Clinical effectiveness of treatment strategies for prosthetic joint infection following total ankle replacement: A systematic review and meta-analysis

Setor K. Kunutsor[1,2], Matthew C. Barrett[3], Michael R. Whitehouse[1,2], Ashley W. Blom[1,2]

[1] *National Institute for Health Research Bristol Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust and University of Bristol, Bristol, UK*

[2]*Translational Health Sciences, Bristol Medical School, Musculoskeletal Research Unit, University of Bristol, Learning & Research Building (Level 1), Southmead Hospital, Bristol, BS10 5NB, UK*

[3]*Barts and The London School of Medicine and Dentistry, 4 Newark St, Whitechapel, London E1 2AT*

Address correspondence to:

Setor K. Kunutsor, Translational Health Sciences, Bristol Medical School, Musculoskeletal Research Unit, University of Bristol, Learning & Research Building (Level 1), Southmead Hospital, Bristol, BS10 5NB, UK; Phone: +44-7539589186; Fax: +44-1174147924;

Email address: skk31@cantab.net / setor.kunutsor@bristol.ac.uk

Financial Disclosure: This study was supported by the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. This article presents independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research program (RP-PG-1210-12005). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Conflict of Interest: MRW undertakes teaching on basic sciences for Orthopaedic trainees preparing for the FRCS, his institution receives market rate payment for this teaching from Heraeus. MRW and AWB are co-applicants on a grant from Stryker investigating the outcome of the Triathlon total knee replacement. MRW and AWB are members of the National Joint Registry lot 2 contract (statistical analysis) team.

Systematic review registration: PROSPERO 2018: CRD42018119102

ABSTRACT

Prosthetic joint infection (PJI) after total ankle replacement (TAR) is a challenging complication, which often requires debridement and implant retention (DAIR) with or without polyethylene exchange; revision surgery; implantation of a cement spacer; conversion to arthrodesis; or even amputation. The optimum treatment for ankle PJI is not well established. We conducted a systematic review and meta-analysis to compare the clinical effectiveness of various treatment strategies for infected ankle prostheses. We searched MEDLINE, Embase, Web of Science, and The Cochrane Library up to December 2018 for studies evaluating the impact of treatment in patient populations with infected ankle prostheses following TAR. Binary data were pooled after arcsine transformation. Six citations comprising of 17 observational design comparisons were included. The re-infection rates (95% CIs) for DAIR with or without polyethylene exchange, one-stage revision, two-stage revision, cement spacer, and arthrodesis were 39.8% (24.4-56.1), 0.0% (0.0-78.7), 0.0% (0.0-8.5), 0.2% (0.0-17.9) and 13.6% (0.0-45.8) respectively. Rates of amputation for DAIR with or without polyethylene exchange and cement spacer were 5.6% (0.0-16.9) and 22.2% (6.3-54.7) respectively. Measures of function, pain, and satisfaction could not be compared because of limited data. One- and two-stage revision strategies seem to be associated with the lowest re-infection rates, but these findings are based on limited data. Arthrodesis and DAIR with or without polyethylene exchange appear to be commonly used in treating infected ankle prosthesis, but are associated with poor infection control. Clear gaps exist in the literature and further research is warranted to evaluate treatment strategies for infected ankle prosthesis.

Level of evidence: 3

Keywords: prosthetic joint infection; ankle replacement; one-stage revision; two-stage revision; arthrodesis; meta-analysis

Fusion or arthrodesis has long been the widely accepted treatment for end-stage osteoarthritis of the ankle. However, with the emergence of third generation three component mobile-bearing implants (1, 2), total ankle replacement (TAR) has become popular and recognised as an equally effective alternative (3, 4). Compared to hip and knee replacements, relatively few ankle replacements are performed. In 2017, approximately 100,000 joint replacements were performed each in knees and hips as recorded in the National Joint Registry for England, Wales and Northern Ireland and the Isle of Man; whereas only 734 ankle replacements were performed (5). Prosthetic joint infection (PJI) is a potentially devastating, albeit uncommon complication of TAR which results in implant failure (6). The incidence of ankle PJI has been reported to range between 1.1% and 8.9% (4, 7, 8), which exceed rates for hip or knee replacement (9). The soft tissue envelope of the ankle joint makes the management of PJI following TAR challenging. Like other joints, the goals of PJI treatment are to eradicate infection, provide substantial pain relief, maintain or restore joint function, and to improve quality of life (10). Several treatment options for ankle PJI exist including long-term suppressive antibiotic treatment without surgical intervention; debridement and implant retention (DAIR) with or without polyethylene exchange; one-stage revision surgery; two-stage revision surgery; prosthesis component removal and implantation of a cement spacer; arthrodesis; and amputation. Below-knee amputation is considered as a last resort after other limb salvage procedures have failed. Though the choice of an appropriate treatment depends on factors which include the timing and the type of infection, the standard treatment strategy for an infected ankle prosthesis is not well defined. Treatment options have generally been based on surgeons' preferences and experiences as well as evidence from hip and knee replacement data. Unlike hip, knee, and shoulder joints, where there is an extensive body of evidence showing the clinical effectiveness of the one- and two-stage revision strategies for managing PJI of these joints (11-14), this is not so for infected ankle joints. Published series on the treatment of infected ankle prostheses are sparse and are characterised by small sample sizes.

