2.75°. Morgenroth, Orendurff ⁴³ also
277 examined trunk angle during walking, however their analysis was based on angle changes of a rigid cluster
278 placed on the 8th thoracic vertebra (T8), with angles relative to the global coordinate system. Thus, they
279 reported that maximum trunk extension of TFA was 26.9° while non-amputee controls were 20.5°. If
280 absolute values were compared, the large maximum angles obtained for TTA's by Morgenroth, Orendurff
281 ⁴³ would drastically alter the differences observed between TTA and TFA across all studies. Therefore,
282 studies which did not examine paired amputee groups (TTA vs TFA or Vascular vs Traumatic) have the
283 potential to drastically alter the results, due to methodological differences in how data were collected.
284 However, if studies recruited both amputees and non-amputees, relative differences compared to non-
285 amputees within the same study could be calculated. Using the example above for Hendershot and Wolf
286 ⁴², relative maximum trunk angle in TTA was 2.1° larger than non-amputee controls and TFA was 2.3°

1
2
3 287 smaller than non-amputee controls, while Morgenroth, Orendurff⁴³ observed TFA was 6.4° larger than
4
5 288 non-amputee controls. Unfortunately, if studies only recruited amputees and did not recruit non-amputee
6
7 289 controls, calculation of relative differences between amputees and non-amputees cannot be calculated.
8
9 290 The diverse range of methodologies included within this review was unexpected and only determinable
10
11 291 due to this systematic review collating the largest number of biomechanical gait studies performed on
12
13 292 amputees to date. Therefore, to ensure rigorous and objective comparison of outcomes between amputee
14
15 293 sub-groups, we have removed 27 studies from screening that did not recruit non-amputee controls (Figure
16
17 294 1), excepting those studies that compared directly between TTA and TFA, or between dysvascular TTA and
18
19 295 traumatic TTA. Challenges we are facing during data extraction highlight the key role non-amputee controls
20
21 296 play during examination of amputee gait, and therefore, studies wishing to compare their results to prior
22
23 297 research should recruit non-amputee participants to facilitate such comparisons.
24
25
26
27
28
29

30

31 299 FUTURE STAGES

32 300 All remaining stages of the protocol encompass the future work yet to be started, with major stages
33
34 301 including risk of bias assessment and data synthesis.
35
36

37

38 302

39 303 OUTCOMES AND PRIORITISATION

40 304 The primary outcomes will be the biomechanical variables listed in Appendix 2. Reporting of outcome
41
42 305 measures will be grouped based on whether previous evidence suggests they may contribute to KOA or
43
44 306 LBP. Kinetic measures not already normalised to body mass will be converted to enable comparison
45
46 307 between studies. Mean/median outcome measures, relative to controls within the same study, will be
47
48 308 compared between amputee groups (TTA vs TFA and Traumatic vs Dysvascular). To directly compare
49
50 309 outcome measures between studies for KOA or LBP, measures will be grouped depending on the type of
51
52 310 movement: preferred speed flat walking, controlled speed flat walking, preferred speed incline/decline
53
54 311 walking, controlled speed incline/decline walking, preferred speed stair climbing or controlled speed stair
55
56 312 climbing. These movements were selected as they are commonly performed in daily living and present
57
58
59
60

1
2
3 313 different challenges for amputees. Thus, to examine differences between amputation level, outcome
4
5 314 measures related to KOA or LBP will be descriptively compared during each movement, between TTA and
6
7 315 TFA, relative to non-amputees. To examine differences between amputation cause, outcome measures
8
9 316 related to KOA or LBP will be descriptively compared during each movement, between transtibial traumatic
10
11 317 and transtibial dysvascular amputees, relative to non-amputees.

318

319 RISK OF BIAS IN INDIVIDUAL STUDIES

320 Risk of bias will be assessed using the modified Downs and Black method ^{44, 45}. In this modified version,
321 question 25 which addresses sample size, will be modified to a yes/no question and studies that performed
322 a sample size calculation/power calculation will be awarded one point, while studies without will be
323 awarded zero ⁴⁴. Randomised controlled trials will be assessed separately to reduce the impact of increased
324 weighting placed on these studies by the Downs and Black method. Randomised controlled trials will only
325 have baseline outcome measures extracted, so while risk of bias will be analysed separately for
326 observational and intervention studies, outcome measures and presentation of the data will be performed
327 identically across all studies. Two reviewers will both assess each study using the Downs and Black criteria.
328 Where there are conflicts, reviewers will meet to discuss and if they cannot agree, a third reviewer will be
329 consulted to make a final decision.

330

331 DATA SYNTHESIS AND DISSEMINATION

332 The primary goal of this systematic review is to descriptively compare biomechanical risk factors for
333 developing KOA and LBP between amputee sub-groups, irrespective of whether KOA or LBP was present.
334 Due to such a large combination of outcome measures (Appendix 2), sub-groups and gait types, meta-
335 analyses will not be performed. Instead, quantitative results will be synthesised and descriptively
336 compared using biomechanical mean/median values of amputee sub-groups relative to non-amputees.
337 Due to the scope of this review, results are expected to be published in three separate manuscripts: 1)
338 Biomechanical risk factors of KOA between TTA and TFA, relative to non-amputees, 2) Biomechanical risk

1
2
3 339 factors of LBP between TTA and TFA, relative to non-amputees, and 3) Biomechanical risk factors of KOA
4
5 340 and LBP between transtibial amputees with traumatic or dysvascular causes, relative to non-amputees.
6
7 341 KOA and LBP will be grouped in the third results paper, as there are far fewer studies that have solely
8
9 342 recruited dysvascular amputees. Systematic review analysis and reporting will be performed using the
10
11 343 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines ⁴⁶.

12
13
14 344

17 345 **META-ANALYSIS AND META-BIAS**

18 346 Due to the high number of movements (e.g. walking, incline walking, decline walking), sub-groups (e.g.
19
20 347 TFA, TTA, dysvascular and traumatic amputation) and outcome variables (temporospatial, kinematic and
21
22 348 kinetic measures), which significantly reduces the number of studies that are able to be statistically
23
24 349 compared for each outcome measure, a meta-analysis will not be performed. Therefore, examination of
25
26 350 meta-bias within this review is not possible.

27
28
29
30
31 351

34 352 **Conclusion**

35 353 Although there have been several systematic reviews examining development of KOA and LBP in amputees,
36
37 354 the number of studies included within these reviews is limited. Furthermore, there have been no
38
39 355 comparisons of biomechanical factors leading to KOA and LBP between amputation level, nor between
40
41 356 traumatic and dysvascular amputation causes. These sub-groups may experience the development of
42
43 357 secondary disorders differently due to altered gait characteristics produced by varying amputation levels
44
45 358 and amputation causes. The following three results papers from this systematic review will hopefully
46
47 359 illustrate which biomechanical measure are key risk factors for different amputee sub-groups.
48
49 360 Understanding these risk factors will hopefully lead to improved personalised rehabilitation programmes
50
51 361 and prosthetic designs by physiotherapists, rehabilitation consultants, clinical biomechanists and
52
53 362 prosthetists.

54
55
56
57
58 363
59
60

Author Contributions

LW is the guarantor. All authors contributed to conception and design of the study. ES and CM developed the search strategy. LW, MPM, CM and ES contributed to the development of selection criteria and performed study selection. LW drafted the manuscript. All authors read, provided feedback and approved the final manuscript.

Funding Statement

This work was supported by the Engineering and Physical Sciences Research Council, through the RCUK Centre for the Analysis of Motion, Entertainment Research and Applications (CAMERA), Bath, United Kingdom, grant number [EP/M023281/1, EP/T014865/1]. This work was also supported by the Versus Arthritis Centre for Sport Exercise, Exercise and Osteoarthritis Research [Ref 21595].

Conflicts of Interest

The authors declare no conflicts of interest

References

1. Ahmad, N., et al., *The prevalence of major lower limb amputation in the diabetic and non-diabetic population of England 2003–2013*. *Diabetes and Vascular Disease Research*, 2016. **13**(5): p. 348-353.
2. Sturma, A., L. Hruby, and M. Diers, *Epidemiology and Mechanisms of Phantom Limb Pain*, in *Bionic Limb Reconstruction*, O.C. Aszmann and D. Farina, Editors. 2021, Springer International Publishing: Cham. p. 103-112.
3. Ziegler-Graham, K., et al., *Estimating the Prevalence of Limb Loss in the United States: 2005 to 2050*. *Archives of Physical Medicine and Rehabilitation*, 2008. **89**(3): p. 422-429.
4. Norvell, D.C., et al., *The prevalence of knee pain and symptomatic knee osteoarthritis among veteran traumatic amputees and nonamputees*. *Archives of Physical Medicine and Rehabilitation*, 2005. **86**(3): p. 487-493.
5. Struyf, P.A., et al., *The Prevalence of Osteoarthritis of the Intact Hip and Knee Among Traumatic Leg Amputees*. *Archives of Physical Medicine and Rehabilitation*, 2009. **90**(3): p. 440-446.

