

CADTH Health Technology Review

Custom-Made Foot Orthotics for People With Lower Limb Conditions

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Abbreviations

DFU	diabetic foot ulcer
GP	general practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ICER	incremental cost-effectiveness ratio
IWGDF	International Working Group on the Diabetic Foot
PEDro	Physiotherapy Evidence Database
QALY	quality-adjusted life-years
RCT	randomized controlled trial

Key Messages

- There were no statistically significant differences between custom-made foot orthotics and prefabricated foot orthotics for plantar heel pain in adults.
- There is limited evidence for short-term pain relief and improved quality of life with custom-made orthotics compared to placebo or no intervention in adults with plantar fasciitis.
- Custom-made foot orthotics are less cost-effective than other interventions (placebo, prefabricated orthotics, usual care) in the short and medium term.
- Two evidence-based guidelines recommended the use of custom-made foot orthotics in patients with diabetes for prevention and treatment of foot ulceration.

Context and Policy Issues

In patients with systemic diseases such as pronated foot, plantar heel pain, rheumatoid arthritis, juvenile idiopathic arthritis, diabetic plantar ulceration, or hallux valgus, the morbidity of the lower limb is compromised. As a result, patients will experience pain, impairment, disability, and reduction in foot function and quality of life.^{1,2} The complications associated with these conditions place the lower limb at risk of infection, deformity, and amputation.² Foot orthotics (also referred to as orthoses) are shoe inserts that are designed to provide proper cushioning, arch support, and corrective biomechanics in people with these conditions.³ Although foot orthotics are sometimes referred to as insoles, these are specialized insoles with a treatment effect for specific foot disorders, as opposed to standard insoles.⁴

Foot orthotics fall under the broader category of conservative, nonsurgical offloading interventions.^{5,6} These are external devices specifically designed to offload local stress, thus relieving mechanical pressure from specific regions of the foot. Foot orthotics vary across different parameters, including materials, design and construction, and customization.³ The most common types are custom-made and prefabricated.⁷ Customized-foot orthotics are uniquely manufactured for the individual from a plaster cast or 3-dimensional laser scan of the foot. These contrast with prefabricated foot orthotics (also referred to as “over-the-counter”), which are mass-produced based on foot sizes.⁷ Other conservative interventions for foot conditions are available, such as magnetized insoles (cushioned insoles with magnetic foil embedded in the foam under the proximal arch),⁸ prefabricated heel lifts,⁹ and resting night splints (braces that hold the foot in place, with the toes pointed up).¹

Custom-made orthotics improve plantar pressure redistribution and gait mechanics^{8,10,11} However, a 2020 CADTH report¹² found inconsistencies regarding the effectiveness of customized or prefabricated foot orthotics compared to control interventions (standard insole, placebo, or none) in alleviating pain and improving foot function in patients with chronic foot pain. Another CADTH¹³ report from 2019 found no difference between custom-made and prefabricated foot orthotics for pain reduction or functional improvement, based on a limited amount of evidence. Neither CADTH report included evidence of cost-effectiveness.

Health insurance plans may cover custom-made foot orthotics to treat diagnosed medical conditions. To ensure that these policies are evidence-based, the objective of this report is to summarize the evidence on the clinical effectiveness of custom-made orthotics for the treatment of people with lower-limb conditions. As custom-made orthotics can be more costly than other conservative options, another objective is to summarize the evidence on

their cost-effectiveness. Additionally, evidence-based guidelines regarding the use of custom-made foot orthotics were sought.

Research Questions

1. What is the clinical effectiveness of custom-made foot orthotics for the treatment of people with lower limb conditions?
2. What is the cost-effectiveness of custom-made foot orthotics for the treatment of people with lower limb conditions?
3. What are the evidence-based guidelines regarding the use of custom-made foot orthotics for the treatment of people with lower limb conditions?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept was custom-made foot orthoses. No filters were applied to limit the retrieval by study type. A separate search was conducted for guidelines, health technology assessments, systematic reviews, meta-analyses, or network meta-analyses on foot orthoses. Comments, newspaper articles, editorials, and letters were excluded. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2017, and January 6, 2022.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, or if they were duplicate publications. Economic evaluations or evidence-based guidelines published before 2017 were excluded. Systematic reviews and randomized controlled trials (RCTs) that were published before 2020 were excluded. Systematic reviews in which all relevant studies were captured in other, more recent or more comprehensive, systematic reviews were excluded.¹⁴⁻²⁰ Primary studies retrieved by the search were excluded if they were captured in 1 or more included systematic reviews.²¹

Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the following tools as a guide: A MeaSurement Tool to Assess Systematic Reviews 2²² for systematic reviews, the Downs and Black checklist²³ for randomized studies, the Drummond checklist²⁴ for economic evaluations, and the Appraisal of Guidelines for Research and Evaluation II instrument²⁵ for guidelines. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 622 citations were identified in the literature search. Following screening of titles and abstracts, 543 citations were excluded and 79 potentially relevant reports from the electronic search were retrieved for full-text review. Ten potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially 89 relevant articles, 74 publications were excluded for various reasons, and 14 publications met the inclusion criteria and were included in this report. These comprised 6 systematic reviews, 5 RCTs, 1 economic evaluation, and 2 evidence-based guidelines. Appendix 1 presents the PRISMA²⁶ flow chart of the study selection.

Additional references of potential interest are provided in Appendix 6.

Summary of Study Characteristics

Six systematic reviews,^{1,5,7,8,27,28} 5 RCTs,^{9,29-32} 1 economic evaluation,³³ and 2 evidence-based guidelines^{34,35} were included in this report.

Table 1: Selection Criteria

Criteria	Description
Population	People with lower limb conditions (e.g., plantar fasciitis, diabetic foot ulcers, Charcot foot, hallux valgus, metatarsal amputation, clubfoot, rheumatoid arthritis)
Intervention	Custom-made foot orthotics (also known as custom-made insoles or custom-made shoe inserts)
Comparator	Q1 to Q2: Alternative interventions (e.g., prefabricated foot orthotics, off-the-shelf foot orthotics, off-the-shelf shoe inserts); no treatment with custom-made foot orthotics (i.e., use of regular footwear) Q3: Not applicable
Outcomes	Q1: Clinical effectiveness (e.g., pain, functionality, quality of life, disability, amputations, safety [e.g., rates of adverse events]) Q2: Cost-effectiveness (e.g., cost per quality-adjusted life-year gained) Q3: Recommendations regarding best practices (e.g., appropriate patient populations, recommended types or features of custom-made foot orthotics, guidance on the replacement of custom-made foot orthotics)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, economic evaluations, evidence-based guidelines

The 6 systematic reviews^{1,5,7,8,27,28} had broader inclusion criteria considered than the present review. Specifically, the systematic reviews investigated other types of mechanical or offloading devices (e.g., orthopedic footwear, shoes with heel lifts, taping, ankle-foot orthoses, fibreglass heel cast)^{1,7,8,27,28} or other interventions (e.g., dermal infrared thermometry, education, extracorporeal shockwave therapy, physiotherapy, stretching).^{5,7,8} Two systematic reviews also included non-randomized studies.^{1,7} Only the subset of primary RCTs meeting the inclusion criteria is presented in this report. There was some overlap in the studies included in the systematic reviews and the degree of overlap is summarized in Appendix 5.

The 2 guidelines also addressed a broader group of interventions than this report. The interventions were offloading devices³⁵ and footwear.³⁴ Only the recommendations on custom-made orthotics are presented within this report. The guideline by Bus et al.³⁵ reported its methodology in a separate publication,³⁶ which was used to supplement the information summarized in this report.

Additional details regarding the characteristics of the included publications are provided in Appendix 2.

Study Design

Of the 6 systematic reviews,^{1,5,7,8,27,28} 1 included meta-analyses.⁸ The number of relevant primary studies included in the systematic reviews ranged between 1 and 8 RCTs. The latest literature search dates were between March 2018 and August 2020.

Of the 5 included RCTs,^{9,29-32} 2 trials were double blinded (participants, investigators, and assessors were blinded),^{31,32} 2 trials were single blinded (participants or investigators and assessors were blinded)^{9,29} and 1 trial was unblinded.³⁰ Two RCTs were conducted at multiple centres,^{29,32} and 3 were conducted at a single clinic.^{9,30,31}

The systematic review by Clarke et al.²⁸ included 2 relevant health economic evaluations: 1 cost-effectiveness analysis and 1 cost-effectiveness analysis plus a cost-utility analysis. Both economic evaluations conducted parallel clinical trials, with time horizons of 8 weeks and 16 weeks. One took the perspective of the health care payer, and the other took the perspectives of the health care payer and patient.

The included economic evaluation³³ was conducted as cost-utility analyses, with a time horizon of 16 weeks. The study used an imputation model; and clinical, cost, and utility inputs were derived from a published RCT (included in this report)³² of custom-made foot orthotics compared to usual care (i.e., no foot orthosis), and the perspectives of health care payers and society were taken. Model parameters included patient characteristics, activity level, and bilateralism of pain. Assumptions were made about absenteeism from paid work and lost productivity.

The 2 evidence-based guidelines^{34,35} were informed by systematic reviews of the literature and included recommendations that were drafted using various consensus-generating methods. Both guidelines^{34,35} were updates to previously published versions and included updated evidence and recommendations.