To bring the existing evidence together, we conducted a systematic review and meta-analysis to compare the clinical effectiveness of the following treatment strategies for the management of PJI following TAR using infection control as a primary outcome: long-term suppressive antibiotic treatment without surgical intervention; debridement, treatment with antibiotics and retention of the prosthesis (DAIR) with or without polyethylene exchange; one-stage revision surgery; two-stage revision surgery; prosthesis component removal and implantation of cement spacer; and arthrodesis. Our secondary objectives included (i) comparing the clinical effectiveness of the above treatment strategies using measures of pain, function, and satisfaction; non-infection related adverse events; conversion to arthrodesis; and amputation and (ii) to identify gaps in the evidence and areas for future research.

Materials and Methods

Data Sources, Search Strategy and Screening

This review was registered in the PROSPERO prospective register of systematic reviews (CRD42018119102) and followed PRISMA and MOOSE guidelines (15, 16) (**Appendix 1-2**). We conducted a systematic electronic search in the following databases from inception to 09 December 2018: MEDLINE, Embase, and The Cochrane library. We constructed the search strategy by combining key words related to the population and outcomes, with no limits on language. Details of the search strategy are reported in **Appendix 3**. All titles and abstracts of studies retrieved from the databases were screened to assess their suitability for inclusion. One reviewer (SKK) initially screened all titles and abstracts for potentially eligible papers and subsequently acquired full text papers. Full text evaluation was conducted by two independent reviewers (SKK and MCB) against the eligibility criteria. Any discrepancies were discussed and the opinion of a third reviewer (MRW) was sought when necessary to achieve consensus. The “cited by” function in Web of Science and the reference lists of included studies and review articles were manually assessed to identify any relevant papers that were not discovered by the initial search.

Eligibility Criteria

We included papers that (i) evaluated the clinical impact of the following strategies: long-term suppressive antibiotic treatment without surgical intervention; DAIR with or without polyethylene exchange; one-stage revision surgery; two-stage revision surgery; prosthesis component removal and implantation of cement spacer; and arthrodesis in a longitudinal observational study or randomized controlled trial (RCT) in patient populations with infected ankle prostheses following TAR and (ii) were followed post-operatively for re-infection (defined as recurrence of infection by the same organism(s) and/or re-infection with a new organism(s)); and/or other clinical outcomes including (a) function, pain, or satisfaction as measured by patient-reported outcomes such as the American Orthopaedic Foot & Ankle Society (AOFAS) hindfoot score, Short Form–36 (SF-36), visual analog scale (VAS), Short Musculoskeletal Function Assessment (SMFA), Foot and Ankle Outcomes Score (FAOS), and American Orthopaedic Foot and Ankle Society score (AOFAS); (b) non-infection related complications (such as implant failure, fracture, re-operation, non-union, loosening, haematoma, postoperative instability); (c) conversion from one of the interventions above to arthrodesis; or (d) conversion from one of the interventions above to amputation.

Data Extraction and Quality Assessment

Using a standardized data extraction form in Microsoft Excel, one reviewer (SKK) independently extracted qualitative and quantitative information from included papers on study design, patient characteristics, nature of interventions, and outcomes. A second reviewer (MCB) independently checked these extracted data with that in the original papers. Discrepancies between the two data extractors (SKK and MCB) were discussed, and the opinion of a third reviewer (MRW) was sought if necessary to achieve consensus. When insufficient data were reported in available papers, we contacted authors to provide further information. We assessed the methodological quality of included studies using the Methodological Index for Non-Randomised Studies (MINORS), a validated instrument designed to assess the quality of non-randomised studies in surgery (17). This tool scores studies from 0-16 using eight pre-defined domains namely: a clearly stated aim, inclusion of consecutive patients, prospective collection of data, endpoints appropriate to the aim of the study, unbiased assessment of the study endpoint, follow-up period appropriate to the aim of the study, loss to follow-up less than 5%, and prospective calculation of the study size. For each item, the instrument assigns a score of 0 for “not reported”, 1 for “reported but inadequate”, or 2 for “reported and adequate”.