- 1
2
3 395 6. Ehde, D.M., et al., *Back pain as a secondary disability in persons with lower limb amputations*. Archives of Physical Medicine and Rehabilitation, 2001. **82**(6): p. 731-734.
- 4 396
- 5 397 7. Stam, H.J., A.-M.V. Dommissie, and H.B.J. Bussmann, *Prevalence of low back pain after*
- 6 398 *transfemoral amputation related to physical activity and other prosthesis-related parameters*.
- 7 399 *Disability and Rehabilitation*, 2004. **26**(13): p. 794-797.
- 8 400 8. Ephraim, P.L., et al., *Phantom Pain, Residual Limb Pain, and Back Pain in Amputees: Results of*
- 9 401 *a National Survey*. Archives of Physical Medicine and Rehabilitation, 2005. **86**(10): p. 1910-
- 10 402 1919.
- 11 403 9. Hammarlund, C.S., et al., *Prevalence of back pain, its effect on functional ability and health-*
- 12 404 *related quality of life in lower limb amputees secondary to trauma or tumour: a comparison*
- 13 405 *across three levels of amputation*. Prosthetics and Orthotics International, 2011. **35**(1): p. 97-
- 14 406 105.
- 15 407 10. Devan, H., et al., *Exploring Factors Influencing Low Back Pain in People With Nondysvascular*
- 16 408 *Lower Limb Amputation: A National Survey*. PM&R, 2017. **9**(10): p. 949-959.
- 17 409 11. Butowicz, C.M., C.L. Dearth, and B.D. Hendershot, *Impact of Traumatic Lower Extremity*
- 18 410 *Injuries Beyond Acute Care: Movement-Based Considerations for Resultant Longer Term*
- 19 411 *Secondary Health Conditions*. Advances in wound care, 2017. **6**(8): p. 269-278.
- 20 412 12. Wasser, J.G., et al., *Potential lower extremity amputation-induced mechanisms of chronic low*
- 21 413 *back pain: role for focused resistance exercise*. Disability and Rehabilitation, 2019: p. 1-9.
- 22 414 13. Spoden, M., U. Nimptsch, and T. Mansky, *Amputation rates of the lower limb by amputation*
- 23 415 *level – observational study using German national hospital discharge data from 2005 to 2015*.
- 24 416 *BMC Health Services Research*, 2019. **19**(1): p. 8.
- 25 417 14. Imam, B., et al., *Incidence of lower limb amputation in Canada*. Canadian Journal of Public
- 26 418 *Health*, 2017. **108**(4): p. 374-380.
- 27 419 15. Cox, P.S.L., W. SKP, and S. Weaver, *Life after lower extremity amputation in diabetics*. West
- 28 420 *indian medical journal*, 2011. **60**(5): p. 536-540.
- 29 421 16. Gailey, R., et al., *Review of secondary physical conditions associated with lower-limb*
- 30 422 *amputation and long-term prosthesis use*. Journal of Rehabilitation Research & Development,
- 31 423 2008. **45**(1).
- 32 424 17. Devan, H., et al., *Spinal, pelvic, and hip movement asymmetries in people with lower-limb*
- 33 425 *amputation: Systematic review*. Journal of Rehabilitation Research & Development, 2015. **52**:
- 34 426 p. 1+.
- 35 427 18. Sivapuratharasu, B., A.M.J. Bull, and A.H. McGregor, *Understanding Low Back Pain in*
- 36 428 *Traumatic Lower Limb Amputees: A Systematic Review*. Archives of Rehabilitation Research
- 37 429 *and Clinical Translation*, 2019. **1**(1): p. 100007.
- 38 430 19. Rosenberg, D.E., et al., *Body mass index patterns following dysvascular lower extremity*
- 39 431 *amputation*. Disability and Rehabilitation, 2013. **35**(15): p. 1269-1275.
- 40 432 20. Lementowski, P.W. and S.B. Zelicof, *Obesity and osteoarthritis*. American Journal of
- 41 433 *Orthopedics-Belle Mead*, 2008. **37**(3): p. 148.
- 42 434 21. Pezzin, L.E., et al., *Use and satisfaction with prosthetic limb devices and related services 11No*
- 43 435 *commercial party having a direct financial interest in the results of the research supporting*
- 44 436 *this article has or will confer a benefit on the author(s) or on any organization with which the*
- 45 437 *author(s) is/are associated*. Archives of Physical Medicine and Rehabilitation, 2004. **85**(5): p.
- 46 438 723-729.
- 47 439 22. Farrokhi, S., et al., *Biopsychosocial risk factors associated with chronic low back pain after*
- 48 440 *lower limb amputation*. Medical Hypotheses, 2017. **108**: p. 1-9.
- 49 441 23. Farrokhi, S., et al., *A Narrative Review of the Prevalence and Risk Factors Associated With*
- 50 442 *Development of Knee Osteoarthritis After Traumatic Unilateral Lower Limb Amputation*.
- 51 443 *Military Medicine*, 2016. **181**(suppl_4): p. 38-44.
- 52 444 24. Kulkarni, J., et al., *Chronic low back pain in traumatic lower limb amputees*. Clinical
- 53 445 *Rehabilitation*, 2005. **19**(1): p. 81-86.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 446 25. Oosterhoff, M., J.H.B. Geertzen, and P.U. Dijkstra, *More than half of persons with lower limb amputation suffer from chronic back pain or residual limb pain: a systematic review with meta-analysis*. Disability and Rehabilitation, 2020: p. 1-21.
- 447
448
449 26. van Eck, C.F. and R.L. McGough, *Clinical outcome of osseointegrated prostheses for lower extremity amputations: a systematic review of the literature*. Current Orthopaedic Practice, 2015. **26**(4).
- 450
451
452 27. Tomaszewski, P.K., et al., *Numerical analysis of an osseointegrated prosthesis fixation with reduced bone failure risk and periprosthetic bone loss*. Journal of Biomechanics, 2012. **45**(11): p. 1875-1880.
- 453
454
455 28. Devan, H., et al., *Asymmetrical movements of the lumbopelvic region: Is this a potential mechanism for low back pain in people with lower limb amputation?* Medical Hypotheses, 2014. **82**(1): p. 77-85.
- 456
457
458 29. Jackson, B.D., et al., *Reviewing knee osteoarthritis — a biomechanical perspective*. Journal of Science and Medicine in Sport, 2004. **7**(3): p. 347-357.
- 459
460 30. Morgenroth, D.C., A.C. Gellhorn, and P. Suri, *Osteoarthritis in the Disabled Population: A Mechanical Perspective*. PM&R, 2012. **4**(5, Supplement): p. S20-S27.
- 461
462 31. Highsmith, M.J., et al., *Low back pain in persons with lower extremity amputation: a systematic review of the literature*. The Spine Journal, 2019. **19**(3): p. 552-563.
- 463
464 32. Iijima, H., et al., *Biomechanical characteristics of stair ambulation in patients with knee OA: A systematic review with meta-analysis toward a better definition of clinical hallmarks*. Gait & Posture, 2018. **62**: p. 191-201.
- 465
466
467 33. Sagawa, Y., et al., *Biomechanics and physiological parameters during gait in lower-limb amputees: A systematic review*. Gait & Posture, 2011. **33**(4): p. 511-526.
- 468
469 34. Shamseer, L., et al., *Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation*. BMJ : British Medical Journal, 2015. **349**: p. g7647.
- 470
471
472 35. Prinsen, E.C., M.J. Nederhand, and J.S. Rietman, *Adaptation Strategies of the Lower Extremities of Patients With a Transtibial or Transfemoral Amputation During Level Walking: A Systematic Review*. Archives of Physical Medicine and Rehabilitation, 2011. **92**(8): p. 1311-1325.
- 473
474
475
476 36. Egloff, C., T. Hügler, and V. Valderrabano, *Biomechanics and pathomechanisms of osteoarthritis*. Swiss Medical Weekly, 2012. **142**(JULY).
- 477
478 37. Davis, E.M., et al., *Longitudinal evidence links joint level mechanics and muscle activation patterns to 3-year medial joint space narrowing*. Clinical Biomechanics, 2019. **61**: p. 233-239.
- 479
480 38. Laird, R.A., et al., *Comparing lumbo-pelvic kinematics in people with and without back pain: a systematic review and meta-analysis*. BMC musculoskeletal disorders, 2014. **15**: p. 229-229.
- 481
482 39. Vonville, H., *Excel workbooks for systematic reviews*. Available at: <https://www.dropbox.com/sh/2q9wh960zfdgc2e/AABc-MEceYIGQMnHwUT8ZWAga>, 2015.
- 483
484 40. Cohen, J., *A Coefficient of Agreement for Nominal Scales*. Educational and Psychological Measurement, 1960. **20**(1): p. 37-46.
- 485
486 41. Rohatgi, A. *WebPlotDigitizer - Version 4.5*. 2021; Available from: <https://automeris.io/WebPlotDigitizer>.
- 487
488 42. Hendershot, B.D. and E.J. Wolf, *Three-dimensional joint reaction forces and moments at the low back during over-ground walking in persons with unilateral lower-extremity amputation*. Clinical Biomechanics, 2014. **29**(3): p. 235-242.
- 489
490
491 43. Morgenroth, D.C., et al., *The Relationship Between Lumbar Spine Kinematics during Gait and Low-Back Pain in Transfemoral Amputees*. American Journal of Physical Medicine & Rehabilitation, 2010. **89**(8): p. 635-643.
- 492
493
494 44. Cindy Ng, L.W., et al., *Does exercise training change physical activity in people with COPD? A systematic review and meta-analysis*. Chronic Respiratory Disease, 2011. **9**(1): p. 17-26.
- 495

- 1
2
3 496 45. Downs, S.H. and N. Black, *The feasibility of creating a checklist for the assessment of the*
4 497 *methodological quality both of randomised and non-randomised studies of health care*
5 498 *interventions*. Journal of Epidemiology and Community Health, 1998. **52**(6): p. 377-384.
6 499 46. Page, M.J., et al., *PRISMA 2020 explanation and elaboration: updated guidance and exemplars*
7 500 *for reporting systematic reviews*. BMJ, 2021. **372**: p. n160.

9 501

10 502

11
12
13
14
15 503 Figure Legend

16
17
18 504 Figure 1: Flow chart of paper selection. Exclusion reasons are: 1) no amputees, 2) upper limb amputation,
19
20 505 3) no adult human participants, 4) language not English, 5) review, 6) no quantitative data, 7) paper not
21
22 506 found/duplicate, 8) no clinical outcomes, 9) single case study), 10) no results for separate amputee groups,
23
24 507 11) no biomechanical parameters, 12) powered prosthesis only.

25
26
27 508
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

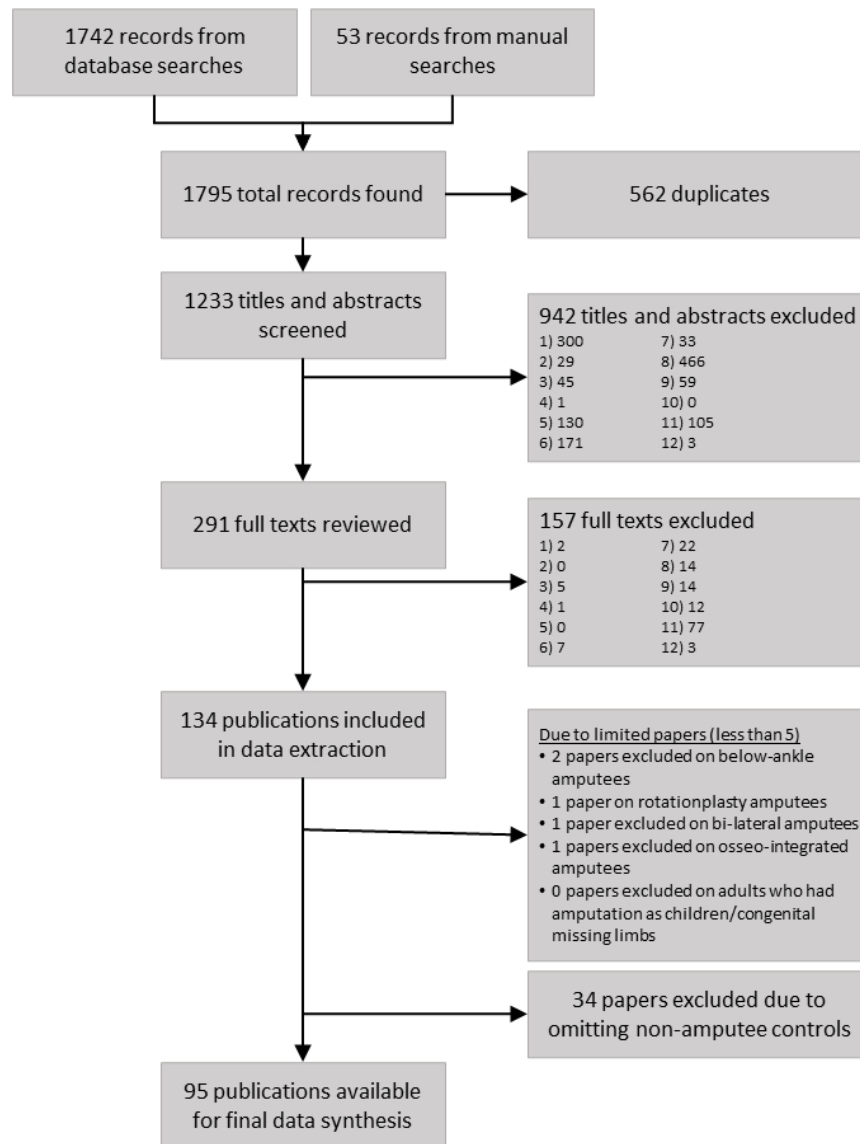


Figure 1: Flow chart of paper selection. Exclusion reasons are: 1) no amputees, 2) upper limb amputation, 3) no adult human participants, 4) language not English, 5) review, 6) no quantitative data, 7) paper not found/duplicate, 8) no clinical outcomes, 9) single case study, 10) no results for separate amputee groups, 11) no biomechanical parameters, 12) powered prosthesis only.