The guideline by van Netten et al.,³⁴ which was developed by Diabetic Foot Australia, used a systematic approach but did not follow a specific guideline development methodology or assess the quality of the evidence. The authors commented that many recommendations

were predominantly based on expert opinion and standard of practice due to limited available evidence and might be seen as “good practice statements.”

The guideline by Bus et al.³⁵ was developed by the International Working Group on the Diabetic Foot (IWGDF), using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology for guideline development. The strength of the recommendations was scored as either strong or weak, based on the quality of evidence, balance between desirable and undesirable effects, values and preferences, resources, and costs, according to the GRADE framework. The quality of the evidence informing the recommendations was graded on study design (classified using the Scottish Intercollegiate Grouping Network criteria), risk of bias, inconsistency of results, publication bias, and presence of a large effect size and/or dose-response relationship.

Country of Origin

The first authors of the systematic reviews were from Australia,²⁸ Brazil,⁷ Spain,²⁷ the Netherlands,¹ and the UK.^{5,8}

The RCTs were conducted in and enrolled patients from Australia,²⁹ Brazil,³⁰ Spain,^{9,31} and the Netherlands.³²

The economic evaluation³³ was conducted in and used data collect from the Netherlands.

The guidelines were intended for use in Australia³⁴ and worldwide.³⁵ The members of the IWGDF guideline group were from 40 countries and 5 continents, and recruited representatives from more than 100 countries around the world to help implement the recommendations.³⁵

Patient Population

Two systematic reviews^{1,8} included patients with plantar fasciitis; 1 review reported on patients with type 1 or type 2 diabetes at risk of foot ulceration;⁵ 1 review reported on people with posterior tibial tendon dysfunction (flatfoot);²⁷ and 2 systematic reviews^{7,28} included patients with various lower limb conditions,⁷ such as rheumatoid arthritis,²⁸ cavus foot,⁷ and flatfoot.⁷ The number of participants in the relevant RCTs included in these systematic reviews ranged from 15 to 400.

Four systematic reviews^{1,5,7,8,27} reported the mean ages in the included RCTs, which ranged from 22 years to 69 years. Two systematic reviews^{7,28} did not report the age of participants in the included studies. The proportion of females varied across studies, ranging from 23% to 89%.

Adult populations were investigated in 3 RCTs, and included people with plantar fasciitis³¹ and rheumatoid arthritis.^{30,32} The number of enrolled participants ranged from 83 to 185, the mean ages varied between 37 and 57 years, and the proportion of females ranged between 54% and 89%. The mean duration of the pain or condition was 6 months in 1 RCT,³² 17 months in the second RCT,³¹ and 11 years in the third RCT.³⁰

Two RCTs investigated pediatric populations, and enrolled children with calcaneal apophysitis (Sever disease)⁹ or with juvenile idiopathic arthritis.²⁹ The number of enrolled children was 66 and 208; the mean ages were 11 and 12 years; and the proportion of females was 17% and 68%. The mean disease duration was 6.5 years in 1 RCT²⁹ and not reported in the other RCT.⁹

Participants in the economic evaluation³³ were the same study population (adults with plantar fasciitis) in the RCT by Rasenberg et al.³²

The target population of the 2 guidelines^{34,35} was people with diabetes at various risk levels of foot ulceration, and the intended users were the clinicians and/or other health care providers who care for these patients.

Interventions and Comparators

In the systematic reviews, the relevant interventions were described as custom-made foot orthotics,²⁸ custom orthoses,⁸ custom or customized insoles,^{1,5,7} customized inserts,⁵ and computer-aided design/computer-aided manufactured insoles (in which computer software was used for designing and producing these custom-made insoles).²⁷ In the RCTs, the interventions were customized preformed foot orthoses,^{29,31} custom-made foot orthoses,^{9,30} and custom insoles.³² For consistency, this report uses the term “custom-made foot orthotics” to refer to these interventions.

Two systematic review^{5,7} provided details about the custom-made orthotics in the included RCTs (e.g., individually moulded ethylene-vinyl acetate insoles with a longitudinal medial arch and heel support⁷; full contact insoles made in ethylene-vinyl acetate and moulded in a negative cast plaster⁷; bespoke orthoses with offloading properties⁵; and customized medium-density cork inserts with a neoprene closed-cell cover).⁵

The comparators in the included systematic reviews and RCTs were prefabricated foot orthotics,^{1,8,27,28} prefabricated heel lifts,⁹ no orthoses (i.e., own footwear^{1,5,30,32} or standard/usual care),^{5,7,32} anterior night splints,¹ and placebo intervention.^{1,5,7,8,27-29,31,32} The placebo intervention consisted of sham insoles (i.e., flat, thin, simple insoles), and its purpose is not to provide no effect, as a true placebo does, but to not provide the main therapeutic element of the custom-made orthotics so as to have minimal impact on the lower limb condition.⁴

In the systematic reviews, the length of time that participants were assigned to the intervention or comparator varied widely, and ranged from a single laboratory visit¹ to 2 years.⁵ In the RCTs, the duration for wearing the intervention or comparator ranged from 4 weeks³⁰ to 1 year.²⁹ In this report, short-term duration is defined as up to 3 months, medium-term duration is between 3 months and 6 months, and long-term duration is more than 6 months.

The economic evaluation³³ examined the cost-effectiveness of custom-made foot orthotics versus usual care led by a general practitioner (GP) after 16 weeks.

Recommendations regarding custom-made orthotics were included in the 2 guidelines.^{34,35}

Outcomes

The clinical effectiveness outcomes reported in the selected systematic reviews included pain,^{1,7,8,27,28} foot function,^{1,7,8} disability,²⁸ health-related quality of life,^{1,28} recurrence of diabetic foot ulcer (DFU).⁵ The RCTs also reported pain,^{9,29-32} foot function,^{30,31} disability,^{29,30} and quality of life.^{29,32}

Pain, foot function, disability, and quality of life were measured in the primary studies of the systematic reviews and RCTs by scores on various patient-reported assessment tools. A frequently used measure of pain severity was the visual analogue scale, a numerical scale with marked points along a 10 cm long horizontal line where 0 equalled no pain and 10 equalled unbearable pain.^{1,8,9,27,29,31} Functionality was measured by the Foot Function Index,

a questionnaire divided into different domains for pain, disability, and functional limitation; with higher values corresponding to higher pain, disability, and limitation.^{1,8,28,30,32} The Foot Health Status Questionnaire was used to measure foot pain and quality of life.^{7,8} One study also used the Numeric Rating Scale to measure foot pain on an 11-point scale from 0 to 10, where higher values indicated better outcomes.³² The Foot and Ankle Outcome score was used to measure function and quality of life, where higher scores indicated optimal foot health.¹ One RCT³¹ used the Roles and Maudsley scale to assess functional valuation. The scale classified the patients into 4 categories, where a score of 1 corresponded to a patient with an excellent quality of life (no symptoms, unlimited walking ability without pain, patient satisfied with the treatment outcome); a score of 2 corresponded to good quality of life; a score of 3 to acceptable quality of life; and a score of 4 to a patient with the worst quality of life possible. The questionnaire contained 8 questions that cover 3 domains of pain, function, and activity, and scores were summated to give a total score out of 100, where higher scores indicated less severe Achilles tendinopathy. The RCT by Fellas²⁹ assessed foot and ankle disability in children with idiopathic rheumatoid arthritis using the Juvenile Arthritis Foot ankle disability index. The 27-item questionnaire is divided into 3 main components: physical impairment, activity limitation, and participation restriction. This study also assessed quality of life using the Pediatric Quality of Life Inventory- Rheumatology Module.²⁹ The Mental Health Component of the Short Form-12 questionnaire was used to collect data about quality of life, with higher values corresponding to lower quality of life.³² The systematic review by Mendes et al.⁷ did not report how pain and function were assessed.

The economic evaluations in the systematic review by Clarke et al.²⁸ and by Rasenberg et al.³³ calculated the benefits and costs of custom-made foot orthotics compared to an alternative intervention. The economic evaluation by Rome et al.²⁸ used the generic preference-based outcome measure EQ-5D to produce utility values that were used to calculate quality-adjusted life-years (QALYs) for each intervention. The economic evaluation by Rasenberg et al.³³ calculated the incremental cost-effectiveness ratio (ICER), expressed as ratios of incremental cost incurred per QALY gained, to compare custom-made orthotics versus standard care.

For the 2 guidelines, the outcomes considered by the guideline panels were DFU prevention and recurrence,^{34,35} harms (adverse events),³⁵ and costs.³⁵

Summary of Critical Appraisal

An overview of the critical appraisal of the included publications is summarized in the following text. Additional details regarding the strengths and limitations of the included publications are provided in Appendix 3.

Systematic Reviews

In the 6 selected systematic reviews,^{1,5,7,8,27,28} the objective and inclusion criteria were clearly stated; a literature search was conducted using multiple databases; the selection of articles was described and a flow chart presented; a list of the included primary studies was presented; and the characteristics of the included studies were described. Providing details of the literature search strategy increases the reproducibility of the review. Five systematic reviews registered their study protocol in PROSPERO.^{5,7,8,27,28} One systematic review¹ did not report whether a protocol had been published before the conduct of the review; therefore, it is unknown whether any significant protocol deviations occurred that may impact the interpretation of the findings of this systematic review.¹

Study selection was done independently by 2 reviewers for 2 systematic reviews,^{5,27} and by 1 reviewer for 2 other systematic reviews.^{1,28} Two other 2 systematic reviews^{7,8} only reported on title and abstract screening, but did not report the approach for full-text screening. Data extraction was done by 2 reviewers in 2 systematic review,^{5,27} and 1 review in 1 systematic review.²⁸ However, in 3 systematic reviews, it was unclear how data extraction was done.^{1,7,8} Therefore, the potential for errors in data extraction is unknown. A list of excluded studies was not presented in any of the reviews. In the absence of justifications for excluding studies, it is unclear if the selection process captured all the relevant studies.