Statistical Analysis

For binary data, rates with 95% confidence intervals (CIs) were used as summary measures across studies and these were estimated using the Freeman-Tukey variance stabilising double arcsine transformation (18). The primary outcome, which was the rate of re-infection, was estimated for each treatment strategy by dividing the number of re-infections within the follow-up period following treatment or revision surgery for infected ankle prostheses by the total number of participants with PJI or number of infected ankle joints. Corresponding rates (with 95% CIs) of non-infection related adverse events, conversion to arthrodesis, and amputation were also estimated. It was planned to compare clinical measures of function, pain, and satisfaction between the treatment strategies using descriptive statistics, but this could not be done because of limited data. Stata version 15 (Stata Corp, College Station, Texas, USA) was used for all statistical analyses.

Results

Study Identification and Selection

A total of 728 citations were retrieved from the search and of this number, 717 (98.5%) citations were excluded based on titles and abstracts. On reviewing the full texts of the remaining 11 (1.5%) articles, we excluded 5 articles because (i) the population was not relevant (n=3) and (ii) intervention not relevant (n=2). This left 6 articles eligible for inclusion in the review (19-24) (**Fig. 1; Table 1**).

Study Characteristics and Study Quality

Table 1 provides details on individual baseline characteristics and methodological quality of individual studies by treatment strategy for infected ankle prostheses. The 6 eligible articles comprised of 17 unique studies or comparisons based on treatment strategies utilized: 4 studies on DAIR with or without polyethylene exchange; 2 studies on one-stage revision surgery; 2 studies on two-stage revision surgery; 3 studies on prosthesis component removal and implantation of antibiotic-loaded cement spacer; and 4 studies on arthrodesis. Overall, there were 105 participants or infected ankle prostheses and 11 re-infections. All included studies were based on retrospective data analyses of observational cohort designs or case series. No RCTs comparing treatment strategies were identified. Studies were carried out in Europe (UK and Switzerland) and North America (United States of America). The methodological quality scores of included studies ranged from 8-11.

Treatment Strategies and Infection Control

Fig. 2 reports the rates of re-infection for the various treatment strategies. In pooled analysis of three studies reporting relevant data, the re-infection rate for DAIR with or without polyethylene exchange was 39.8% (95% CI: 24.4-56.1). The rates for one- and two-stage revision surgeries were 0.0% (95% CI: 0.0-78.7) and 0.0% (95% CI:0.0-8.5) respectively. That for antibiotic-loaded cement spacer and arthrodesis as a primary treatment were 0.2% (95% CI: 0.0-17.9) and 13.6% (95% CI: 0.0-45.8) respectively.

Treatment Strategies and Other Post-operative Clinical Outcomes

DAIR with or without polyethylene Rates of conversion to arthrodesis and amputation were 18.9% (95% CI: 6.6-34.3) and 5.6% (95% CI: 0.0-16.9) respectively. In one study that reported on satisfaction outcomes, all 14 patients who were infection free after the treatment were satisfied with their outcomes.(20) In another study that reported on patient-reported measures of function, pain, and satisfaction, there were statistically significant improvements in VAS, SMFA Function, SMFA

Bother, SF-36 Physical, and AOFAS Hindfoot scores when postoperative PJI treatment scores were compared with preoperative primary TAR scores.(24)

Implantation of antibiotic-loaded cement spacer Rates of non-infection related adverse events and amputation were 18.6% (95% CI: 1.9-43.2) and 22.2% (95% CI: 6.3-54.7) respectively. In one study of 9 patients, all 7 patients who retained their spacer insitu were able to mobilize with full weight bearing, had no or experienced occasional mild pain, and were satisfied with their outcomes.(19)

Arthrodesis Four studies reported on arthrodesis as a primary treatment for infected ankle prosthesis. None of the studies reported on any non-infection related adverse events. One study reported on a series of 6 patients, of which 3 patients failed to have their infection cleared and therefore required below knee amputation (22).

No studies reported on mortality outcomes and none of the one- or two-stage revision studies reported on complications, conversion to arthrodesis, or amputations following revision arthroplasty.