190x250mm (96 x 96 DPI)

Appendix 1: Search strategies for each of the five databases used in this systematic review

Database	keywords
Web of Science	TS=("transtibial amput*" OR "transfemoral amput*" OR amput* OR "Lower limb amput*" OR "Lower extremity amput*" OR "Leg prosthesis") AND TS=(walking OR running OR gait OR locomotion OR biomechanics OR kinematics OR kinetics OR "biomechanical parameter*" OR *symmetr* OR forc* OR angle* OR moment* OR power OR EMG OR electromyogra*) AND TS=(Osteoporosis OR Osteopenia OR "Back Pain" OR Backache OR Osteoarthritis OR "musculoskeletal diseases*" OR "musculoskeletal condition*" OR "secondary diseases*") Limited from 2017-2019
Scopus	(TITLE-ABS-KEY ("transtibial amput*" OR "transfemoral amput*" OR amput* OR "Lower limb amput*" OR "Lower extremity amput*" OR "Leg prosthesis") AND TITLE-ABS-KEY (walking OR running OR gait OR locomotion OR biomechanics OR kinematics OR kinetics OR "biomechanical parameter*" OR *symmetr* OR forc* OR angle* OR moment* OR power OR emg OR electromyogra*) AND TITLE-ABS-KEY (osteoporosis OR osteopenia OR "Back Pain" OR backache OR osteoarthritis OR "musculoskeletal diseases*" OR "musculoskeletal condition*" OR "secondary diseases*")) AND (LIMIT-TO (LANGUAGE , "English") OR LIMIT-TO (LANGUAGE , "German") OR LIMIT-TO (LANGUAGE , "Italian")) AND (LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017))
Pubmed	((("Amputees"[Mesh] OR "Amputation"[Mesh] OR Amput* OR "Amputation, Traumatic"[Mesh] OR "Amputation, Congenital" [Supplementary Concept] OR "lower limb amputation" OR "lower limb amputee" OR "lower extremity amputee" OR "Artificial Limb"[Mesh]) AND ("Walking"[Mesh] OR "Running"[Mesh] OR "Gait"[Mesh] OR gait OR "Locomotion"[Mesh] OR Locomotion OR "Biomechanical Phenomena"[Mesh] OR biomechanic* OR biomechanical parameter*" OR symmetr* OR angle OR angles OR force OR "Ground Reaction forces" OR power OR "kinetics"[Mesh] OR "Kinematics"[Mesh] OR kinetic* OR kinematic* OR EMG) AND ("Osteoarthritis"[Mesh] OR "osteoporosis"[Mesh] OR osteopenia OR "Back Pain"[Mesh] OR backache OR "musculoskeletal disease*" [Mesh] OR "secondary diseases*" OR "secondary condition" OR "knee osteoarthritis" OR "hip osteoarthritis")))) AND ("2017/07/05"[Date - Publication] : "2019/05/06"[Date - Publication])
Embase	Option A ('transtibial amputation'/exp OR 'transtibial amputation' OR 'transfemoral amputation'/exp OR 'transfemoral amputation' OR 'amputee'/exp OR 'amputee' OR 'amputees'/exp OR 'amputees' OR 'individual with amputation'/exp OR 'individual with amputation' OR 'person with amputation'/exp OR 'person with amputation' OR 'artificial leg'/exp OR 'artificial leg' OR 'artificial legs'/exp OR 'artificial legs' OR 'leg prostheses'/exp OR 'leg prostheses' OR 'leg prosthesis'/exp OR 'leg prosthesis' OR 'leg prosthetics'/exp OR 'leg prosthetics' OR 'leg, artificial'/exp OR 'leg, artificial'

	<p>OR 'legs, artificial'/exp OR 'legs, artificial' OR 'lower extremity prosthesis'/exp OR 'lower extremity prosthesis' OR 'lower limb prostheses'/exp OR 'lower limb prostheses' OR 'lower limb prosthesis'/exp OR 'lower limb prosthesis' OR 'prostheses, leg'/exp OR 'prostheses, leg' OR 'prosthesis, leg'/exp OR 'prosthesis, leg' OR 'walking prosthesis'/exp OR 'walking prosthesis' OR 'amputation, traumatic'/exp OR 'amputation, traumatic' OR 'traumatic amputation'/exp OR 'traumatic amputation' OR 'congenital amputation'/exp OR 'congenital amputation') AND ('walking'/exp OR 'walking' OR 'runner'/exp OR 'runner' OR 'running'/exp OR 'running' OR 'kinematics'/exp OR 'kinematics' OR 'human kinetics'/exp OR 'human kinetics' OR 'kinetic analysis'/exp OR 'kinetic analysis' OR 'kinetic mechanism'/exp OR 'kinetic mechanism' OR 'kinetic model'/exp OR 'kinetic model' OR 'kinetics'/exp OR 'kinetics' OR 'biomechanical phenomena'/exp OR 'biomechanical phenomena' OR 'biomechanical phenomenon'/exp OR 'biomechanical phenomenon' OR 'biomechanics'/exp OR 'biomechanics' OR 'biomechanism'/exp OR 'biomechanism' OR 'behavior, locomotor'/exp OR 'behavior, locomotor' OR 'behaviour, locomotor'/exp OR 'behaviour, locomotor' OR 'locomotion'/exp OR 'locomotion' OR 'locomotion pattern'/exp OR 'locomotion pattern' OR 'locomotor activity'/exp OR 'locomotor activity' OR 'locomotor response'/exp OR 'locomotor response' OR 'biped gait'/exp OR 'biped gait' OR 'gait'/exp OR 'gait' OR 'gait analysis'/exp OR 'gait analysis' OR 'gait training'/exp OR 'gait training' OR 'pattern, walking'/exp OR 'pattern, walking' OR 'walking pattern'/exp OR 'walking pattern') AND ('decalcification, pathologic'/exp OR 'decalcification, pathologic' OR 'endocrine osteoporosis'/exp OR 'endocrine osteoporosis' OR 'osteoporosis'/exp OR 'osteoporosis' OR 'osteoporotic decalcification'/exp OR 'osteoporotic decalcification' OR 'osteoarthritis'/exp OR 'osteoarthritis' OR 'back ache'/exp OR 'back ache' OR 'back pain'/exp OR 'back pain' OR 'back pain syndrome'/exp OR 'back pain syndrome' OR 'backache'/exp OR 'backache' OR 'backpain'/exp OR 'backpain' OR 'dorsalgia'/exp OR 'dorsalgia' OR 'pain, back'/exp OR 'pain, back' OR 'musculoskeletal disease'/exp OR 'musculoskeletal disease' OR 'secondary disease'/exp OR 'secondary disease') AND [3-7-2017]/sd NOT [3-5-2019]/sd</p>
CINAHL	<p>OPTION A: Straight search of terms (no subheading selection)</p> <p>("transtibial amput*" OR "transfemoral amput*" OR amput* OR "Lower limb amput*" OR "Lower extremity amput*" OR "Leg prosthesis")</p> <p>AND</p> <p>("Walking" OR "Running" OR "Gait" OR gait OR "Locomotion" OR Locomotion OR "Biomechanical Phenomena" OR biomechanic* OR "biomechanical parameter*" OR symmetr* OR angle OR angles OR force OR "Ground Reaction forces" OR power OR "kinetics" OR "Kinematics" OR kinetic* Or kinematic OR "EMG" OR electromyog)</p> <p>AND</p>

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

	(“Osteoarthritis” OR “osteoporosis” OR osteopenia OR “Back Pain” OR backache OR “musculoskeletal disease*” OR “secondary diseas*” OR “secondary condition” OR “knee osteoarthritis” OR “hip osteoarthritis”)
--	--

For peer review only

Appendix 2: Outcome variable to be extracted from experimental studies

Temporospatial	Kinematics		Kinetics	
BMI	Knee adduction range of motion (ROM)	Knee	Peak knee adduction moment (KAM)	Knee
Walking speed	Knee sagittal ROM		KAM loading rate (rate of force development)	
Stride width (from midline)	Hip-knee-ankle adduction angle		KAM impulse	
Stride/step length/symmetry	Varus/valgus angle - knee adduction angle		Peak knee joint contact forces	
Stance/contact time	Knee flexion at heel strike		Joint reaction force at terminal stance	
Leg length discrepancy	Knee flexion at toe off		Peak knee sagittal/flexion/extension plane moments	
Cadence		Knee rotation moment early stance		
		Knee flexion moment at loading response		
Ground Reaction Force (GRF)	Peak hip extension	Hip	Flexion moment at terminal stance	Knee
Vertical GRF at heel strike	Peak hip flexion angle		Net work	
Horizontal GRF at heel strike	Hip flexion at toe off		Positive work	
Vertical GRF loading rate	Hip ROM sagittal		Negative work	
Prosthetic horizontal GRF at push-off	Hip flexion at loading response			
Peak vertical GRF			Peak hip extension moment	
	Peak trunk flexion angle	Trunk/Pelvis		Trunk/Pelvis
	Peak lumbar spine extension		Lumbar-pelvic lateral joint reaction force	
	Lumbar-pelvis spine extension		Anterior lateral joint reaction force - lumbar-pelvic	
	Peak coronal/frontal/lateral/contralateral pelvic tilt		Mediolateral shear joint reaction force of trunk	
	Peak anterior-posterior/sagittal pelvic tilt		Anterior-posterior shear joint reaction force of trunk	
	Pelvic ROM in frontal plane		Compression joint reaction force forces of trunk	
	Pelvic ROM in sagittal plane		Lumbar/pelvic joint power	
	Lumbar transverse plane rotation ROM		Lower back joint contact force	
	Sagittal plane pelvis angle		Joint work L5/S1 (frontal and sagittal plane)	
	Side flexion of trunk-pelvis			
	Mediolateral trunk sway			
	Lumbar lordosis angle			

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Completed
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Yes
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Yes
Sponsor	5b	Provide name for the review funder and/or sponsor	Yes
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits such that it could be repeated	Yes

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Yes
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently in duplicate), any processes for obtaining and confirming data from investigators	Yes
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Yes
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Yes
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	Yes
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I ² , Kendall's τ)	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	N/A
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	N/A
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	Yes