The quality of the included studies was assessed in all 6 systematic reviews.^{1,5,7,8,27,28} Three systematic reviews^{1,5,27} used the Cochrane Risk of Bias tool to assess risk of bias. In the systematic review by Gomez-Juardo et al.,²⁷ the included trial had 3 domains assessed as high risk of bias using the Cochrane tool. In the systematic review by Crawford et al.,⁵ 3 included trials were judged to be high risk and 1 trial was judged to be low risk of bias on the Cochrane tool. In the systematic review by Schuitema et al., the included studies had 1 or more domains assessed as high risk of bias on the Cochrane Risk of Bias tool.¹ One systematic review⁷ used the Physiotherapy Evidence Database (PEDro) scale, and the included trials were given a score of 7 out of 10 to 9 out of 10, where a higher score equalled greater quality. In the systematic review by Morrissey et al.,⁸ RCTs were evaluated using both the PEDro scale and the Cochrane Risk of Bias tool. The relevant RCTs scored 8 out of 10 or 9 out of 10 on the PEDRO scale. These same RCTs were assessed as low risk on the Cochrane tool, with the exception of 1 RCT, which had some concerns due to selective reporting.⁸ The PEDro scale and Cochrane tool have been shown to be valid, reliable, and frequently used tools for assessing methodological quality and risk of bias.

In the systematic review of health economic evaluations,²⁸ the extended version of the Consensus on Health Economic Criteria was used to assess risk of bias in individual studies. The 2 included economic evaluations used appropriate designs, perspectives, and benefits; however, methodological issues were identified, such as, intervention groups that differed on clinical factors that would likely have influenced the benefit outcome, sample sizes that were too small, time horizons that were too short, limitations in the model input data, and the absence of sensitivity analyses to manage uncertainty.²⁸

Meta-analyses were conducted in the systematic review by Morrissey et al.,⁸ and were appropriate. In the systematic review by Crawford et al.,⁵ meta-analyses were also conducted; however, data on custom-made foot orthotics was pooled with orthopedic footwear (i.e., shoes) and non-custom-made orthotics. Therefore, only data from the individual studies (and not the meta-analyses) has been included in this report.

In 5 systematic reviews,^{5,7,8,27,28} the authors reported that there were no conflicts of interest. In 1 systematic review,¹ conflicts of interest were not reported.

Randomized Controlled Trials

In the 5 selected RCTs,^{9,29-32} the objective, selection criteria, patient characteristics, interventions, and outcomes were described. The method of randomization was described and was appropriate in 4 RCTs²⁹⁻³² and was not described in 1 RCT.⁹ In 2 RCTs,^{31,32} both the investigator and the participants were blinded. In 1 RCT,²⁹ the participants were blinded but the investigators were not; in another RCT,⁹ the investigators and assessors were blinded but the participants were not; and in 1 RCT,^{30,37-40} there was no blinding. Lack of blinding

has the potential of introducing detection and performances biases, as the outcomes were mainly subjective.

Sample size calculations were undertaken in all 5 RCTs,^{9,29-32} and the appropriate number of participants were recruited in 4 trials.^{9,29,31,32} In the fourth trial,³⁰ the necessary sample size was not achieved, which reduced the statistical power to extrapolate the results to the overall population.

In 3 RCTs,^{9,31,32} the discontinuation in each treatment group was less than 10%; therefore, unlikely to introduce attrition bias. In 2 RCTs,^{29,30} the discontinuation rates in the intervention and control groups ranged between 11% and 18%; therefore, there is potential for attrition bias, but the direction of impact is unclear. The reasons for discontinuation were mainly loss to follow-up, unwillingness to wear orthotics, or personal reasons (e.g., medical emergency unrelated to intervention).

The authors reported that there were no conflicts of interest in for any of the 5 RCTs.^{9,29-32}

Economic Evaluation

The economic evaluation³³ had the following strengths: the research question and its economic importance were stated; sources of clinical effectiveness estimates, primary outcome, details of the imputation model, and methods for the estimation of unit costs were described; the time horizon and details of statistical tests and sensitivity analyses were given; the incremental analysis was reported; conclusions were given; and the authors stated that they had no conflicts of interest. The economic evaluation³³ also had the following limitations: the sample size was insufficient to show statistically significant differences; and the discount rate and current price adjustments for inflation were not provided.

Evidence-Based Guidelines

The 2 guidelines^{34,35} provided a clear description of their scope and purpose. Overall objectives, health questions covered in the guideline, target population, and target users were described. The guideline development groups included individuals from all relevant professional groups, as well as the views and perspectives of patients. In both guidelines,^{34,35} the systematic methods used to identify evidence and the selection criteria were described. The explicit link between evidence and recommendations was clearly described. The recommendations were unambiguous and easy to identify. A procedure for updating the evidence base and recommendations was described. The guidelines were externally reviewed by stakeholders and experts before publication.^{34,35}

The overall strengths and limitations of the evidence and the methods for formulating and developing the recommendations were reported in both guidelines.^{34,35} The IWGDF guideline rated the strength of the recommendations using the GRADE system and rated the quality of the evidence using the Scottish Intercollegiate Grouping Network criteria³⁵; but the Diabetic Foot Australia guideline did not rate the strength of the recommendations nor the quality of the evidence supporting the recommendations.³⁴

The 2 guidelines^{34,35} described the facilitators and barriers to the implementation of the recommendations and addressed the potential resource implications. The IWGDF guideline provided monitoring criteria,³⁵ but the Diabetic Foot Australia guideline did not.³⁴ Finally, while the funding sources did not influence the recommendations in the IWGDF guideline,³⁵ this was unclear in the Diabetic Foot Australia guideline.³⁴

Summary of Findings

Clinical Effectiveness of Custom-Made Foot Orthotics

The main findings from the included systematic reviews are summarized in the following sections and Appendix 4. There was some overlap in the primary studies that were included in the systematic reviews; therefore, to avoid duplication of reporting, outcomes data from an individual RCT is reported only once as part of 1 systematic review. If study outcomes were included in the meta-analyses by Morrissey et al.,⁸ they are reported only in the pooled estimates (and not the individual study level results). A citation matrix illustrating the degree of overlap is presented in Appendix 5.

Foot Pain in Adults

There was no statistically significant difference in foot pain with custom-made orthotics compared to prefabricated orthotics reported by the 5 RCTs included in the 3 systematic reviews.^{1,8,27} Four trials were conducted in adults with plantar fasciitis^{1,8} and 1 study in adults with flatfoot.²⁷ In general, both custom-made and prefabricated orthotics caused pain to decrease in these studies; but no statistically significant differences were found between groups.^{1,8,27}

The meta-analysis by Morrissey et al.⁸ showed a statistically significant effect on foot pain with custom-made foot orthotics versus sham orthotics in the short term (i.e., up to 3 months) in people with plantar fasciitis. However, there was moderate statistical heterogeneity. In the same systematic review,⁸ 1 RCT found a statistically significant improvement in foot pain in the medium term (i.e., > 3 months and up to 6 months), and another RCT found no effect in the long term (i.e., > 6 months). Two RCTs in patients with plantar fasciitis^{27,31} also found a statistically significant improvement in short-term and medium-term pain with custom-made foot orthoses compared to sham insoles. However, 2 other trials in people with plantar fasciitis^{1,32} found no statistically significant difference in pain between custom-made orthotics and sham insoles in the short term. A trial that included patients with cavus foot⁷ found statistically significant improvement with custom-made foot orthoses compared to sham insoles (follow-up time not reported); but another RCT of patients with rheumatoid arthritis²⁸ found no statistically significant difference in pain between custom-made orthotics and sham insoles in the short term.

Compared to no orthotics, 2 trials reported that custom-made orthotics significantly reduced foot pain in the short term in patients with rheumatoid arthritis³⁰ and plantar fasciitis.³² However, 2 studies included in 2 systematic reviews^{1,7} reported no significant difference in function after wearing custom-made orthotics compared to no foot orthotics in the short term in people with plantar fasciitis,¹ or compared to standard care in the short term and long term in patients with flatfoot.⁷

One RCT in the systematic review by Schuitema et al.,¹ found no statistically significant difference between custom-made orthotics and night splints for pain due to plantar fasciitis. In another RCT included in the same systematic review,¹ people with plantar fasciitis were randomized to receive foot orthoses, foot orthoses and night splints, or night splints alone. At 1 year, pain reduction was statistically significantly higher in the 2 groups using custom-made foot orthoses compared to those in the anterior night splint only group.

Foot Pain in Children

One RCT⁹ reported that pain relief was statistically significantly higher with custom-made foot orthoses compared to prefabricated heel lifts in children with calcaneal apophysitis in

the short term. Another RCT²⁹ reported that pain was statistically significantly improved in children with idiopathic rheumatoid arthritis with custom-made foot orthoses compared to sham insoles in the short term, but there was no statistically significant difference in pain in the medium term or long term.