Discussion

Compared to infected total knee and hip replacements, the standard treatment strategy of infected ankle prostheses is not well defined. We have attempted to compare the clinical effectiveness of several treatment strategies for infected ankle prosthesis using a literature-based systematic meta-analysis. Treatment strategies were compared using infection control as a primary outcome and other clinical measures such as pain, function, satisfaction, non-infection related adverse events, conversion to arthrodesis, and amputation. Based on the limited data available, one- and two-stage revision strategies were associated with the lowest re-infection rates. A high re-infection rate was observed for DAIR with or without polyethylene exchange, followed by arthrodesis. DAIR with or without polyethylene exchange and use of a cement spacer were also associated with moderately high rates of conversion to arthrodesis and amputation respectively. No complications, conversion to arthrodesis, or amputations were reported by any of the one- or two-stage revision studies. Measures of function, pain, and satisfaction could not be compared effectively because the majority of studies did not report this data.

Data on treatment strategies for infected ankle prostheses is very limited and hence it is challenging to make any evidence-based conclusions on which treatment strategy is more clinically effective. However, it does appear that the one- and two-stage revision rates are associated with the lowest re-infection rates. Furthermore, published studies do not report any non-infection related adverse events related to these strategies. These findings are not surprising given that these two treatment strategies are the obvious choices for the treatment of chronic PJI in other joints such as the hips, knees, and shoulders (11-14). This review has also identified substantial gaps in the existent literature; though TARs are associated with higher incidence of PJIs compared with hip or knee replacements (25-27), there is a general lack of evidence on the optimal treatment strategies for managing infected ankle joint replacements. Of the over 700 retrieved citations, only 6 published articles were found to be relevant to the topic. Given the extensive body of published evidence on PJI treatment in hip and knee joints, it is puzzling that only a handful of studies have been published on the management of infected ankle prostheses. It is likely that the paucity of data on treatment of ankle PJI is due to the lower incidence of TAR utilization. For example, whereas about 100,000 joint replacements were performed each in knees and hips in England, Wales and Northern Ireland and the Isle of Man in 2017, only about 700 ankle replacements were performed that same year (5). Though there is clear evidence from other joints such as the hips, knees, or shoulders that the two-stage revision is the standard treatment for PJI, the current findings suggest that arthrodesis as a primary treatment and DAIR with or without polyethylene exchange are more commonly used in treating infected ankle prosthesis. This is likely to be due to arthrodesis being an accepted and commonly used treatment for the degenerative ankle, which is not the case for the hip and knee, and the challenge of surgical reconstruction of the ankle in terms of bone stock and soft tissues if more invasive revision strategies are employed. Although DAIR with or without polyethylene exchange is associated with acceptable infection control rates in other joints, it is more beneficial in the early post-operative period or for acute postoperative infections (28). Our current findings suggest that

DAIR with or without polyethylene in the ankle is associated with low infection control rates in comparison to other joints. Indeed, DAIR with or without polyethylene has been reported to have high rates of failure when used for treating PJI following TAR (29). Arthrodesis as a primary treatment for infected ankle prosthesis is considered to be a salvage procedure, but as range of motion of the ankle joint is of lower concern to patients with an infected joint replacement than it is in the hip or knee, it is more acceptable. Performing arthrodesis in a previously replaced ankle is challenging due to poor bone stock and involves prolonged surgical and medical treatment with multidisciplinary teams (30). The one- and two-stage revision strategies are commonly associated with high infection control rates in lower limb replacement (11, 12) and shoulder arthroplasty (13), but their role in treating infected ankle prosthesis seems less established particularly in the case of one-stage revision where only two cases were reported. Given the limited data available, it appears orthopaedic surgeons must apply treatment principles from infected hip and knee replacements to infected ankle prostheses. Infections following TAR seem to run a completely different clinical course compared to that of other joints; the majority of cases of PJI of the ankles seem to originate from exogenous sources, infection is difficult to diagnose and requires a high index of suspicion, and there seems to be no consensus on the definition of PJI following TAR (29). It is thus possible that the principles of PJI treatment in other joints may not apply to that of ankles. The overall societal cost of PJI is high and the experience of managing infected ankle replacements is more limited due to the lower number of cases, hence we encourage units with experience of the management of infected ankle replacements to report their results and add to the evidence base.