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

BMJ Open

Biomechanical risk factors for knee osteoarthritis and lower back pain in lower limb amputees: protocol for a systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-066959.R1
Article Type:	Protocol
Date Submitted by the Author:	03-Nov-2022
Complete List of Authors:	Wade, Logan; University of Bath, Department for Health McGuigan, M. Polly; University of Bath, Department for Health McKay, Carly; University of Bath, Department for Health Bilzon, James; University of Bath, Department for Health Seminati, Elena; University of Bath, Department for Health
Primary Subject Heading:	Research methods
Secondary Subject Heading:	Sports and exercise medicine, Research methods, Reproductive medicine
Keywords:	Diabetic nephropathy & vascular disease < DIABETES & ENDOCRINOLOGY, REHABILITATION MEDICINE, SPORTS MEDICINE

SCHOLARONE™
Manuscripts

BIOMECHANICAL RISK FACTORS FOR KNEE OSTEOARTHRITIS AND LOWER BACK PAIN IN LOWER LIMB AMPUTEES: PROTOCOL FOR A SYSTEMATIC REVIEW

Logan Wade^{a,b}, M. Polly McGuigan^{a,b}, Carly McKay^{a,c,d}, James Bilzon^{a,b,d}, Elena Seminati^{a,b}

a) Department for Health, University of Bath, Bath UK

b) Centre for Analysis of Motion, Entertainment Research and Applications, University of Bath, United Kingdom

c) Centre for Health and Illness and Injury Prevention in Sport, University of Bath, Bath UK

d) Centre for Sport Exercise and Osteoarthritis Research Versus Arthritis, University of Bath, Bath UK

Corresponding Author:

Logan Wade

lw2175@bath.ac.uk

University of Bath

1 West, Office 5.111, Bath, BA2 7AY, United Kingdom

Email:

Logan Wade - lw2175@bath.ac.uk, M. Polly McGuigan - mpm21@bath.ac.uk, Carly McKay - cdm47@bath.ac.uk, James Bilzon - jb438@bath.ac.uk, Elena Seminati - es685@bath.ac.uk

Registration

In accordance with guidelines, this protocol was submitted and approved with the International Prospective Register of Systematic reviews (PROSPERO) on 03/02/2020 and was last updated 21/01/2022 (ID: CRD42020158247).

1
2
3 28
4
5 29
6
7
8 30
9
10 31
11
12
13 32
14
15 33
16
17 34
18
19 35
20
21 36
22
23 37
24
25 38
26
27 39
28
29
30 40
31
32 41
33
34 42
35
36 43
37
38 44
39
40 45
41
42 46
43
44 47
45
46 48
47
48 49
49
50 50
51
52 51
53
54 52
55
56 53
57
58 54
59
60 55

Abstract

Introduction: There is limited research exploring biomechanical risk factors for the development of knee osteoarthritis (KOA) and lower back pain (LBP) between lower limb amputee sub-groups, [e.g., transtibial amputees (TTA) vs transfemoral amputees (TFA), or TTA dysvascular vs TTA traumatic]. Previous reviews have focussed primarily on studies where symptoms of KOA or LBP are present, however, due to limited study numbers, this hinders their scope and ability to compare between amputee sub-groups. Therefore, the aim of this systematic review is to descriptively compare biomechanical risk factors for developing KOA and LBP between lower limb amputee sub-groups, irrespective of whether KOA or LBP was present.

Methods and analysis: This review is currently in progress and screening results are presented alongside the protocol to highlight challenges encountered during data extraction. Five electronic databases were searched (Medline – Web of Science, PubMed, CINAHL, Embase and Scopus). Eligible studies were observational or interventional, reporting biomechanical gait outcomes for individual legs in adult lower limb amputees during flat walking, incline/decline walking or stair ascent/descent. Two reviewers screened for eligibility and level of agreement was assessed using Cohen’s Kappa. Data extraction is ongoing. Risk of bias will be assessed using a modified Downs and Black method, and outcome measures will be descriptively synthesised.

Ethics and dissemination: There are no ethical considerations for this systematic review. Due to its scope, results are expected to be published in three separate manuscripts: 1) Biomechanical risk factors of KOA between TTA and TFA, relative to non-amputees, 2) Biomechanical risk factors of LBP between TTA and TFA, relative to non-amputees, and 3) Biomechanical risk factors of KOA and LBP between transtibial amputees with traumatic or dysvascular causes, relative to non-amputees.

PROSPERO registration number: CRD42020158247).

1
2
3 54
4
5
6
7 55
8
9 56
10
11 57
12
13 58
14
15 59
16
17 60
18
19 61
20
21 62
22
23 63
24
25
26 64
27
28
29
30 65
31
32 66
33
34 67
35
36 68
37
38 69
39
40 70
41
42 71
43
44 72
45
46 73
47
48 74
49
50 75
51
52 76
53
54 77
55
56 78
57
58 79
59
60

Strength and Limitations

- This systematic review protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines.
- Biomechanical gait will be compared between amputee sub-groups (transtibial vs transfemoral amputees, and transtibial dysvascular vs transtibial traumatic amputees).
- Studies must include at least one temporospatial, joint kinematic or joint kinetic outcome measure for individual legs.
- Only amputee studies that included non-amputee controls will be included in the systematic review.

Introduction

Lower limb amputations of the hip, knee and ankle considerably alter walking gait and function, with over 42 000 major lower limb amputations performed over a ten year period (2003-2013) in the UK ¹. In 2005, major lower limb amputations in the USA and UK accounted for over 90% of all major limb amputations ², ³ and compared to healthy populations, lower-limb amputees have significantly higher rates of secondary disorders such as knee osteoarthritis ^{4, 5} and lower back pain ⁶⁻¹¹. While there are many biopsychosocial factors that may contribute to the higher rates of secondary disorders, (e.g. mental health, diet, access to facilities or social organisations), the biomechanical factors which result in altered gait of amputee populations will potentially also play a major role ¹². Stable lower limb amputee gait often requires the intact leg to support greater load, which introduces gait asymmetries that over the lifetime, may result in overuse and greater wear of joints and muscles compared to non-amputees. Furthermore, differences between amputation levels (below ankle, below knee and above knee) and amputation causes (traumatic, vascular disease, cancer, congenital) may produce different functional impairments, which could increase the risk of developing knee osteoarthritis (KOA) and lower back pain (LBP) in these different amputee populations.

1
2
3 80
4
5

6 81 Considering the prevalence of lower limb amputations, transfemoral (above the level of the knee)
7
8 82 amputees (TFA) and through knee (at the level of the knee joint) amputees account for 17-23% of all
9
10 83 amputations^{13,14}. Transtibial (below the level of the knee) amputees (TTA) and through ankle (at the level
11
12 84 of the ankle joint) amputees account for 12-32%, while partial foot amputees account for 15-26% of all
13
14 85 amputations^{13,14}. Minor amputations of the foot make up the remaining percentages, however these
15
16 86 generally do not substantially alter gait and are therefore not a focus of this review. As amputation level
17
18 87 moves up the leg, functional mobility and quality of life is reduced¹⁵, requiring greater altered gait
19
20 88 mechanics to accommodate the limited power output and instability of the prosthetic limb during stance
21
22 89¹². Thus, above knee amputees are at an increased risk of developing knee pain⁴ and KOA in the intact limb
23
24 90 compared to below knee amputees, with OA of the intact knee occurring in roughly 60% of TFAs and 40%
25
26 91 of TTAs, compared to just 20% of non-amputees¹⁶. Similarly, prevalence of LBP is found in roughly 50-76%
27
28 92 of lower limb amputees, compared to 35% of non-amputees¹⁰⁻¹². Evidence suggests that there may not be
29
30 93 a difference in prevalence or intensity of LBP between TTA and TFA¹⁷, although a previous systematic
31
32 94 review of LBP in lower limb amputees was unable to draw comparisons between TTA and TFA due to limited
33
34 95 studies in TTA¹⁸. Thus, there is a need to explore biomechanical gait differences between TTAs and TFAs,
35
36 96 to understand how biomechanical risk factors associated with the development of and potential
37
38 97 predisposition to KOA and LBP differ between groups.
39
40
41
42
43 98

44
45 99 While amputation level plays a crucial role in altered gait mechanics, cause of amputation likely also
46
47 100 contributes significantly to the development of secondary musculoskeletal symptoms. The two primary
48
49 101 causes of amputation are vascular diseases and traumatic accidents, with cancer and congenital causes
50
51 102 only making up 1-3% of all amputations^{3,14}. Prevalence of amputation cause varies worldwide, with
52
53 103 traumatic amputations making up 6 - 45% of all amputations^{3,14} and patients primarily characterised as
54
55 104 being young and fit³. Alternatively, dysvascular amputations have increased significantly in recent decades
56
57 105 due to the increasing prevalence of diabetes and dysvascular disease, making up 65%-91% of all
58
59
60

1
2
3 106 amputations^{3,14}. This population is generally older than other amputee cause types³ and commonly have
4
5 107 a higher body mass index¹⁹, which additionally puts individuals at a greater risk of KOA²⁰. Dysvascular
6
7 108 amputees also have poorer uptake of prosthetic devices, which further increases their risk of sedentary
8
9 109 lifestyle and weight gain after amputation²¹. Counterintuitively, some research suggests that this lower
10
11 110 activity status and prosthetic use may result in TFAs having a reduced risk of developing LBP compared to
12
13 111 traumatic amputees^{16,18}. Unfortunately, despite a much higher prevalence of dysvascular amputations,
14
15 112 gait biomechanics research within this population is relatively limited, especially compared to the high
16
17 113 proportion of research surrounding traumatic amputations^{4,11,18,22-25}. We therefore need to determine
18
19 114 whether current research, investigating the development of secondary disorders primarily in traumatic
20
21 115 amputees, is generalisable to dysvascular amputees, and if there are any additional biomechanical factors
22
23 116 specific to dysvascular amputees that would increase or decrease their likelihood of developing KOA and
24
25 117 LBP.
26
27
28
29
30
31

32 119 Additional sub-groups include bi-lateral amputees, osseo-integrated amputees and adult amputees who
33
34 120 had an amputation as children or were born without a limb (i.e. congenital amputees). Bilateral amputees
35
36 121 have a high variation between individuals, often presenting with multiple amputation levels (e.g. one leg
37
38 122 with a trans-tibial amputation and the other with a trans-femoral amputation), which can dramatically alter
39
40 123 gait and may influence development of secondary disorders. Osseo-integrated amputees generally do not
41
42 124 suffer from skin problems, ill-fitting prosthesis issues or bone degeneration issues of their socket wearing
43
44 125 counterparts. Thus, this population may have greater prosthetic use and increased risk of KOA and LBP,
45
46 126 although they also have alternate complications such a recurring infections and risk of bone fractures^{26,27}.
47
48 127 Finally, adult amputees who experienced amputations during childhood, or were congenital amputees,
49
50 128 have spent the most time with their amputation. This group may have altered gait patterns as a function
51
52 129 of growing with their prosthesis, which may place them at an increased risk of developing secondary
53
54 130 symptoms much earlier in life. Across all amputee sub-groups, the primary barrier to understanding altered
55
56 131 biomechanical gait is in recruiting a sufficient sample from each population, especially in these latter
57
58 132 specialised sub-groups. Furthermore, longitudinal cohort studies, following patients throughout their life
59
60