Foot Function in Adults

The effectiveness of custom-made orthotics versus prefabricated orthotics on foot function in people with plantar fasciitis was examined by 3 RCTs identified in 1 systematic review,⁸ which reported no significant difference in function in the short term and long term. However, 1 RCT³¹ reported a statistically significant improvement in foot function in the medium term in people with plantar fasciitis.

The meta-analysis by Morrissey et al.⁸ found no statistically significant difference in foot function with custom-made orthotics compared to placebo insoles in the short-term for plantar fasciitis. Two individual RCTs in the same review of people with plantar fasciitis⁸ also reported no statistically significant difference in the medium and long term. In the systematic review by Mendes et al.,⁷ 1 RCT of people with cavus foot reported statistically significant improvement in foot function with custom-made orthotics compared to sham insoles, and another RCT in the same review⁷ reported no significant difference in people with Achilles tendinopathy (follow-up times not reported). One RCT³² also reported that, compared to sham orthotics, there was no significant difference in foot function at 26 weeks in people with plantar fasciitis.

Two RCTs, 1 in adults with rheumatoid arthritis³⁰ and 1 in adults with plantar fasciitis³² reported statistically significant improvement in foot function with custom-made orthotics compared to no orthotics³⁰ or standard care.³²

One RCT included in the systematic review by Schuitema et al.,¹ reported no statistically significant difference in long-term foot function between custom-made foot orthoses and anterior night splints in people with plantar fasciitis.

Disability in Adults

The impact of custom-made orthotics on disability was assessed in 2 RCTs of adults with plantar fasciitis. In the RCT by Gaino et al.,³⁰ there was a statistically significant improvement in short-term disability with custom-made orthotics compared to simple insoles. The other RCT included in a systematic review²⁸ reported no statistically significant difference in short-term disability between custom-made orthotics and no foot orthotics.

Disability in Children

The RCT of children with idiopathic rheumatoid arthritis²⁹ reported no statistically significant improvement in disability with custom-made foot orthoses compared to sham insoles in the short term (3 months), medium term (6 months) or long term (1 year).

Quality of Life in Adults

One RCT of people with plantar fasciitis³² showed that custom-made orthotics resulted in a statistically significant improvement in short-term quality of life compared to sham insoles and compared to standard care. An RCT included in the systematic review by Schuitema et al.,¹ reported no statistically significant difference in long-term quality of life between custom-made foot orthoses and anterior night splints in people with plantar fasciitis.

Quality of Life in Children

The RCT of children with idiopathic rheumatoid arthritis²⁹ reported no statistically significant improvement in quality of life with custom-made foot orthoses compared to sham insoles in the short or medium term. There was an improvement in quality of life in the long term; however, this difference was only statistically significant when measured by parent-report and not statistically significant when self-reported by the children.²⁹

Recurrence of Diabetic Foot Ulcer

Four RCTs in 1 systematic review⁵ reported the effects of custom-made foot orthotics on the recurrence of DFU. One RCT⁵ found a reduction in DFUs at 15 months when compared to prefabricated foot orthotics. Two RCTs⁵ found a reduction in DFU rates at 1 year among participants who wore custom-made foot orthotics compared to no orthotics or usual care. The fourth RCT⁵ randomized patients with diabetes to 3 groups: therapeutic footwear with custom-made cork orthotics, therapeutic footwear with prefabricated polyurethane orthotics, and usual footwear. At 2 years, there was no statistically significant difference in ulcer relapse between the 3 groups.⁵

Safety

No systematic reviews or primary studies included adverse events as an outcome. However, 3 RCTs did report how many participants dropped out of the study due to negative effects of the trial interventions. The RCT by Fellas et al.²⁹ in children with idiopathic rheumatoid arthritis reported that 1 child (3%) in the custom-made foot orthotics group withdrew due to discomfort with the assigned orthotics. The child reported the presence of blistering shortly after wearing them and opted to withdraw from the study. The RCT by Cohena-Jimenez et al. of adults with plantar fasciitis³¹ reported that 1 adult (2%) in the custom-made foot orthotics group and 2 adults (5%) in the placebo orthotics group dropped out due to increased pain after 24 weeks. In the RCT by Gaino et al.,³⁰ 1 adult (2%) with rheumatoid arthritis in the custom-made orthotics group discontinued the intervention because that person could not adapt to using the orthotics due to the tightness of the footwear.

Cost-Effectiveness of Custom-Made Foot Orthotics

The systematic review by Clarke et al.²⁸ reported that custom-made foot orthotics were less cost-effective than simple insoles in people with rheumatoid arthritis, based on the cost-utility analysis by Rome et al. There was a small, statistically insignificant QALY loss of -0.03 when comparing custom-made orthotics to simple insoles, controlling for baseline utility. The simple insoles group was dominant, having an incremental gain in QALY at a lower cost compared to the custom-made orthotics group. That is, custom-made orthotics were far more expensive with no significant cost per QALY gain, in comparison to simple insoles. The same systematic review²⁸ also reported that custom-made foot orthotics were less cost-effective than prefabricated foot orthotics in people with heel pain, based on the cost-effectiveness analysis by Ring and Otter.²⁸ No ICER was reported in either economic evaluation.

The economic evaluation³³ reported that custom-made foot orthotics were not cost-effective in comparison to GP-led usual care in people with plantar fasciitis, with an ICER of € -150,548 per QALY gained from a health care payer perspective.

Guidelines

Prevention and Treatment of Diabetic Foot Ulcers

The 2 evidence-based guidelines^{34,35} made recommendations regarding the use of custom-made orthotics for people with diabetes. The IWGDF guideline³⁵ made a strong recommendation, based on low-quality evidence, for the use of therapeutic footwear in people with diabetes at moderate risk of DFU or with a healed non-plantar DFU, as well as the consideration of foot orthotics in people with foot deformity or pre-ulcerative signs. Another strong recommendation, based on moderate-quality evidence, was made in favour of therapeutic footwear (including custom-made foot orthotics) for people with a healed plantar DFU to help prevent recurrence.

The Diabetic Foot Australia guideline³⁴ also recommended custom-made foot orthotics for people with foot deformities or pre-ulcerative lesions, but the strength of the recommendation was not provided, and the quality of the evidence was not rated. The guideline³⁴ also recommend medical-grade footwear plus orthoses or insoles for people with healed plantar DFUs, based on 2 RCTs and alignment with IWDF recommendations; however, the strength of the recommendation and quality of evidence were not included. The Diabetic Foot Australia guideline³⁴ included a recommendation that health care providers review prescribed orthotics every 3 months for continued fit, protection, and support. This recommendation was based on 1 RCT and was aligned with the Australian National Health and Medical Research Council guideline.

Appendix 4 presents the main study findings and authors' conclusions.

Limitations

There are several limitations that prevent a definitive conclusion regarding the clinical effectiveness of custom-made foot orthotics for all patients with lower-limb conditions. Most of the included RCTs, as well as the economic evaluations, were limited by relatively small sample sizes: 65% of included trials involved fewer than 100 participants and a small percentage of studies (1%) had more than 200 participants. In the meta-analyses conducted by Morrissey et al.,⁸ there were between 214 and 254 adults in the pooled analyses. Results can be imprecise when studies include relatively few patients and few events.

There were also several reporting issues in the systematic reviews, such as inconsistent (or lack of) detail about the study population, settings, development of the custom-made orthotics (e.g., design, manufacturing, and adaption of orthotics to footwear or patient), interventions (e.g., characteristics, frequency of wearing orthotics), and findings (e.g., outcome data, effect sizes, P values). There was considerable heterogeneity among the RCTs identified in the systematic reviews^{1,5,7,8,27,28} in terms of customization of orthotics, application of cointervention (e.g., orthopedic footwear, exercise program, information booklets), duration of intervention, and assessment of outcomes. The risk of bias ranged from low to high for the RCTs in the included systematic reviews (as assessed by the systematic review authors).^{1,5,7,8,27,28} Common methodological limitations included unclear allocation concealment (selection bias), nonblinding of participants and personnel (performance bias), nonblinding of outcome assessment (detection bias), incomplete outcome data (attrition

bias), and selective reporting. Any quality issues from the primary studies causes uncertainty in the findings presented in the systematic review.

The 2 economic evaluations included in the systematic review by Clarke et al.²⁸ had time horizons shorter than 6 months, which is insufficient time to capture all material differences in costs and benefits, and may overstate the cost-effectiveness of less durable interventions (e.g., replacement of simple insoles) for people with long-term or chronic lower limb conditions. The systematic review authors²⁸ identified other limitations, including inadequate measurement of costs, no reporting of discounting, and no sensitivity analyses.

In the IWGDF guideline,³⁵ the level of evidence of the recommendations varied. The Diabetic Foot Australia guideline³⁴ did not assess the strength of their recommendations or the level of evidence. The studies making up the evidence base for the guideline recommendations were also small, with varying risks of bias.^{34,35}

Evidence on clinical effectiveness was available for people with the following conditions: plantar fasciitis,^{1,8,31} DFUs,⁵ rheumatoid arthritis,²⁸⁻³⁰ flatfoot,^{7,27} calcaneal apophysitis,⁹ cavus foot,⁷ and heel pain.³² Evidence on cost-effectiveness was available for people with rheumatoid arthritis²⁸ and heel pain.^{28,33} The included guidelines targeted people with diabetes.^{34,35} None of the selected primary studies or guidelines included people with Charcot foot, hallux valgus, gout, or metatarsal amputation. Also, no studies were identified that reported the effect of custom-made orthotics on amputation in people with lower-limb conditions.