The evidence on the topic is scanty and sparse, hence the need for a systematic review to bring the evidence together and identify any gaps in the literature. This study represents the first attempt to achieve this. Our search was comprehensive and it spanned several databases including “cited by” search in Web of Science, with manual reference scanning. Although outcome data was limited, our data extraction was thorough which enabled some pooling to enhance interpretation of findings. We employed appropriate statistical tests to take into account the low event rates. Finally, we conducted a detailed assessment of the methodological quality of the included studies using a validated tool. There were limitations to the review which were mostly inherent to the included studies. A head-to-head comparison of the clinical effectiveness of the treatment strategies evaluated could not be robustly done because of the limited number of studies, small sample sizes, and selective reporting of outcomes. Attempts to get investigators of these studies to contribute missing data did not yield any results.

In conclusion, one- and two-stage revision strategies seem to be associated with the lowest re-infection rates, but these are based on very limited data. Arthrodesis and DAIR with or without polyethylene exchange appear to be commonly used in treating infected ankle prosthesis, but these are associated with relatively low infection control rates. The current findings are timely and relevant because they provide insight on the large gaps in the existing literature. Further investigation is warranted on this topic.

References

1. Saltzman CL, Kadoko RG, Suh JS. Treatment of isolated ankle osteoarthritis with arthrodesis or the total ankle replacement: a comparison of early outcomes. Clin Orthop Surg 2: 1, 2010
2. Courville XF, Hecht PJ, Tosteson AN. Is total ankle arthroplasty a cost-effective alternative to ankle fusion? Clin Orthop 469: 1721, 2011
3. Easley ME, Adams SB, Jr., Hembree WC, DeOrio JK. Results of total ankle arthroplasty. J Bone Joint Surg Am 93: 1455, 2011
4. Zaidi R, Cro S, Gurusamy K, Siva N, Macgregor A, Henricson A, Goldberg A. The outcome of total ankle replacement: a systematic review and meta-analysis. Bone Joint J 95-B: 1500, 2013
5. National Joint Registry for England and Wales: 15th Annual Report. Accessed from http://www.njrreports.org.uk/Portals/0/PDFdownloads/NJR%2015th%20Annual%20Report%202018.pdf. 2018
6. Glazebrook MA, Arsenault K, Dunbar M. Evidence-based classification of complications in total ankle arthroplasty. Foot Ankle Int 30: 945, 2009
7. Kessler B, Sendi P, Graber P, Knupp M, Zwicky L, Hintermann B, Zimmerli W. Risk factors for periprosthetic ankle joint infection: a case-control study. J Bone Joint Surg Am 94: 1871, 2012
8. Althoff A, Cancienne JM, Cooper MT, Werner BC. Patient-Related Risk Factors for Periprosthetic Ankle Joint Infection: An Analysis of 6977 Total Ankle Arthroplasties. J Foot Ankle Surg 57: 269, 2018
9. Huotari K, Peltola M, Jamsen E. The incidence of late prosthetic joint infections: a registry-based study of 112,708 primary hip and knee replacements. Acta Orthop 86: 321, 2015
10. Santos AL, Demange MK, Prado MP, Fernandes TD, Giglio PN, Hintermann B. Cartilage lesions and ankle osteoarthrosis: review of the literature and treatment algorithm. Rev Bras Ortop 49: 565, 2014
11. Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD, Inform Team. Re-infection outcomes following one- and two-stage surgical revision of infected hip prosthesis: A systematic review and meta-analysis. PloS one 10: e0139166, 2015
12. Kunutsor SK, Whitehouse MR, Lenguerrand E, Blom AW, Beswick AD, Inform Team. Re-infection outcomes following one- and two-stage surgical revision of infected knee prosthesis: A systematic review and meta-analysis. PloS one 11: e0151537, 2016
13. Kunutsor SK, Wylde V, Beswick AD, Whitehouse MR, Blom AW. One- and two-stage surgical revision of infected shoulder prostheses following arthroplasty surgery: A systematic review and meta-analysis. Scientific Reports, 2018 (In Press)
14. Kunutsor SK, Whitehouse MR, Blom AW, Board T, Kay P, Wroblewski BM, Zeller V, Chen SY, Hsieh PH, Masri BA, Herman A, Jenny JY, Schwarzkopf R, Whittaker JP, Burston B, Huang R, Restrepo C, Parvizi J, Rudelli S, Honda E, Uip DE, Bori G, Munoz-Mahamud E, Darley E, Ribera A, Canas E, Cabo J, Cordero-Ampuero J, Redo MLS, Strange S, Lenguerrand E, Gooberman-Hill R, Webb J, MacGowan A, Dieppe P, Wilson M, Beswick AD, Global Infection Orthopaedic Management C. One- and two-stage surgical revision of peri-prosthetic joint infection of the hip: a pooled individual participant data analysis of 44 cohort studies. Eur J Epidemiol 33: 933, 2018
15. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB, Group ftM-aOOSiE. Meta-analysis of Observational Studies in Epidemiology. JAMA: The Journal of the American Medical Association 283: 2008, 2000
16. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 6: e1000097, 2009
17. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. ANZ J Surg 73: 712, 2003
18. Freeman MF, Tukey JW. Transformations Related to the Angular and the Square Root. Ann Math Statist: 607, 1950