1
2
3 133 are very rare, with most studies being performed cross-sectionally. Therefore, a large-scale systematic
4
5 134 review that examines biomechanical gait between amputee sub-groups is presently the best available
6
7 135 option for exploring which biomechanical gait factors may contribute to development of KOA or LBP
8
9 136 between lower limb amputee populations.
10

11
12 137
13
14

15 138 Several reviews have examined amputee biomechanical gait with a focus on KOA and LBP. However, the
16
17 139 majority of these reviews have not been performed using systematic methods ^{11, 22, 23, 28-30}, and generally
18
19 140 have not described differences between amputee sub-groups, often only including a single sub-group (e.g.
20
21 141 only traumatic or transtibial amputees). Moreover, those few systematic reviews on gait and secondary
22
23 142 disorders in amputees have generally only been performed on a single amputee subgroup, using studies
24
25 143 where symptoms of KOA or LBP are present, which severely limits their scope (11-17 studies per review)
26
27 144 and ability to compare between amputee groups ^{16, 18, 31, 32}. Due to such small study numbers included
28
29 145 within these systematic reviews, knowledge of the biomechanical gait characteristics associated with KOA
30
31 146 and LBP and their prevalence between amputee sub-groups is considerably limited. Sagawa, Turcot ³³ has
32
33 147 performed a large-scale systematic review (89 studies) of altered biomechanical gait factors across all lower
34
35 148 limb amputees, aiming to broadly characterise biomechanics and physiological parameters during gait.
36
37 149 They identified that TTA knee flexion during heel strike is limited to 9-12°, while TFA knee flexion was zero
38
39 150 or negative (extension). Additionally, TFAs had twice the pelvic ROM compared to healthy individuals which
40
41 151 may contribute to the development of LBP. Unfortunately, their review was very broad, was not targeted
42
43 152 at gait characteristics of KOA and LBP and generally did not make any comparisons or conclusions between
44
45 153 sub-groups (e.g., amputation level or amputation cause). To fill this gap in the literature, a large-scale
46
47 154 systematic review targeted at identifying how biomechanical risk factors of KOA and LBP differ between
48
49 155 amputee sub-groups is needed. Understanding what biomechanical factors influence gait will help facilitate
50
51 156 specific and personalised rehabilitation programmes and prosthetic designs.
52
53
54
55

56 157
57
58
59
60

OBJECTIVES

While previous systematic reviews have been limited by only including studies with amputees who are diagnosed with KOA and LBP, there is a substantial amount of experimental literature that has examined lower limb amputee gait and posture where no KOA or LBP has been recorded. Because of the high prevalence of KOA and LBP, it is likely that biomechanical abnormalities leading to these secondary disorders will be present across the majority of amputees. Therefore, the aim of this systematic review is to descriptively compare biomechanical risk factors for developing KOA and LBP between amputee sub-groups, irrespective of whether KOA or LBP was present. Amputee sub-groups will be categorised by level of amputation (below ankle, below knee and above knee), cause of amputation (vascular disease, traumatic injury, cancer, congenital) and special sub-groups (bilateral amputees, osseo-integrated amputees, adult amputees who had an amputation or congenital missing limb as children. Individual sub-groups will only be included for analysis if sufficient data is available to support comparisons (see data extraction section).

Methods

This systematic review is currently in progress with the first search complete on 03/07/2017 and a projected end date of 01/12/2023. Screening results are presented within this paper to highlight challenges encountered during data extraction. This approach was chosen to ensure the transparency of our methods and increase the replicability of the review.

ELIGIBILITY CRITERIA

In accordance with PRISMA-P guidelines³⁴, this protocol was submitted and approved by the International Prospective Register of Systematic reviews (PROSPERO) on 03/02/2020 and was last updated 21/01/2022 (ID: CRD42020158247). This protocol has adhered to the PRISMA-P guide and checklist for publishing systematic review protocols³⁴.

STUDY CHARACTERISTICS

Studies included in this review had to be observational studies such as cross-sectional/cohort studies and longitudinal studies. Intervention and randomised control trial (RCT) studies were included in this review but only the control amputee group or baseline measures were extracted (observational data). Review papers, case studies, conference proceedings and animal studies were excluded. Studies that included quantitative biomechanical measures of lower limb amputees were included if results were reported for individual legs (intact leg and prosthetic leg presented separately). To ensure application of valid and thorough biomechanical technique and analysis, data had to include at least one temporospatial, joint kinematic or joint kinetic outcome measure for individual legs (see Appendix 1 for a full list of extracted outcome measures). Outcome variables were determined from previous reviews that outlined biomechanical differences between: amputees and non-amputee populations^{12, 17, 22, 23, 28, 33, 35}; healthy non-amputee populations and KOA and LBP non-amputee populations³⁶⁻³⁸; and healthy amputees and amputees with KOA and LBP^{12, 16, 18, 31, 32}. While ground reaction force (GRF) outcome measures for individual strides were extracted, studies that only reported GRF measures were not included in this review, as GRF is a measure of full body force and is not specific to the knee joint or lower back region. Observational studies had to be performed during walking on flat, incline or stair surfaces, at either preferred or controlled walking speeds. Studies that only investigated running-specific prostheses or running gaits were not included. Studies that examined powered ankles were included in this review, but only if an unpowered condition was performed. All microprocessor-controlled ankles and knees (devices that do not add energy to the system) were included in this review.

PARTICIPANTS

Lower limb amputees were included in this review, but only if results were separated by different amputation levels (e.g., studies that combined results of transtibial and transfemoral amputees were not included). Due to the differences between child and adult gait, and the focus on development of secondary disorders which primarily occurs in adults, studies performed only on children (younger than 18 years) were not included.

210

211 PATIENT AND PUBLIC INVOLVEMENT

212 None

213

214 INFORMATION SOURCES

215 Literature searches were performed across five databases: Medline – Web of Science, PubMed, CINAHL,
216 Embase and Scopus. Manual searches were conducted using the reference lists within previous reviews
217 and reference lists within papers obtained from database searches, to ensure all relevant literature was
218 identified (Figure 1).

219

220 SEARCH STRATEGY

221 Studies were only examined if they were published in English. Only peer-reviewed studies were included.
222 No publication date limit was imposed on the search criteria. Search terms included a combination of
223 amputation terms AND gait/biomechanics terms AND secondary disorders. While inclusion for this
224 systematic review did not require the presence of secondary disorders, this term helped to refine the
225 search and identify papers with outcome measures of relevance to the development of secondary
226 disorders in amputee populations. An example search strategy is presented below and a table of the full
227 search strategy, formatted for each database, can be found in Appendix 2.

- 228 1) Amputee: "transtibial amput*" OR "transfemoral amput*" OR amput* OR "Lower limb amput*"
229 OR "Lower extremity amput*" OR "Leg prosthesis"
- 230 2) Activity: walking OR running OR gait OR locomotion OR biomechanics OR kinematics OR kinetics
231 OR "biomechanical parameter*" OR *symmetr* OR forc* OR angle* OR moment* OR power EMG
232 OR electromyogra*)
- 233 3) Secondary disorder: Osteoporosis OR Osteopenia OR "Back Pain" OR Backache OR Osteoarthritis
234 OR "musculoskeletal diseas*" OR "musculoskeletal condition*" OR "secondary diseas*

1
2
3
4 2355
6 236 **DATA MANAGEMENT AND SELECTION PROCESS**

7 237 Records retained for abstract and full paper screening were compiled using an excel spreadsheet designed
8
9 238 for systematic reviews³⁹. Two reviewers individually applied the eligibility criteria to all records based on
10
11 239 the inclusion/exclusion criteria outlined in Figure 1. Where conflicts arose, reviewers met to discuss and if
12
13 240 agreement still could not be made, a third reviewer was consulted to make the final decision. Review stages
14
15 241 progressed from title and abstract review to full paper review (Figure 1). For the title and abstract stage,
16
17 242 there were four reviewers, with one person reviewing all papers and the remaining three people each
18
19 243 reviewing a third of the papers. For the full paper stage, there were three reviewers, with one person
20
21 244 reviewing all papers and the remaining two people reviewing half of the papers each. Level of agreement
22
23 245 was assessed using Cohens Kappa⁴⁰. Agreement for the title and abstract review stage was 0.76, while
24
25 246 agreement for the full paper review stage was 0.64, where agreement between 0.61-0.80 represents
26
27 247 substantial agreement between reviewers. A minimum of five studies that evaluated a specific sub-group
28
29 248 were required to be included for evaluation of said sub-group within this systematic review. Due to a
30
31 249 limited number of papers included after full text review, studies that examined below ankle amputation (2
32
33 250 papers), rotationplasty amputation (1 paper), bi-lateral amputation (1 paper), osseo-integration (1
34
35 251 papers), and adult amputees who had an amputation or congenital missing limb as children (0 papers) were
36
37 252 ultimately excluded.

38
39
40
41
42 25343
44
45 25446
47
48 255 **CURRENT STAGE**

49 256 This systematic review is currently at the stage of performing data extraction.
50
51
52
53 257

54
55
56 258 **DATA COLLECTION PROCESS**

57 259 Data is currently being extracted from studies using a standardised excel spreadsheet. All data are being
58
59 260 extracted by a single reviewer to ensure consistency, though a random sample of 20% of the data are also

1
2
3 261 being extracted by a second reviewer to assess the risk of bias in the extraction process. Where necessary,
4
5 262 extraction from figures is being performed using the desktop version of WebPlotDigitizer ⁴¹, which is a
6
7 263 data extraction tool for plots, images and maps.
8
9

10 264

13 265 DATA ITEMS

15 266 Data items being extracted include manuscript title, authors, journal, year, country where data was
16
17 267 collected, study type, amputee population, number of participants, amputation level, age, biological sex,
18
19 268 body mass, height, time since amputation, cause of amputation, type of prosthetic, years of prosthetic use,
20
21 269 secondary symptoms, tasks performed in the study and outcome variables (temporospatial, joint
22
23 270 kinematics and joint kinetics). For a detailed list of all biomechanical outcome variables, see Appendix 1.
24
25 271 Mean/median values, along with standard deviation/ranges are being extracted. For intervention studies,
26
27 272 only the baseline measure will be extracted, thus all data included within this review will be observational
28
29 273 and cross-sectional in nature.
30
31