None of the included systematic reviews or RCTs reported adverse events; as a result, this report focused on the benefits of custom-made orthotics. Without also assessing harms, results may be unbalanced and biased toward favouring the intervention.

One systematic review²⁸ reported the countries in which the included studies were conducted (England), but 5 systematic reviews^{1,5,7,8,27} did not report this information. The RCTs^{9,29-32} and economic evaluation³³ were not conducted in Canada. Similarly, the 2 included guidelines^{34,35} were not specifically intended for use in Canada, although the IWGDF guideline³⁵ was intended for worldwide use. Taken together, the generalizability of the findings and recommendations to the Canadian context are unknown because of substantial variations in health care systems and available resources for delivering health services across countries. The information provided in the included studies was also insufficient to determine the generalizability of the findings to populations belonging to specific geographical, ethnic, or cultural groups in Canada.

Conclusions and Implications for Decision- or Policy-Making

This review comprised 6 systematic reviews,^{1,5,7,8,27,28} 5 RCTs,^{9,29-32} 1 economic evaluation,³³ and 2 evidence-based guidelines.^{34,35} Most of the evidence included in this report pertained to adults with plantar fasciitis^{1,8,31-33} and diabetes mellitus.^{5,34,35}

Clinical Effectiveness of Custom-Made Foot Orthotics Compared to Prefabricated Orthotics in Adults

Evidence from meta-analyses⁸ and individual trials^{1,27} found no effect of custom-made orthotics compared to prefabricated foot orthotics on pain reduction and foot function in the short term and long term in adults with plantar fasciitis. Evidence on prevention of DFU recurrence with custom-made orthotics compared to prefabricated orthotics in the long term was conflicting;⁵ 1 trial with low risk of bias (according to systematic review authors)⁵ reported long-term reduction in DFU recurrence with custom-made foot orthotics, but another trial with uncertain risk or bias (according to systematic review authors)⁵ found no statistically significant difference in recurrence of DFU between groups.

Clinical Effectiveness of Custom-Made Foot Orthotics Compared to Sham Orthotics in Adults

The meta-analysis by Morrissey et al.⁸ reported strong evidence (according to systematic review authors) of a positive effect of custom-made orthotics on short-term pain reduction, limited evidence of a positive effect on medium-term pain reduction, and moderate evidence of no effect for long-term pain relief in patients with plantar fasciitis. Findings from RCTs supported the positive effect of custom-made orthotics on short-term pain in people with flatfoot²⁷ and cavus foot,⁷ and the positive effect on medium-term pain in people with plantar fasciitis.³¹ However, 3 other RCTs found no effect on short-term pain in patients with rheumatoid arthritis²⁸ or plantar fasciitis.^{1,32}

Moderate evidence (according to systematic review authors) from the meta-analysis⁸ found no statistically significant difference in foot function with custom-made orthotics compared to sham orthotics in the short term, medium term, and long term. Two small RCTs^{7,32} also found no effect of custom-made orthotics on short-term foot function, but 1 trial in people with cavus foot did find a positive effect on foot function.⁷ One RCT also found that custom-made foot orthotics improved disability compared to sham orthotics,⁷ and another RCT reported that custom-made foot orthotics improved short-term health-related quality of life.³²

Clinical Effectiveness of Custom-Made Foot Orthotics Compared to No Intervention or Standard Care in Adults

Compared to no orthotics, custom-made orthotics significantly reduced foot pain and improved quality of life in the short term,^{30,32} but did not affect foot function.^{1,7} Two trials with varying risks of bias (according to systematic review authors)⁵ reported long-term reduction in DFU recurrence with custom-made foot orthotics compared to no orthotics or usual care. However, another trial with uncertain risk of bias (according to systematic review authors)⁵ found no statistically significant difference in recurrence of DFU between custom-made orthotics and no orthotics.

Clinical Effectiveness of Custom-Made Foot Orthotics Compared to Night Splints in Adults

Custom-made orthotics were compared to tension night splints in people with plantar fasciitis.¹ There was no significant difference between groups regarding pain at short term, according to 1 trial with high risk of bias (according to systematic reviews).¹ There was significantly lower pain, similar foot function, and similar quality of life with custom-

made orthotics at long term, according to another trial with low risk of bias (according to systematic reviews).¹

Clinical Effectiveness of Custom-Made Foot Orthotics in Children

Custom-made orthotics provided significantly improved pain relief to children in the short term,^{9,29} but not in the medium or long term when compared to prefabricated heel lifts for calcaneal apophysitis⁹ and not compared to sham orthotics for idiopathic rheumatoid arthritis.²⁹ In children with idiopathic rheumatoid arthritis, custom-made orthotics did not improve disability,²⁹ and their effect on quality of life in the long term differed between self-report and parent-report.²⁹

Cost-Effectiveness of Custom-Made Foot Orthotics

The included economic evaluations were consistent in their results; custom-made foot orthotics were less cost-effective than simple insoles,²⁸ prefabricated foot orthotics,²⁸ and GP-led usual care.³³

Evidence-Based Guidelines

The 2 evidence-based guidelines for people with diabetes^{34,35} made similar recommendations in favour of the use of custom-made orthotics by people with diabetes at moderate risk of DFU, with healed DFU, and with foot deformity or pre-ulcerative lesions.

Conclusions

In general, this review found that custom-made foot orthotics had a beneficial or neutral effect on clinical outcomes compared to other interventions, which is similar to the findings of the 2020 CADTH report.¹² There were no differences between custom-made and prefabricated foot orthotics on pain reduction and foot function in adults with plantar heel pain.^{1,8,27} These results are similar to those of the 2019 CADTH report.¹³ Custom-made orthotics were better than or similar to prefabricated orthotics, no orthotics, or standard care in preventing DFU relapse in patients with diabetes.⁵ These results are in alignment with the guideline recommendations in support of custom-made orthotics for the prevention of new and recurring DFU.^{34,35}

Although no studies reported that custom-made orthotics had a negative impact on clinical outcomes compared to other interventions, the dearth of evidence about adverse events creates uncertainty about these positive results. Further research set in Canada on both benefits and harms, and based on adequately powered high-quality RCTs with long-term follow-up, is needed to better understand the clinical effectiveness of custom-made foot orthotics in people with lower-limb conditions.

Custom-made foot orthotics were not cost-effective in comparison to placebo insoles, prefabricated orthotics, and GP-led usual care in the short term and medium term.^{28,33} Further economic evaluations, also set in Canada, with longer-term time horizons, proper cost measurements, discounting, and sensitivity analyses, are warranted.

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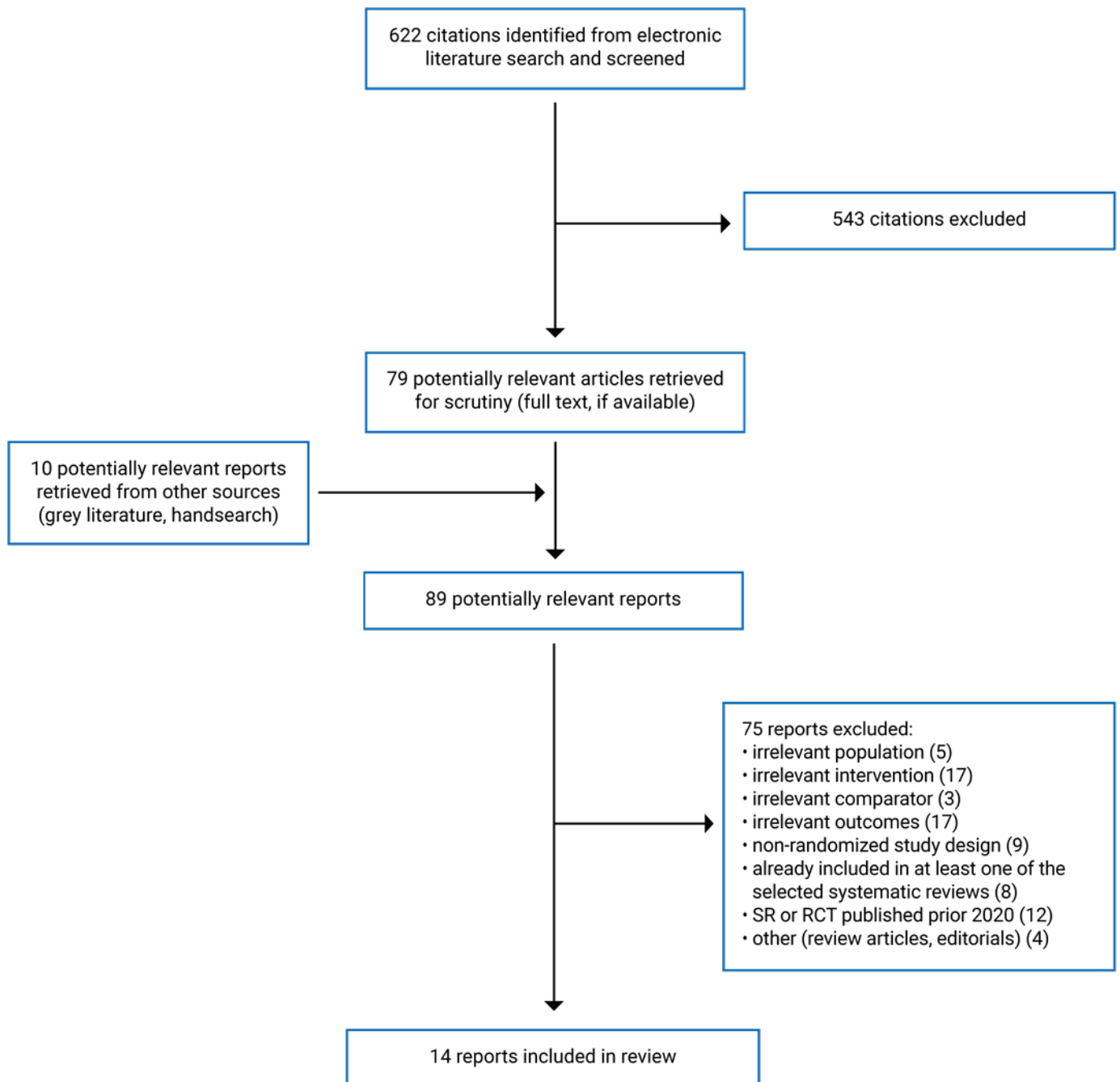
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Appendix 1: Selection of Included Studies

Note that this appendix has not been copy-edited.