19. Ferrao P, Myerson MS, Schuberth JM, McCourt MJ. Cement spacer as definitive management for postoperative ankle infection. Foot Ankle Int 33: 173, 2012
20. Kessler B, Knupp M, Graber P, Zwicky L, Hintermann B, Zimmerli W, Sendi P. The treatment and outcome of peri-prosthetic infection of the ankle: a single cohort-centre experience of 34 cases. Bone Joint J 96-B: 772, 2014
21. Kotnis R, Pasapula C, Anwar F, Cooke PH, Sharp RJ. The management of failed ankle replacement. J Bone Joint Surg Br 88: 1039, 2006
22. Myerson MS, Shariff R, Zonno AJ. The management of infection following total ankle replacement: demographics and treatment. Foot Ankle Int 35: 855, 2014
23. Patton D, Kiewiet N, Brage M. Infected Total Ankle Arthroplasty: Risk Factors and Treatment Options. Foot & Ankle International 36: 626, 2015
24. Lachman JR, Ramos JA, DeOrio JK, Easley ME, Nunley JA, Adams SB. Outcomes of Acute Hematogenous Periprosthetic Joint Infection in Total Ankle Arthroplasty Treated With Irrigation, Debridement, and Polyethylene Exchange. Foot Ankle Int 39: 1266, 2018
25. Morrey BF, Bryan RS. Infection after total elbow arthroplasty. J Bone Joint Surg Am 65: 330, 1983
26. Park SE, Kim JY, Cho SW, Rhee SK, Kwon SY. Complications and revision rate compared by type of total elbow arthroplasty. J Shoulder Elbow Surg 22: 1121, 2013
27. Kasten MD, Skinner HB. Total elbow arthroplasty. An 18-year experience. Clin Orthop: 177, 1993
28. Kunutsor SK, Beswick AD, Whitehouse MR, Wylde V, Blom AW. Debridement, antibiotics and implant retention for periprosthetic joint infections: A systematic review and meta-analysis of treatment outcomes. J Infect, 2018
29. Buckley PS, Raikin SM. Operative Treatment of Infections in the Foot and Ankle. Operative Techniques in Orthopaedics 26: 45, 2016
30. Klouche S, El-Masri F, Graff W, Mamoudy P. Arthrodesis with internal fixation of the infected ankle. J Foot Ankle Surg 50: 25, 2011