32 274

33 275

34
35
36
37
38 276 During data extraction, it has become evident that some outcome measures may appear very high or very
39
40 277 low for both amputee and non-amputee groups within the same study. For example, Hendershot and Wolf
41
42 278 ⁴² examined trunk angle during walking gait using inverse dynamics, identifying that maximum extension
43
44 279 for TTA was 4.89°, TFA was 0.48° and non-amputee controls were 2.75°. Morgenroth, Orendurff ⁴³ also
45
46 280 examined trunk angle during walking, however their analysis was based on angle changes of a rigid cluster
47
48 281 placed on the 8th thoracic vertebra (T8), with angles relative to the global coordinate system. Thus, they
49
50 282 reported that maximum trunk extension of TFA was 26.9° while non-amputee controls were 20.5°. If
51
52 283 absolute values were compared, the large maximum angles obtained for TTA's by Morgenroth, Orendurff
53
54 284 ⁴³ would drastically alter the differences observed between TTA and TFA across all studies. Therefore,
55
56 285 studies which did not examine paired amputee groups (TTA vs TFA or Vascular vs Traumatic) have the
57
58 286 potential to drastically alter the results, due to methodological differences in how data were collected.
59
60

1
2
3 287 However, if studies recruited both amputees and non-amputees, relative differences compared to non-
4
5 288 amputees within the same study could be calculated. Using the example above for Hendershot and Wolf
6
7 289 ⁴², relative maximum trunk angle in TTA was 2.1° larger than non-amputee controls and TFA was 2.3°
8
9 290 smaller than non-amputee controls, while Morgenroth, Orendurff ⁴³ observed TFA was 6.4° larger than
10
11 291 non-amputee controls. Unfortunately, if studies only recruited amputees and did not recruit non-amputee
12
13 292 controls, calculation of relative differences between amputees and non-amputees cannot be calculated.
14
15 293 The diverse range of methodologies included within this review was unexpected and only determinable
16
17 294 due to this systematic review collating the largest number of biomechanical gait studies performed on
18
19 295 amputees to date. Therefore, to ensure rigorous and objective comparison of outcomes between amputee
20
21 296 sub-groups, we have removed 27 studies from screening that did not recruit non-amputee controls (Figure
22
23 297 1), excepting those studies that compared directly between TTA and TFA, or between dysvascular TTA and
24
25 298 traumatic TTA. Challenges we are facing during data extraction highlight the key role non-amputee controls
26
27 299 play during examination of amputee gait, and therefore, studies wishing to compare their results to prior
28
29 300 research should recruit non-amputee participants to facilitate such comparisons.
30
31
32
33
34 301

37 302 FUTURE STAGES

38 303 All remaining stages of the protocol encompass the future work yet to be started, with major stages
39
40 304 including risk of bias assessment and data synthesis.
41
42
43
44 305

47 306 OUTCOMES AND PRIORITISATION

48 307 The primary outcomes will be the biomechanical variables listed in Appendix 1. Reporting of outcome
49
50 308 measures will be grouped based on whether previous evidence suggests they may contribute to KOA or
51
52 309 LBP. Kinetic measures not already normalised to body mass will be converted to enable comparison
53
54 310 between studies. Mean/median outcome measures, relative to controls within the same study, will be
55
56 311 compared between amputee groups (TTA vs TFA and Traumatic vs Dysvascular). To directly compare
57
58 312 outcome measures between studies for KOA or LBP, measures will be grouped depending on the type of
59
60

1
2
3 313 movement: preferred speed flat walking, controlled speed flat walking, preferred speed incline/decline
4
5 314 walking, controlled speed incline/decline walking, preferred speed stair climbing or controlled speed stair
6
7 315 climbing. These movements were selected as they are commonly performed in daily living and present
8
9 316 different challenges for amputees. Thus, to examine differences between amputation level, outcome
10
11 317 measures related to KOA or LBP will be descriptively compared during each movement, between TTA and
12
13 318 TFA, relative to non-amputees. To examine differences between amputation cause, outcome measures
14
15 319 related to KOA or LBP will be descriptively compared during each movement, between transtibial traumatic
16
17 320 and transtibial dysvascular amputees, relative to non-amputees.
18
19
20
21 321
22
23

322 RISK OF BIAS IN INDIVIDUAL STUDIES

24
25 323 Risk of bias will be assessed using the modified Downs and Black method ^{44, 45}. In this modified version,
26
27 324 question 25 which addresses sample size, will be modified to a yes/no question and studies that performed
28
29 325 a sample size calculation/power calculation will be awarded one point, while studies without will be
30
31 326 awarded zero ⁴⁴. Randomised controlled trials will be assessed separately to reduce the impact of increased
32
33 327 weighting placed on these studies by the Downs and Black method. Randomised controlled trials will only
34
35 328 have baseline outcome measures extracted, so while risk of bias will be analysed separately for
36
37 329 observational and intervention studies, outcome measures and presentation of the data will be performed
38
39 330 identically across all studies. Two reviewers will both assess each study using the Downs and Black criteria.
40
41 331 Where there are conflicts, reviewers will meet to discuss and if they cannot agree, a third reviewer will be
42
43 332 consulted to make a final decision.
44
45
46
47
48 333
49
50

51 DATA SYNTHESIS AND DISSEMINATION

52 335 The primary goal of this systematic review is to descriptively compare biomechanical risk factors for
53
54 336 developing KOA and LBP between amputee sub-groups, irrespective of whether KOA or LBP was present.
55
56 337 Due to such a large combination of outcome measures (Appendix 1), sub-groups and gait types, meta-
57
58 338 analyses will not be performed. Instead, quantitative results will be synthesised and descriptively
59
60

1
2
3 339 compared using biomechanical mean/median values of amputee sub-groups relative to non-amputees.
4
5 340 Due to the scope of this review, results are expected to be published in three separate manuscripts: 1)
6
7 341 Biomechanical risk factors of KOA between TTA and TFA, relative to non-amputees, 2) Biomechanical risk
8
9 342 factors of LBP between TTA and TFA, relative to non-amputees, and 3) Biomechanical risk factors of KOA
10
11 343 and LBP between transtibial amputees with traumatic or dysvascular causes, relative to non-amputees.
12
13 344 KOA and LBP will be grouped in the third results paper, as there are far fewer studies that have solely
14
15 345 recruited dysvascular amputees. The quality of evidence for all outcomes will be judged using the Grading
16
17 346 of Recommendations Assessment, Development and Evaluation (GRADE) working group methodology.
18
19 347 Systematic review analysis and reporting will be performed using the Preferred Reporting Items for
20
21 348 Systematic Reviews and Meta-Analyses (PRISMA) guidelines ⁴⁶.
22
23
24
25
26
27
28

350 META-ANALYSIS AND META-BIAS

351 Due to the high number of movements (e.g. walking, incline walking, decline walking), sub-groups (e.g.
352 TFA, TTA, dysvascular and traumatic amputation) and outcome variables (temporospatial, kinematic and
353 kinetic measures), which significantly reduces the number of studies that are able to be statistically
354 compared for each outcome measure, a meta-analysis will not be performed. Therefore, examination of
355 meta-bias within this review is not possible.
36
37
38
39
40
41
42
43
44

357 Author Contributions

358 LW is the guarantor. LW, MPM, CM, JB and ES contributed to conception and design of the study. ES and
359 CM developed the search strategy. LW, MPM, CM, JB and ES contributed to the development of selection
360 criteria. LW, MPM, CM and ES and performed study selection. LW drafted the manuscript. LW, MPM, CM,
361 JB and ES read, provided feedback and approved the final manuscript.
362

Funding Statement

This work was supported by the Engineering and Physical Sciences Research Council, through the RCUK Centre for the Analysis of Motion, Entertainment Research and Applications (CAMERA), Bath, United Kingdom, grant number [EP/M023281/1, EP/T014865/1]. This work was also supported by the Versus Arthritis Centre for Sport Exercise, Exercise and Osteoarthritis Research [Ref 21595].

Conflicts of Interest

The authors declare no conflicts of interest

References

1. Ahmad, N., et al., *The prevalence of major lower limb amputation in the diabetic and non-diabetic population of England 2003–2013*. *Diabetes and Vascular Disease Research*, 2016. **13**(5): p. 348-353.
2. Sturma, A., L. Hruby, and M. Diers, *Epidemiology and Mechanisms of Phantom Limb Pain*, in *Bionic Limb Reconstruction*, O.C. Aszmann and D. Farina, Editors. 2021, Springer International Publishing: Cham. p. 103-112.
3. Ziegler-Graham, K., et al., *Estimating the Prevalence of Limb Loss in the United States: 2005 to 2050*. *Archives of Physical Medicine and Rehabilitation*, 2008. **89**(3): p. 422-429.
4. Norvell, D.C., et al., *The prevalence of knee pain and symptomatic knee osteoarthritis among veteran traumatic amputees and nonamputees*. *Archives of Physical Medicine and Rehabilitation*, 2005. **86**(3): p. 487-493.
5. Struyf, P.A., et al., *The Prevalence of Osteoarthritis of the Intact Hip and Knee Among Traumatic Leg Amputees*. *Archives of Physical Medicine and Rehabilitation*, 2009. **90**(3): p. 440-446.
6. Ehde, D.M., et al., *Back pain as a secondary disability in persons with lower limb amputations*. *Archives of Physical Medicine and Rehabilitation*, 2001. **82**(6): p. 731-734.
7. Stam, H.J., A.-M.V. Dommissie, and H.B.J. Bussmann, *Prevalence of low back pain after transfemoral amputation related to physical activity and other prosthesis-related parameters*. *Disability and Rehabilitation*, 2004. **26**(13): p. 794-797.
8. Ephraim, P.L., et al., *Phantom Pain, Residual Limb Pain, and Back Pain in Amputees: Results of a National Survey*. *Archives of Physical Medicine and Rehabilitation*, 2005. **86**(10): p. 1910-1919.
9. Hammarlund, C.S., et al., *Prevalence of back pain, its effect on functional ability and health-related quality of life in lower limb amputees secondary to trauma or tumour: a comparison across three levels of amputation*. *Prosthetics and Orthotics International*, 2011. **35**(1): p. 97-105.
10. Devan, H., et al., *Exploring Factors Influencing Low Back Pain in People With Nondysvascular Lower Limb Amputation: A National Survey*. *PM&R*, 2017. **9**(10): p. 949-959.