Figure 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews

Study citation, country, funding source(s)	Study objectives, last search dates, numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Outcomes, length of follow-up
Clarke et al. 2021 ²⁸ Australia Funding source: No funding	Study objective: To critically appraise the existing orthotic/prosthetic health economic evaluation literature and therefore determine evidence gaps, critical method design issues, and the extent to which the literature informs orthotic policy and investment decisions Last search date: January 2019 Number of relevant studies: 2 economic evaluations (1 RCT + cost-effectiveness + cost-utility; 1 cost-effectiveness)	People with acute and chronic clinical presentations, including plantar fasciitis and rheumatoid arthritis Sample size: 41 to 69 Mean age: NR % female: NR	Intervention: CMFO Comparator: Prefabricated FO; Simple insoles	Outcomes: <ul style="list-style-type: none"> • Pain (FFI) • Disability (FFI) • Costs • QALY (EQ-5D utility index) Time horizons: 8 to 16 weeks
Gómez-Jurado et al., 2021 ²⁷ Spain Funding source: No funding	Study objective: To investigate whether orthotic treatment is effective for the treatment of posterior tibial tendon dysfunction stages I and II (flat foot) Last search date: August 2020 Number of relevant primary studies: 1 RCT	Adults diagnosed with posterior tibial tendon dysfunction stages I and II (flat foot) Sample size: 67 Mean age: 22 years % female: 58	Intervention: CADCAM orthotics Comparators: Conventional FO; Flat insoles Cointervention: Home-based exercise program	Outcomes: Pain (VAS) Follow-up: 8 weeks
Morrissey et al. 2021 ⁹ UK Funding source: National Institute for Health Research	Study objective: To develop a best practice guide for managing people with plantar fasciitis, informed by a systematic review Last search date: October 2019 Number of relevant primary studies: 5 RCTs	People with plantar fasciitis experiencing plantar heel pain Sample size: 60 to 142 Mean age: 44 to 53 years % female: 63 to 89	Intervention: CMFO Comparators: Prefabricated FO; sham FO	Outcomes: <ul style="list-style-type: none"> • Pain (VAS, FFI, FHSQ) • Function (FFI, FHSQ) Follow-up: 3 to 52 weeks

Study citation, country, funding source(s)	Study objectives, last search dates, numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Outcomes, length of follow-up
Crawford et al. 2020 ⁵ UK Funding sources: NIHR HTA Programme	Study objective: To systematically review the evidence from RCTs for effective interventions to prevent foot ulceration in people with diabetes Last search date: February 2019 Number of relevant primary studies: 4 RCTs	People with a diagnosis of type 1 or type 2 diabetes, with or without a history of ulceration Sample size: 69 to 400 Mean age: 56.5 to 67 years % female: 23 to 38	Intervention: CMFO Comparators: Prefabricated FO; sham FO; standard care; no FO Cointervention: Orthopedic shoes	Outcomes: DFU recurrence Follow-up: 1 to 2 years
Mendes et al. 2020 ⁷ Brazil Funding source: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil	Study objective: To identify the main types of insoles described in the literature that are used to treat musculoskeletal alterations of lower limbs and to analyze the existence of previous evaluation for the prescription of these insoles Last search date: July 2018 Number of relevant primary studies: 5 RCTs	People with musculoskeletal disorders of the lower limbs, including plantar fasciitis, cavus foot, Achilles tendinopathy, and flatfoot Sample size: NR % female: NR Mean age: NR	Intervention: CMFO Comparators: Sham FO; standard care	Outcomes: • Pain (measure NR) • Function (measure NR) Follow-up: 3 to 12 months
Schuitema et al. 2020 ¹ The Netherlands Funding source: OIM Orthopedie, Assen, The Netherlands	Study designs: SR of RCTs with a minimum number of 5 participants Last search date: March 2018 Number of relevant primary studies: 8 RCTs	Adults with plantar fasciitis Sample size: 15 to 142 Mean age: 44 to 53 years % Female: 65 to 89	Intervention: CMFO Comparators: Prefabricated FO; sham FO; no FO; night splint Cointervention: Rocker shoes	Outcomes: • Pain (VAS, FFI) • Function (FAOS) • QoL (FAOS) Follow-up: Single visit to 52 weeks

CMFO = custom-made foot orthotics; FAOS ADL = Foot and Ankle Outcome Score; FFI = Foot Function Index; FO = foot orthotics; JAFI = juvenile arthritis foot ankle disability index; HTA = Health Technology Assessment; NIHR = National Institute of Health Research; NR = not reported; PedsQL = Pediatric Quality of Life Rheumatology Module version 3; RoB = Risk of Bias; QALY = quality-adjusted life-years; QoL = quality of life; SF12 = 12-Item Short Form Health Survey; SR = systematic review; VAS = visual analogue scale.

Note: This table has not been copy-edited.

Table 3: Characteristics of Included Primary Clinical Studies

Study citation, country, funding source	Study design and setting	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Alfaro-Santafé et al. 2021 ⁹ Spain Funding: No funding	Parallel RCT Single centre: podiatry clinic	Physically active children diagnosed radiologically with calcaneal apophysitis (Sever's disease) (n=208 randomized) Mean age: 11 years (range 9-12) Mean disease duration: NR Mean BMI: 19.3 kg/m ² % Female: 17	Intervention: CMFO (n=100) Comparator: Prefabricated heel lifts (n=99)	Outcomes: Pain (VAS) Follow-up: 12 weeks
Coheña-Jiménez et al. 2021 ³¹ Spain Funding source: No funding	Parallel RCT Single centre: private rehabilitation and physiotherapy and podiatry unit	Adults with plantar fasciitis (n=83 randomized) Mean age: 36.5 years Mean pain duration: 17 months Mean BMI: 25.81 kg/m ² % Female: 54	Intervention: CMFO (n=39) Comparator: Placebo FO (n=37) Co-interventions: Stretches of the posterior muscle chain; extracorporeal shock wave therapy	Outcomes: • Pain (VAS) • Function (RM) Follow-up: 6 months
Fellas et al. 2021 ²⁹ Australia Funding source: PHD funding and scholarship program	Parallel RCT Multi-centre: 3 children's hospitals	Children with a diagnosis of juvenile idiopathic rheumatoid arthritis (n=66 randomized) Mean age: 12 years (range 5-18) Mean disease duration: 6.5 years Mean BMI: NR % Female: 68	Intervention: CMFO (n=29) Comparator: Placebo FO (n=27)	Outcomes: • Pain (VAS) • Disability (JAFI) • QoL (PedsQL) Follow-up: 12 months
Gaino et al. 2021 ³⁰ Brazil Funding source: No funding	RCT Single centre: outpatient rheumatology clinic	Adults with rheumatoid arthritis (n=94 randomized) Mean age: 56.7 years Mean disease duration: 11.4 years Mean BMI: 27.7 kg/m ² % Female: 86	Intervention: CMFO (n=40) Comparator: No FO (n=41)	Outcomes: • Pain (FFI) • Function (FFI) • Disability (FFI) Follow-up: 4 weeks

Study citation, country, funding source	Study design and setting	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Rasenberg et al. 2021a ³² The Netherlands Funding: The Netherlands Organisation for Health Research and Development; The Dutch Association of Podiatrist	Parallel RCT Multi-centre: 175 GPs and 6 sports physicians	Adults with clinical diagnosis of plantar fasciitis (n=185) Mean age: 47.6 years (range 18-65) Mean pain duration: 6.2 months Mean BMI: 29.7 kg/m ² % Female: 69	Intervention: CMFO (n=70) Comparators: GP-led usual care (n=46); Sham FO (n=69) Co-interventions: Information booklet on plantar heel pain; Information of stretching and strengthening exercises	Outcomes: <ul style="list-style-type: none"> • Pain (NRS, FFI) • QoL (SF12) Follow-up: 26 weeks

CMFO = custom-made foot orthotics; FFI = Foot Function Index; FO = foot orthotics; GP = general practitioner; JAFI = juvenile arthritis foot ankle disability index; NR = not reported; NRS = numerical rating scale; PedsQL = Pediatric Quality of Life Rheumatology Module version 3; RM = Roles and Maudsley scale; QoL = quality of life; SF12 = 12-Item Short Form Health Survey; VAS = visual analogue scale.