Figure legends

Figure 1 PRISMA flow diagram

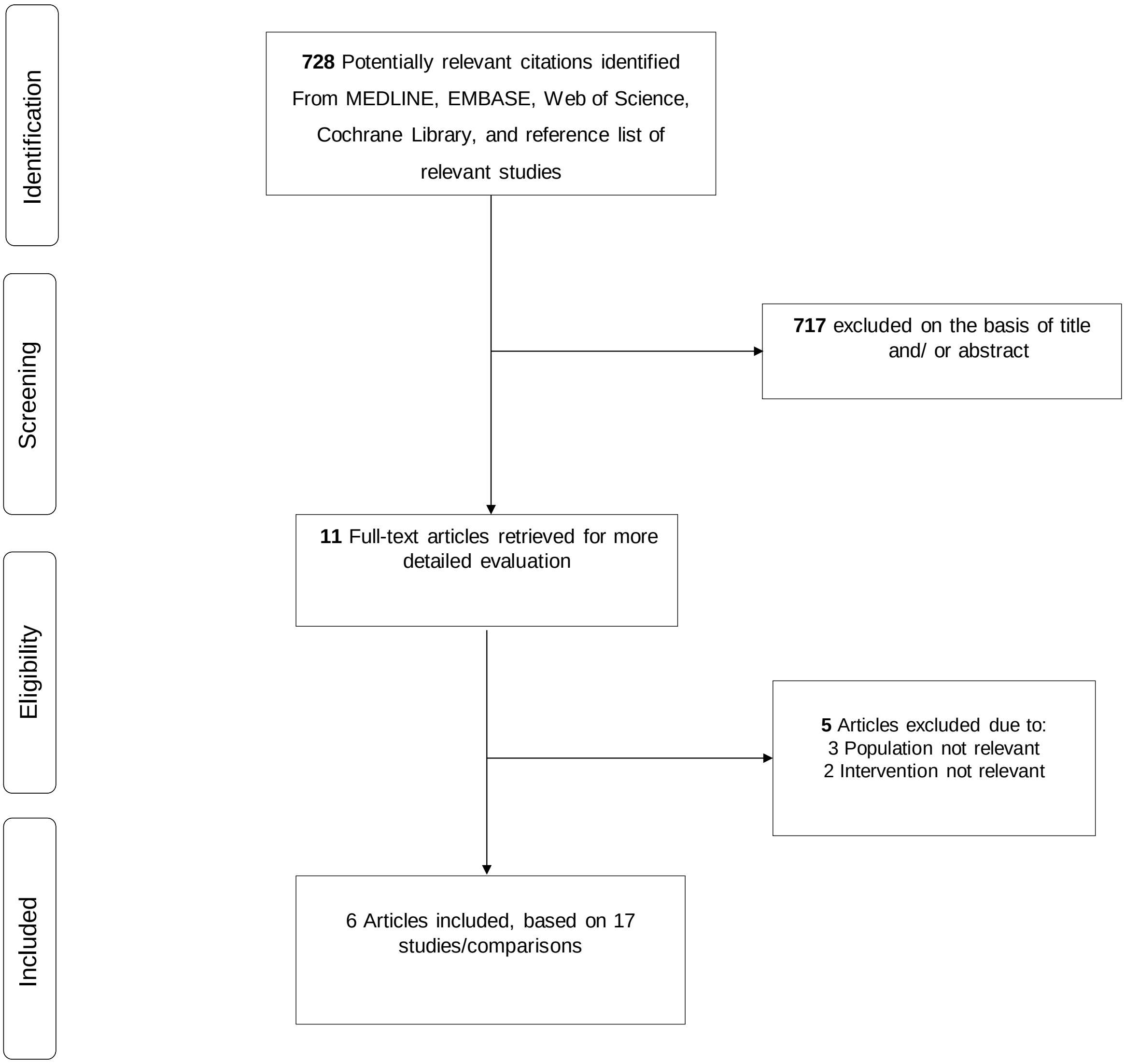
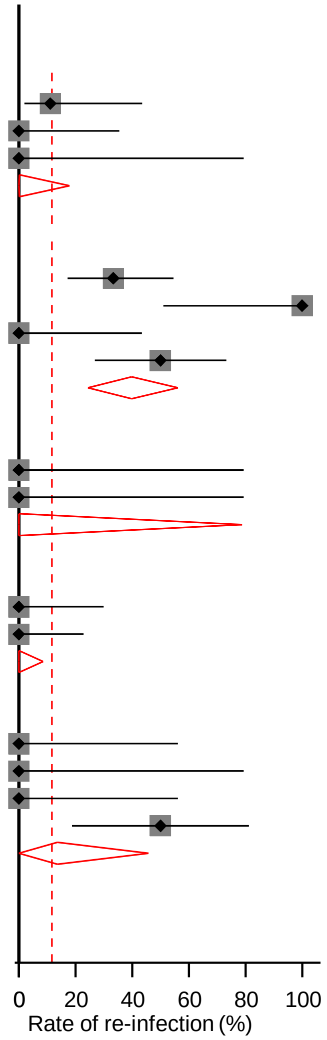


Figure 2 Rates of re-infection in infected ankle prostheses by treatment strategies

Author, year of publication	No. of re-infections	No. of participants/ infected ankle joints	Rate of re-infection (95% CI)
Cement spacer			
Ferrao, 2012	1	9	11.1 (2.0, 43.5)
Myerson, 2014	0	7	0.0 (0.0, 35.4)
Patton, 2015	0	1	0.0 (0.0, 79.3)
Subtotal			0.2 (0.0, 17.9)
DAIR with/without polyethylene exchange			
Kessler, 2014	7	21	33.3 (17.2, 54.6)
Myerson, 2014	4	4	100.0 (51.0, 100.0)
Patton, 2015	0	5	0.0 (0.0, 43.4)
Lachman, 2018	7	14	50.0 (26.8, 73.2)
Subtotal			39.8 (24.4, 56.1)
One-stage revision			
Kessler, 2014	0	1	0.0 (0.0, 79.3)
Patton, 2015	0	1	0.0 (0.0, 79.3)
Subtotal			0.0 (0.0, 78.7)
Two-stage revision			
Kessler, 2014	0	9	0.0 (0.0, 29.9)
Patton, 2015	0	13	0.0 (0.0, 22.8)
Subtotal			0.0 (0.0, 8.5)
Arthrodesis			
Kessler, 2014	0	3	0.0 (0.0, 56.1)
Kotnis, 2006	0	1	0.0 (0.0, 79.3)
Patton, 2015	0	3	0.0 (0.0, 56.1)
Myerson, 2014	3	6	50.0 (18.8, 81.2)
Subtotal			13.6 (0.0, 45.8)