- 1
2
3 401 11. Butowicz, C.M., C.L. Dearth, and B.D. Hendershot, *Impact of Traumatic Lower Extremity*
4 402 *Injuries Beyond Acute Care: Movement-Based Considerations for Resultant Longer Term*
5 403 *Secondary Health Conditions*. *Advances in wound care*, 2017. **6**(8): p. 269-278.
- 6 404 12. Wasser, J.G., et al., *Potential lower extremity amputation-induced mechanisms of chronic low*
7 405 *back pain: role for focused resistance exercise*. *Disability and Rehabilitation*, 2019: p. 1-9.
- 8 406 13. Spoden, M., U. Nimptsch, and T. Mansky, *Amputation rates of the lower limb by amputation*
9 407 *level – observational study using German national hospital discharge data from 2005 to 2015*.
10 408 *BMC Health Services Research*, 2019. **19**(1): p. 8.
- 11 409 14. Imam, B., et al., *Incidence of lower limb amputation in Canada*. *Canadian Journal of Public*
12 410 *Health*, 2017. **108**(4): p. 374-380.
- 13 411 15. Cox, P.S.L., W. SKP, and S. Weaver, *Life after lower extremity amputation in diabetics*. *West*
14 412 *indian medical journal*, 2011. **60**(5): p. 536-540.
- 15 413 16. Gailey, R., et al., *Review of secondary physical conditions associated with lower-limb*
16 414 *amputation and long-term prosthesis use*. *Journal of Rehabilitation Research & Development*,
17 415 2008. **45**(1).
- 18 416 17. Devan, H., et al., *Spinal, pelvic, and hip movement asymmetries in people with lower-limb*
19 417 *amputation: Systematic review*. *Journal of Rehabilitation Research & Development*, 2015. **52**:
20 418 p. 1+.
- 21 419 18. Sivapuratharasu, B., A.M.J. Bull, and A.H. McGregor, *Understanding Low Back Pain in*
22 420 *Traumatic Lower Limb Amputees: A Systematic Review*. *Archives of Rehabilitation Research*
23 421 *and Clinical Translation*, 2019. **1**(1): p. 100007.
- 24 422 19. Rosenberg, D.E., et al., *Body mass index patterns following dysvascular lower extremity*
25 423 *amputation*. *Disability and Rehabilitation*, 2013. **35**(15): p. 1269-1275.
- 26 424 20. Lementowski, P.W. and S.B. Zelicof, *Obesity and osteoarthritis*. *American Journal of*
27 425 *Orthopedics-Belle Mead-*, 2008. **37**(3): p. 148.
- 28 426 21. Pezzin, L.E., et al., *Use and satisfaction with prosthetic limb devices and related services 11No*
29 427 *commercial party having a direct financial interest in the results of the research supporting*
30 428 *this article has or will confer a benefit on the author(s) or on any organization with which the*
31 429 *author(s) is/are associated*. *Archives of Physical Medicine and Rehabilitation*, 2004. **85**(5): p.
32 430 723-729.
- 33 431 22. Farrokhi, S., et al., *Biopsychosocial risk factors associated with chronic low back pain after*
34 432 *lower limb amputation*. *Medical Hypotheses*, 2017. **108**: p. 1-9.
- 35 433 23. Farrokhi, S., et al., *A Narrative Review of the Prevalence and Risk Factors Associated With*
36 434 *Development of Knee Osteoarthritis After Traumatic Unilateral Lower Limb Amputation*.
37 435 *Military Medicine*, 2016. **181**(suppl_4): p. 38-44.
- 38 436 24. Kulkarni, J., et al., *Chronic low back pain in traumatic lower limb amputees*. *Clinical*
39 437 *Rehabilitation*, 2005. **19**(1): p. 81-86.
- 40 438 25. Oosterhoff, M., J.H.B. Geertzen, and P.U. Dijkstra, *More than half of persons with lower limb*
41 439 *amputation suffer from chronic back pain or residual limb pain: a systematic review with meta-*
42 440 *analysis*. *Disability and Rehabilitation*, 2020: p. 1-21.
- 43 441 26. van Eck, C.F. and R.L. McGough, *Clinical outcome of osseointegrated prostheses for lower*
44 442 *extremity amputations: a systematic review of the literature*. *Current Orthopaedic Practice*,
45 443 2015. **26**(4).
- 46 444 27. Tomaszewski, P.K., et al., *Numerical analysis of an osseointegrated prosthesis fixation with*
47 445 *reduced bone failure risk and periprosthetic bone loss*. *Journal of Biomechanics*, 2012. **45**(11):
48 446 p. 1875-1880.
- 49 447 28. Devan, H., et al., *Asymmetrical movements of the lumbopelvic region: Is this a potential*
50 448 *mechanism for low back pain in people with lower limb amputation?* *Medical Hypotheses*,
51 449 2014. **82**(1): p. 77-85.
- 52 450 29. Jackson, B.D., et al., *Reviewing knee osteoarthritis — a biomechanical perspective*. *Journal of*
53 451 *Science and Medicine in Sport*, 2004. **7**(3): p. 347-357.

- 1
2
3 452 30. Morgenroth, D.C., A.C. Gellhorn, and P. Suri, *Osteoarthritis in the Disabled Population: A Mechanical Perspective*. PM&R, 2012. **4**(5, Supplement): p. S20-S27.
- 4 453
5 454 31. Highsmith, M.J., et al., *Low back pain in persons with lower extremity amputation: a systematic review of the literature*. The Spine Journal, 2019. **19**(3): p. 552-563.
- 6 455
7 456 32. Iijima, H., et al., *Biomechanical characteristics of stair ambulation in patients with knee OA: A systematic review with meta-analysis toward a better definition of clinical hallmarks*. Gait & Posture, 2018. **62**: p. 191-201.
- 8 457
9 458
10 459 33. Sagawa, Y., et al., *Biomechanics and physiological parameters during gait in lower-limb amputees: A systematic review*. Gait & Posture, 2011. **33**(4): p. 511-526.
- 11 460
12 461 34. Shamseer, L., et al., *Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation*. BMJ : British Medical Journal, 2015. **349**: p. g7647.
- 13 462
14 463
15 464 35. Prinsen, E.C., M.J. Nederhand, and J.S. Rietman, *Adaptation Strategies of the Lower Extremities of Patients With a Transtibial or Transfemoral Amputation During Level Walking: A Systematic Review*. Archives of Physical Medicine and Rehabilitation, 2011. **92**(8): p. 1311-1325.
- 16 465
17 466
18 467
19 468 36. Egloff, C., T. Hügler, and V. Valderrabano, *Biomechanics and pathomechanisms of osteoarthritis*. Swiss Medical Weekly, 2012. **142**(JULY).
- 20 469
21 470 37. Davis, E.M., et al., *Longitudinal evidence links joint level mechanics and muscle activation patterns to 3-year medial joint space narrowing*. Clinical Biomechanics, 2019. **61**: p. 233-239.
- 22 471
23 472 38. Laird, R.A., et al., *Comparing lumbo-pelvic kinematics in people with and without back pain: a systematic review and meta-analysis*. BMC musculoskeletal disorders, 2014. **15**: p. 229-229.
- 24 473
25 474 39. Vonville, H., *Excel workbooks for systematic reviews*. Available at: <https://www.dropbox.com/sh/2q9wh960zfdgc2e/AABc-MEceYIGQMnHwUT8ZWAgA>, 2015.
- 26 475
27 476 40. Cohen, J., *A Coefficient of Agreement for Nominal Scales*. Educational and Psychological Measurement, 1960. **20**(1): p. 37-46.
- 28 477
29 478 41. Rohatgi, A. *WebPlotDigitizer - Version 4.5*. 2021; Available from: <https://automeris.io/WebPlotDigitizer>.
- 30 479
31 480 42. Hendershot, B.D. and E.J. Wolf, *Three-dimensional joint reaction forces and moments at the low back during over-ground walking in persons with unilateral lower-extremity amputation*. Clinical Biomechanics, 2014. **29**(3): p. 235-242.
- 32 481
33 482
34 483 43. Morgenroth, D.C., et al., *The Relationship Between Lumbar Spine Kinematics during Gait and Low-Back Pain in Transfemoral Amputees*. American Journal of Physical Medicine & Rehabilitation, 2010. **89**(8): p. 635-643.
- 35 484
36 485
37 486 44. Cindy Ng, L.W., et al., *Does exercise training change physical activity in people with COPD? A systematic review and meta-analysis*. Chronic Respiratory Disease, 2011. **9**(1): p. 17-26.
- 38 487
39 488 45. Downs, S.H. and N. Black, *The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions*. Journal of Epidemiology and Community Health, 1998. **52**(6): p. 377-384.
- 40 489
41 490
42 491 46. Page, M.J., et al., *PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews*. BMJ, 2021. **372**: p. n160.
- 43 492
44 493
45 494
46 495

Figure Legend

1
2
3 496 Figure 1: Flow chart of paper selection. Exclusion reasons are: 1) no amputees, 2) upper limb amputation,
4
5 497 3) no adult human participants, 4) language not English, 5) review, 6) no quantitative data, 7) paper not
6
7 498 found/duplicate, 8) no clinical outcomes, 9) single case study), 10) no results for separate amputee groups,
8
9 499 11) no biomechanical parameters, 12) powered prosthesis only.
10
11
12 500
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

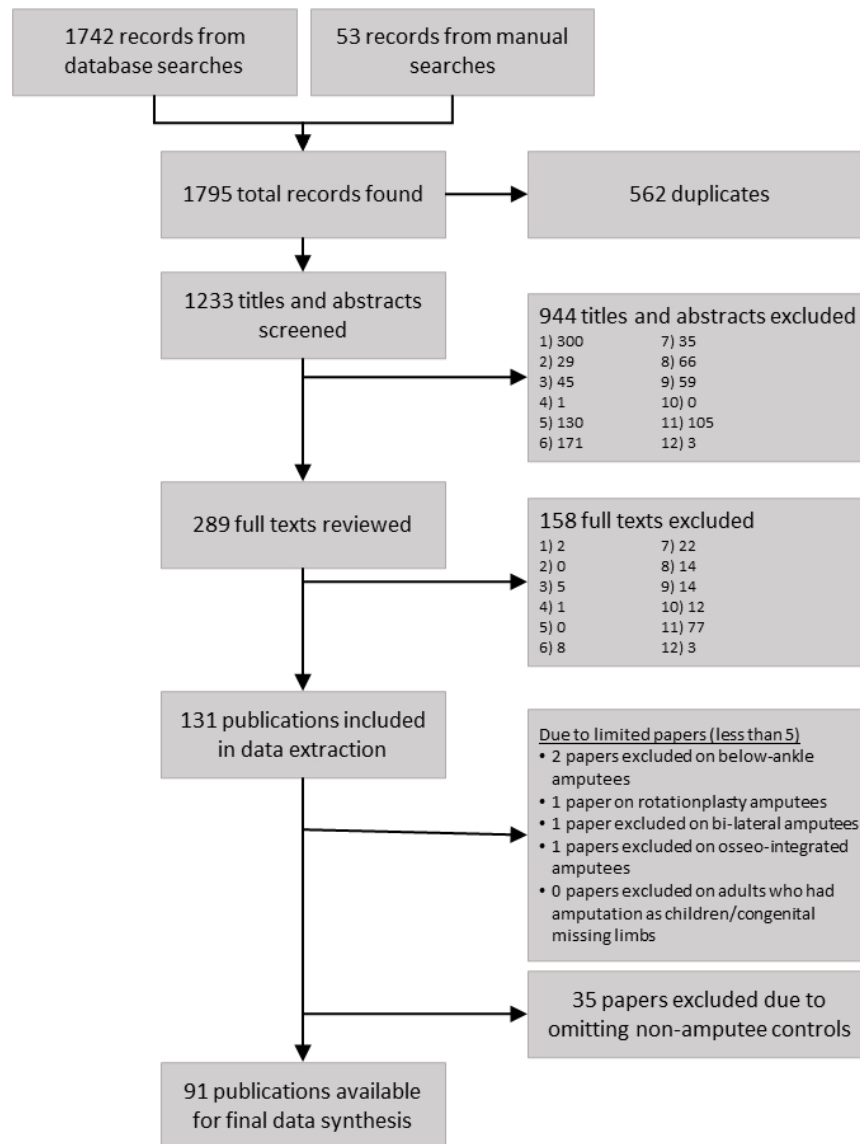


Figure 1: Flow chart of paper selection. Exclusion reasons are: 1) no amputees, 2) upper limb amputation, 3) no adult human participants, 4) language not English, 5) review, 6) no quantitative data, 7) paper not found/duplicate, 8) no clinical outcomes, 9) single case study, 10) no results for separate amputee groups, 11) no biomechanical parameters, 12) powered prosthesis only.