Note: This table has not been copy-edited.

Table 4: Characteristics of Included Economic Evaluations

Study citation country, funding source	Type of analysis, time horizon, perspective(s)	Population characteristics	Intervention and comparator(s)	Approach	Source of clinical, cost, and utility data used in analysis	Main assumptions
<p>Rasenberg et al. 2021b³³</p> <p>The Netherlands</p> <p>Funding source: The Netherlands Organisation for Health Research and Development; The Dutch Association of Podiatrist</p>	<p>Analyses: Cost-utility analysis and cost-effectiveness analysis</p> <p>Time horizon: 26 weeks</p> <p>Perspectives: Health care payer; societal</p>	<p>Participants from RCT³² with clinical diagnosis of plantar fasciitis</p> <p>Mean age: 47.6 years (range 18-65)</p> <p>% Female: 69</p>	<p>Intervention: CMFO (n=70)</p> <p>Comparators: GP-led usual care (no FO, n=46)</p>	<p>An imputation model was created containing all variables included in the analysis models, and variables that were statistically different between groups at baseline, related to missingness or related to the outcomes (age, gender, BMI, activity level, bilateralism of pain). Missing cost and effectiveness data were imputed using multiple imputation by chained equations.</p> <p>Differences in QALYs and total societal costs between groups were estimated using a linear regression model.</p> <p>Uncertainty around cost differences estimated using non-parametric bootstrap.</p>	<p>Clinical effectiveness, cost, and utility data collected during RCT³² using online questionnaires. Costs included health care costs (i.e., primary care, secondary care, medical devices, medication) and lost productivity costs (i.e., absenteeism from paid and unpaid work, presenteeism). Utilization of health care services was valued using Dutch standard costs, if available. Otherwise, tariffs recommended by professional organizations were used. Costs of insoles used were reported by study podiatrists. Medication was valued using the cost per daily defined dose.</p>	<p>Absenteeism from paid work was valued using the friction cost approach. Absenteeism from unpaid work was valued using a shadow price based on the costs for</p> <p>a legally employed cleaner. Lost productivity was subsequently valued using mean wage rates stratified by sex.</p>

CMFO = custom-made foot orthotics; FO = foot orthotics; GP = general practitioner; HRQoL = Health-related quality of life; NHS = National Health Service; NICE = National Institute for Health and Care Excellence.

Note: This table has not been copy-edited.

Table 5: Characteristics of Included Guidelines

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
IWGDF, 2019 Update³⁵						
<p>Intended users: Clinicians and other health care professionals</p> <p>Target population: Diabetic patients at risk of DFU</p>	Interventions for the prevention of foot ulcers in people with diabetes	Benefits (prevention of DFU incidence and DFU recurrence) and harms (adverse events), financial costs (resource utilization)	Using GRADE system, evidence came from systematic reviews, and expert opinion where evidence was not available	SIGN grading system was used as an initial guide for assigning level of evidence (excluding levels 3 and 4). Level 1 referred to RCTs and was considered “high”, and level 2 referred to case control, cohort, controlled before-and after designs, or interrupted time series and was considered “low”. The quality of evidence could then be lowered based on the presence of risk of bias, inconsistency of results and publication bias. The quality of evidence could also be raised based on the presence of a large effect size or evidence of a dose-response relationship (for observational studies only).	<p>Guideline developed using GRADE methodology</p> <p>The initial guidelines, and each subsequent update, were developed by a consensus process and written by a panel of experts. Utilizing a multistep review process, the guidelines were revised by the IWGDF Editorial Board, followed by critical evaluation by global IWGDF representatives, culminating in an agreed upon text.</p> <p>All members of the working group participated in the discussion of the conclusions for each clinical question, reaching consensus on the content of the evidence statements and the strength of the recommendations.</p>	The members of the IWGDF Editorial Board met in person on a number of occasions to thoroughly review guideline chapter, which were then revised by the working groups based on this editorial review. The working groups then sent the guideline to the panel of independent international external experts for their critical review. The working group subsequently revised the document further based on these comments, after which, the IWGDF Editorial Board did a final review of the recommendations and the rationale provided.

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
Diabetic Foot Australia 2018³⁴						
<p>Intended Users: Health care providers</p> <p>Target Population: People with diabetes at risk of DFU</p>	Medical-grade footwear	DFU prevention; DFU recurrence	Information from the 2013 footwear guideline was updated by the primary author by reviewing and incorporating any new footwear-related recommendations from the most recent Australian NHMRC diabetic foot guideline and IWGDF guidance documents. The primary author then reviewed and incorporated common findings from all recent systematic reviews on footwear interventions for people with diabetes, recent RCTs included in these reviews, and any further studies obtained from hand searching reference lists of these articles and an additional non-systematic search of the literature.	NR	The first draft of this guideline was written by the first author and sent to 2 coauthors for critical review and expert opinion. A second draft incorporating consensus feedback from the 3 authors was written by the first author.	Drafts of the guideline incorporating feedback from all coauthors was sent to all coauthors for review, until consensus was reached from all authors, leading to the final version of the guideline, approved by all authors

DFU = diabetic foot ulcer; GRADE = Grading of Recommendations Assessment, Development and Evaluation; IWGDF = International Working Group on the Diabetic Foot; NHMRC = National Health and Medical Research Council; NR = not reported; RCT = randomized controlled trial; SIGN = SR = systematic review.

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Appendix 3: Critical Appraisal of Included Publications

Note that this appendix has not been copy-edited.

Table 6: Strengths and Limitations of Systematic Reviews and Meta-Analyses Using AMSTAR 2²²

Strengths	Limitations
Clarke et al. 2021²⁸	
<ul style="list-style-type: none"> • The research question and inclusion criteria for the review were clearly stated • The choice of included study designs was explained • Explicit statement that the review methods were established before the conduct of the review • Comprehensive literature search strategy and detailed methods were described • The search was conducted in multiple databases and key search terms were provided • Data extraction was performed by one reviewer and independently reviewed by a second reviewer; and disagreements were resolved through discussion with input from a third reviewer as needed • Adequate details about the included studies were described • The Consensus on Health Economic Criteria - Extended was used to assess risk of bias in individual studies • The authors accounted for risk of bias in individual studies where interpreting/discuss the results of the review • Authors reported that no funding was received and declared that they had no conflicts of interest 	<ul style="list-style-type: none"> • Study selection was performed by a sole reviewer; and second or third opinion was sought only if required and disagreement resolved by discussion until consensus. • Authors did not provide a list of excluded studies with justifications for exclusion • Indicated whether individual studies reported their sources of funding; however, the sources of funding themselves were not reported
Gómez-Jurado et al., 2021²⁷	
<ul style="list-style-type: none"> • The research question and inclusion criteria for the review included the components of PICO • Explicit statement that the review methods were established before the conduct of the review • Comprehensive literature search strategy and detailed methods were described • The search was conducted in multiple databases and key search terms were provided • Study selection was performed in duplicate, and disagreements were resolved through consensus or involving a third reviewer • Adequate details about the included studies were described • The Cochrane Risk of Bias tool was used to assess risk of bias in individual studies • Authors reported that no funding was received and declared that they had no conflicts of interest 	<ul style="list-style-type: none"> • Data extraction was performed by a sole reviewer • Authors did not provide justification for eligible study designs • Authors did not provide a list of excluded studies with justifications for exclusion • Sources of funding for individual studies included in the review were not reported • The authors did not account for risk of bias in individual studies where interpreting/discuss the results of the review

Strengths	Limitations
Morrisey et al. 2021⁸	
<ul style="list-style-type: none"> • The research question and inclusion criteria for the review include the components of PICO • Explicit statement that the review methods were established before the conduct of the review • Authors provided justification for eligible study designs • Comprehensive literature search strategy and detailed methods were described • The search was conducted in multiple databases, key search terms were provided, and the reference lists of included articles were hand-searched for additional relevant literature • Adequate details about the included studies were described • The PEDro scale and Cochrane Risk of Bias tool were used to assess risk of bias in individual studies • Authors accounted for risk of bias in included studies when discussing results of review • Appropriate methods were used for meta-analyses • Authors assess the potential impact of risk of bias in individual studies on the results of the meta-analysis • Authors provided a satisfactory explanation and discussion of heterogeneity observed in the results of the review • Authors reported their funding sources and declared that they had no competing interests • Authors stated that funders had no role in the design, conduct or reporting of the research 	<ul style="list-style-type: none"> • Abstracts were screened independently by 2 reviewers; however, it is unclear if full-text review and data extraction were also performed in duplicate • Authors did not provide a list of excluded studies with justifications for exclusion • Authors did not investigate publication bias (small study bias) • Sources of funding for individual studies included in the review were not reported
Crawford et al. 2020⁵	
<ul style="list-style-type: none"> • The research question and inclusion criteria for the review included the components of PICO • Explicit statement that the review methods were established before the conduct of the review • Authors provided justification for eligible study designs • Comprehensive literature search strategy and methods were described • The search was conducted in multiple databases • Adequate details about the included studies were described • Full-text review and data extraction were performed in duplicate • The Cochrane Risk of Bias tool was used to assess risk of bias in individual studies • Authors accounted for risk of bias in included studies when discussing results of review • Authors provided a satisfactory explanation and discussion of heterogeneity observed in the results of the review • Authors reported their funding source and declared that they had no competing interests 	<ul style="list-style-type: none"> • Key search terms were not provided • Title and abstracts were screened by a sole reviewer and a 10% sample was checked by a second reviewer • Authors did not provide a list of excluded studies with justifications for exclusion • Meta-analysis was performed, but the authors pooled studies on custom-made foot orthotics with other custom footwear and offloading interventions (i.e., shoes without orthotics, shear-reducing insoles) • Sources of funding for individual studies included in the review were not reported