CI, confidence interval (bars); DAIR, debridement and implant retention of the prosthesis

Table 1. Baseline characteristics of individual studies included in review

Lead author, publication date	Location	Year of study	Mean/median age (years)	% male	Mean/median follow-up (years)	No. of re-infections	No. of non-infection related adverse events	Conversion to arthrodesis	Amputation	No. of participants or ankles	Function outcome post-intervention	Pain outcome post-intervention	Satisfaction outcome post-intervention	Quality score
DAIR with or without polyethylene exchange														
Kessler, 2014	Switzerland	2006-2011	62.1*	14.0*	2.6*	7	NR	3	1	21	NR	NR	14 patients who were infection free had satisfactory function	11
Myerson, 2014	USA	2002-2011	65.5*	58*	2.2*	4	NR	1	NR	4	NR	NR	NR	10
Patton, 2015	USA	1995-2012	54.5*	53*	4.6*	0	NR	NR	NR	5	NR	NR	NR	8
Lachman, 2018	USA	2005-2015	60.9	35.7	2.8	7	NR	4	1	14	SMFA Function, SF-36 Physical, and AOFOS Hindfoot scores were comparable to preoperative primary TAR scores	FAOS Pain score comparable to pre-intervention score	SF-36 Mental and Bother were comparable to pre-intervention scores	11
One-stage revision surgery														
Kessler, 2014	Switzerland	2006-2011	62.1*	14.0*	2.6*	0	NR	NR	NR	1	NR	NR	NR	11
Patton, 2015	USA	1995-2012	78	0	4.6*	0	NR	NR	NR	1	NR	NR	NR	8
Two-stage revision surgery														
Kessler, 2014	Switzerland	2006-2011	62.1*	14.0*	2.6*	0	NR	NR	NR	9	NR	NR	NR	11
Patton, 2015	USA	1995-2012	60.6	61.5	2.6*	0	NR	NR	NR	13	NR	NR	NR	8
Implantation of antibiotic-loaded cement spacer														
Ferrao, 2012	USA	2004-2009	63.3	66.7	Up to 4.3 years	1	2	NR	2	9	7 patients with spacer insitu mobilized full weight bearing	7 patients with spacer insitu had no or occasional mild pain	7 patients had spacer insitu at final follow-up and were satisfied with outcome	9

Lead author, publication date	Location	Year of study	Mean/median age (years)	% male	Mean/median follow-up (years)	No. of re-infections	No. of non-infection related adverse events	Conversion to arthrodesis	Amputation	No. of participants or ankles	Function outcome post-intervention	Pain outcome post-intervention	Satisfaction outcome post-intervention	Quality score
Myerson, 2014	USA	2002-2011	65.1%	100	1.1	0	2	NR	NR	7	NR	NR	NR	10
Patton, 2015	USA	1995-2012	65	100	4.6*	0	NR	NR	NR	1	NR	NR	NR	8
Arthrodesis														
Kotnis, 2006	UK	1999-2004	52.0	0.0	NR	0	NR	NA	NR	1	NR	NR	NR	9
Kessler, 2014	Switzerland	2006-2011	62.1*	14.0*	2.6*	0	NR	NA	NR	3	None of the 3 patients had intact function	NR	NR	11
Myerson, 2014	USA	2002-2011	63.7	50.0	2.2*	3	NR	NA	3	6	NR	NR	NR	10
Patton, 2015	USA	1995-2012	50.3	33.3	4.6*	0	NR	NA	NR	3	NR	NR	NR	8

*, for all participants; AOFAS, American Orthopaedic Foot and Ankle Society score; DAIR, debridement and implant retention; FAOS, Foot and Ankle Outcomes Score; Short Form–36; SMFA, Short Musculoskeletal Function Assessment; NA, not applicable; NR, not reported; TAR, total ankle replacement