190x250mm (96 x 96 DPI)

Appendix 1: Outcome variable to be extracted from experimental studies

Temporospatial	Kinematics		Kinetics	
BMI	Knee adduction range of motion (ROM)	Knee	Peak knee adduction moment (KAM)	Knee
Walking speed	Knee sagittal ROM		KAM loading rate (rate of force development)	
Stride width (from midline)	Hip-knee-ankle adduction angle		KAM impulse	
Stride/step length/symmetry	Varus/valgus angle - knee adduction angle		Peak knee joint contact forces	
Stance/contact time	Knee flexion at heel strike		Joint reaction force at terminal stance	
Leg length discrepancy	Knee flexion at toe off		Peak knee sagittal/flexion/extension plane moments	
Cadence		Knee rotation moment early stance		
Ground Reaction Force (GRF)	Peak hip extension	Hip	Knee flexion moment at loading response	Knee
Vertical GRF at heel strike	Peak hip flexion angle		Flexion moment at terminal stance	
Horizontal GRF at heel strike	Hip flexion at toe off		Net work	
Vertical GRF loading rate	Hip ROM sagittal		Positive work	
Prosthetic horizontal GRF at push-off	Hip flexion at loading response		Negative work	
Peak vertical GRF				
	Peak trunk flexion angle	Trunk/Pelvis	Peak hip extension moment	Hip
	Peak lumbar spine extension		Lumbar-pelvic lateral joint reaction force	Trunk/Pelvis
	Lumbar-pelvis spine extension		Anterior lateral joint reaction force - lumbar-pelvic	
	Peak coronal/frontal/lateral/contralateral pelvic tilt		Mediolateral shear joint reaction force of trunk	
	Peak anterior-posterior/sagittal pelvic tilt		Anterior-posterior shear joint reaction force of trunk	
	Pelvic ROM in frontal plane		Compression joint reaction force forces of trunk	
	Pelvic ROM in sagittal plane		Lumbar/pelvic joint power	
	Lumbar transverse plane rotation ROM		Lower back joint contact force	
	Sagittal plane pelvis angle		Joint work L5/S1 (frontal and sagittal plane)	
	Side flexion of trunk-pelvis			
	Mediolateral trunk sway			
	Lumbar lordosis angle			

mjopen-2022-066959
 2022
 November 09, 2022
 Downloaded from <http://bmjopen.bmj.com/> on April 25, 2024 by guest. Protected by copyright.

Appendix 2: Search strategies for each of the five databases used in this systematic review

Database	keywords
Web of Science	TS=("transtibial amput*" OR "transfemoral amput*" OR amput* OR "Lower limb amput*" OR "Lower extremity amput*" OR "Leg prosthesis") AND TS=(walking OR running OR gait OR locomotion OR biomechanics OR kinematics OR kinetics OR "biomechanical parameter*" OR *symmetr* OR forc* OR angle* OR moment* OR power OR emg OR electromyogra*) AND TS=(Osteoporosis OR Osteopenia OR "Back Pain" OR Backache OR Osteoarthritis OR "musculoskeletal diseas*" OR "musculoskeletal condition*" OR "secondary diseas*")
Scopus	(TITLE-ABS-KEY ("transtibial amput*" OR "transfemoral amput*" OR amput* OR "Lower limb amput*" OR "Lower extremity amput*" OR "Leg prosthesis") AND TITLE-ABS-KEY (walking OR running OR gait OR locomotion OR biomechanics OR kinematics OR kinetics OR "biomechanical parameter*" OR *symmetr* OR forc* OR angle* OR moment* OR power OR emg OR electromyogra*) AND TITLE-ABS-KEY (osteoporosis OR osteopenia OR "Back Pain" OR backache OR osteoarthritis OR "musculoskeletal diseas*" OR "musculoskeletal condition*" OR "secondary diseas*")) AND (LIMIT-TO (LANGUAGE , "English") OR LIMIT-TO (LANGUAGE , "German") OR LIMIT-TO (LANGUAGE , "Italian"))
Pubmed	((("Amputees"[Mesh] OR "Amputation"[Mesh] OR Amput* OR "Amputation, Traumatic"[Mesh] OR "Amputation, Congenital" [Supplementary Concept] OR "lower limb amputation" OR "lower limb amputee" OR "lower extremity amputee" OR "Artificial Limb"[Mesh]) AND ("Walking"[Mesh] OR "Running"[Mesh] OR "Gait"[Mesh] OR gait OR "Locomotion"[Mesh] OR Locomotion OR "Biomechanical Phenomena"[Mesh] OR biomechanic* OR biomechanical parameter*" OR symmetr* OR angle OR angles OR force OR "Ground Reaction forces" OR power OR "kinetics"[Mesh] OR "Kinematics"[Mesh] OR kinetic* Or kinematic* OR EMG) AND ("Osteoarthritis"[Mesh] OR "osteoporosis"[Mesh] OR osteopenia OR "Back Pain"[Mesh] OR backache OR "musculoskeletal disease*" [Mesh] OR "secondary diseas*" OR "secondary condition" OR "knee osteoarthritis" OR "hip osteoarthritis"))))
Embase	Option A (('transtibial amputation'/exp OR 'transtibial amputation' OR 'transfemoral amputation'/exp OR 'transfemoral amputation' OR 'amputee'/exp OR 'amputee' OR 'amputees'/exp OR 'amputees' OR 'individual with amputation'/exp OR 'individual with amputation' OR 'person with amputation'/exp OR 'person with amputation' OR 'artificial leg'/exp OR 'artificial leg' OR 'artificial legs'/exp OR 'artificial legs' OR 'leg prostheses'/exp OR 'leg prostheses' OR 'leg prosthesis'/exp OR 'leg prosthesis' OR 'leg prosthetics'/exp OR 'leg prosthetics' OR 'leg, artificial'/exp OR 'leg, artificial' OR 'legs, artificial'/exp OR 'legs, artificial' OR 'lower extremity prosthesis'/exp OR 'lower extremity prosthesis' OR 'lower limb prostheses'/exp OR 'lower limb prostheses' OR 'lower limb prosthesis'/exp OR 'lower limb prosthesis' OR 'prostheses, leg'/exp OR 'prostheses, leg' OR 'prosthesis, leg'/exp OR 'prosthesis, leg' OR 'walking prosthesis'/exp OR 'walking prosthesis' OR 'amputation, traumatic'/exp OR 'amputation, traumatic' OR 'traumatic amputation'/exp OR

	<p>'traumatic amputation' OR 'congenital amputation'/exp OR 'congenital amputation') AND ('walking'/exp OR 'walking' OR 'runner'/exp OR 'runner' OR 'running'/exp OR 'running' OR 'kinematics'/exp OR 'kinematics' OR 'human kinetics'/exp OR 'human kinetics' OR 'kinetic analysis'/exp OR 'kinetic analysis' OR 'kinetic mechanism'/exp OR 'kinetic mechanism' OR 'kinetic model'/exp OR 'kinetic model' OR 'kinetics'/exp OR 'kinetics' OR 'biomechanical phenomena'/exp OR 'biomechanical phenomena' OR 'biomechanical phenomenon'/exp OR 'biomechanical phenomenon' OR 'biomechanics'/exp OR 'biomechanics' OR 'biomechanism'/exp OR 'biomechanism' OR 'behavior, locomotor'/exp OR 'behavior, locomotor' OR 'behaviour, locomotor'/exp OR 'behaviour, locomotor' OR 'locomotion'/exp OR 'locomotion' OR 'locomotion pattern'/exp OR 'locomotion pattern' OR 'locomotor activity'/exp OR 'locomotor activity' OR 'locomotor response'/exp OR 'locomotor response' OR 'biped gait'/exp OR 'biped gait' OR 'gait'/exp OR 'gait' OR 'gait analysis'/exp OR 'gait analysis' OR 'gait training'/exp OR 'gait training' OR 'pattern, walking'/exp OR 'pattern, walking' OR 'walking pattern'/exp OR 'walking pattern') AND ('decalcification, pathologic'/exp OR 'decalcification, pathologic' OR 'endocrine osteoporosis'/exp OR 'endocrine osteoporosis' OR 'osteoporosis'/exp OR 'osteoporosis' OR 'osteoporotic decalcification'/exp OR 'osteoporotic decalcification' OR 'osteoarthritis'/exp OR 'osteoarthritis' OR 'back ache'/exp OR 'back ache' OR 'back pain'/exp OR 'back pain' OR 'back pain syndrome'/exp OR 'back pain syndrome' OR 'backache'/exp OR 'backache' OR 'backpain'/exp OR 'backpain' OR 'dorsalgia'/exp OR 'dorsalgia' OR 'pain, back'/exp OR 'pain, back' OR 'musculoskeletal disease'/exp OR 'musculoskeletal disease' OR 'secondary disease'/exp OR 'secondary disease')</p>
<p>CINAHL</p>	<p>OPTION A: Straight search of terms (no subheading selection)</p> <p>("transtibial amput*" OR "transfemoral amput*" OR amput* OR "Lower limb amput*" OR "Lower extremity amput*" OR "Leg prosthesis")</p> <p>AND</p> <p>("Walking" OR "Running" OR "Gait" OR gait OR "Locomotion" OR Locomotion OR "Biomechanical Phenomena" OR biomechanic* OR "biomechanical parameter*" OR symmetr* OR angle OR angles OR force OR "Ground Reaction forces" OR power OR "kinetics" OR "Kinematics" OR kinetic* OR kinematic OR "EMG" OR electromyo*)</p> <p>AND</p> <p>("Osteoarthritis" OR "osteoporosis" OR osteopenia OR "Back Pain" OR backache OR "musculoskeletal disease*" OR "secondary diseas*" OR "secondary condition" OR "knee osteoarthritis" OR "hip osteoarthritis")</p>

bmjopen-2022-066959 on 24 November 2022 Downloaded from <http://bmjopen.bmj.com/> on April 20, 2024 by guest. Protected by copyright.

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Completed
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Yes – Page 1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes – Page 1 & 7
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes – Page 1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes – Page 14
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Yes – Page 14
Sponsor	5b	Provide name for the review funder and/or sponsor	Yes – Page 14
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes – Page 3-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes - Page 6-7
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes – Page 7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes – Page 9
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits such that it could be repeated	Yes – Page 9

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Yes – Page 9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes – Page 9-10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently in duplicate), any processes for obtaining and confirming data from investigators	Yes – Page 10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes – Page 11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Yes – Page 12-13
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Yes – Page 13
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	Yes – Page 13-14
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	N/A
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	N/A
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	Yes – Page 13-14

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.