Strengths	Limitations
Mendes et al. 2020⁷	
<ul style="list-style-type: none"> • The research question and inclusion criteria for the review included the components of PICO • Explicit statement that the review methods were established before the conduct of the review • Comprehensive literature search strategy and detailed methods described • The search was conducted in multiple databases and key search terms were provided • Adequate details about the included studies were described • The PEDro scale was used to assess risk of bias in individual studies • Authors reported their funding sources and declared that they had no competing interests 	<ul style="list-style-type: none"> • Authors did not provide justification for eligible study designs • Abstracts were screened independently by 2 reviewers; however, it is unclear if full-text review and data extraction were also performed in duplicate • Authors did not provide a list of excluded studies with justifications for exclusion • Details on study design, methods and sample characteristics of included studies were lacking • Sources of funding for individual studies included in the review were not reported • Authors did not account for risk of bias in included studies when discussing results of review
Schuitema et al. 2020¹	
<ul style="list-style-type: none"> • The research question and inclusion criteria for the review included the components of PICO • Authors explained their selection of study designs for inclusion in the review • Comprehensive literature search strategy and detailed methods described • Study selection was performed in duplicated • The search was conducted in multiple databases and key search terms were provided • Adequate details about the included studies were described • The Cochrane Risk of Bias tool was used to assess risk of bias in individual studies • Authors accounted for risk of bias in included studies when discussing results of review • Authors reported their funding source 	<ul style="list-style-type: none"> • Unclear whether review methods were established before the conduct of the review • Unclear if data extraction was performed in duplicate • Authors did not provide a list of excluded studies with justifications for exclusion • Sources of funding for individual studies included in the review were not reported • Authors did not discuss whether heterogeneity was observed in the results of the review • Authors did not disclose whether they had any conflicts of interest

AMSTAR 2 = A Measurement Tool to Assess systematic Reviews 2; PEDro = Physiotherapy Evidence Database; PICO = population/participants, intervention, comparison, outcomes.

Table 7: Strengths and Limitations of Clinical Studies Using the Downs and Black Checklist²³

Strengths	Limitations
Alfaro-Santafé et al. 2021⁹	
<ul style="list-style-type: none"> • The aim of the study was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, interventions, and outcomes were described • Randomization was performed by a third party with no involvement in the recruitment or treatment of participants • The investigators and assessors were blinded • Sample size estimation was conducted, and the appropriate number of patients were recruited • Discontinuation and associated reasons were reported: 3.8% in the CMFO group and 4.8% in the prefabricated heel lifts group • The authors reported reasonable compliance with the allocated interventions • ITT analysis was conducted • P values were reported • The authors declared no conflict of interest 	<ul style="list-style-type: none"> • Method or randomization and allocation concealment were not described • Non-blinded (Participants (children) and their parents were not blinded)
Coheña-Jiménez et al. 2021³¹	
<ul style="list-style-type: none"> • The objective of the study was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, intervention, comparator, and outcomes were described • Method of randomization (sequence generator) and allocation concealment (sealed opaque envelopes) appeared appropriate. An external assistant not involved in the trial safeguarded the randomization sequence. • Sample size calculation was conducted, and the appropriate number of patients were recruited • Double blinded (participants and researchers/assessors were blinded) • Discontinuation and associated reasons were reported: 7.1% in the CMFO group and 9.8% in the placebo insoles group • ITT analysis was conducted • P values were reported • The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of the article 	<ul style="list-style-type: none"> • There were statistically significant differences between the intervention and control groups in relation to age and BMI; the mean age and BMI were lower in CMFO group

Strengths	Limitations
Fellas et al. 2021²⁹	
<ul style="list-style-type: none"> • The aim of the study was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, intervention, comparator, and outcomes were described • Method of randomization (computerized randomization sequence generator) and allocation concealment (sealed opaque envelopes) appeared appropriate. • Sample size calculation was conducted, and the appropriate number of patients were recruited • Single blinded (participants were blinded) • Discontinuation and associated reasons were reported: 12.1% in the CMFO group and 18% in the placebo insoles group • ITT analysis was conducted • P values were reported • The authors declared no conflicts of interest 	<ul style="list-style-type: none"> • Investigators/assessors were not blinded • Adjusted analysis indicated changes to medication and disease status may have impacted on the validity of results. Child reported pain results appeared to be affected the most when medication-changed participants were removed in a subgroup analysis.
Gaino et al. 2021³⁰	
<ul style="list-style-type: none"> • The objective of the study was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, intervention, comparator, and outcomes were described • Method of randomization (drawn from a closed bag by an independent person not involved in patient's evaluation or delivery of intervention) and allocation concealment (sequentially number, sealed, opaque envelopes) appeared appropriate. • Sample size calculation was conducted, and the appropriate number of patients were recruited • Discontinuation and associated reasons were reported: 16.6% in the CMFO group and 10.9% in the control group • ITT analysis was conducted • P values were reported • The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of the article 	<ul style="list-style-type: none"> • Non-blinded (participants and investigators/assessors were not blinded) • Sample size calculation was conducted; however, the necessary sample size was not achieved • The intervention and control groups different in relation to comorbidities and race

Strengths	Limitations
Rasenberg et al. 2021a³²	
<ul style="list-style-type: none"> • The objective of the study was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, interventions (CMFO, sham insoles, GP-led usual care) and outcomes were described • Method of randomization (computer-generated randomization list) appeared appropriate. The randomization list was created by an independent person and the sequence was hidden from all involved researchers. • Participants and GPs were blinded. Podiatrists were blinded during the first consultation but received information necessary to fabricate the insoles and were no longer blinded afterwards. • Sample size estimation was conducted, and the appropriate number of patients were recruited • Discontinuation and associated reasons were reported: 1.4% in the CMFO group, 0 in the sham insole group, and 8.7% in the usual care group • ITT analysis was conducted • P values were reported • The authors declared no competing interests 	<ul style="list-style-type: none"> • The GP-led usual care group had more access to co-interventions (e.g., corticosteroid injections, pain medication), which may have enhance the treatment effects in this group

BMI = body mass index; CMFO = custom-made foot orthotics; GP = general practitioner; ITT = intention to treat.

Table 8: Strengths and Limitations of Economic Evaluation Using the Drummond Checklist²⁴

Strengths	Limitations
Rasenberg et al. 2021b³³	
<p>Study design</p> <ul style="list-style-type: none"> • The research question was stated • The economic importance of the research question was stated • The viewpoint of the analysis was clearly stated and justified • The choice of form of economic evaluation was justified in relation to the questions addressed <p>Data collection</p> <ul style="list-style-type: none"> • The sources of effectiveness estimates used were stated • The primary outcome measures for the economic evaluation were clearly stated • Details of the subjects from whom valuations were obtained were given • Methods for the estimation of costs were described • Currency and price data were recorded • Details of the imputation model were given 	<ul style="list-style-type: none"> • Model inputs were taken from a single trial, rather than a synthesis or meta-analysis of estimates from multiple sources • The power of the study was too low to show statistically significant differences in costs and effects • The small sample size of the study led to imputation of data being necessary • The discount rate is not stated • No description of current price adjustments for inflation was provided

Strengths	Limitations
<p>Analysis and interpretation</p> <ul style="list-style-type: none"> • Time horizon of costs and benefits were stated • Details of statistical tests were given • The approach to sensitivity analysis was given • The choice of variables for sensitivity analysis were justified • Confidence intervals were reported • Relevant alternatives are compared • Incremental analysis was reported • The answer to the study question was given • Conclusions following from the data were reported • Conclusions were accompanied by the appropriate caveats (limitations) <p>Miscellaneous</p> <ul style="list-style-type: none"> • Authors disclosed all conflicts of interest related to the study • Source of funding was disclosed 	

Table 9: Strengths and Limitations of Guidelines Using AGREE II²⁵

Item	IWGDF, 2019 Update ³⁵	Diabetic Foot Australia 2018 ³⁴
Domain 1: Scope and Purpose		
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes	Yes
Domain 2: Stakeholder Involvement		
4. The guideline development group includes individuals from all relevant professional groups.	Yes	Yes
5. The views and preferences of the target population (patients, public, etc.) have been sought.	Yes	No
6. The target users of the guideline are clearly defined.	Yes	Yes
Domain 3: Rigour of Development		
7. Systematic methods were used to search for evidence.	Yes	Yes
8. The criteria for selecting the evidence are clearly described.	Yes	Yes
9. The strengths and limitations of the body of evidence are clearly described.	Yes	Partially
10. The methods for formulating the recommendations are clearly described.	Yes	Yes
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Yes	Yes
12. There is an explicit link between the recommendations and the supporting evidence.	Yes	Yes
13. The guideline has been externally reviewed by experts prior to its publication.	Yes	Yes

Item	IWGDF, 2019 Update ³⁵	Diabetic Foot Australia 2018 ³⁴
14. A procedure for updating the guideline is provided.	Yes	Yes
Domain 4: Clarity of Presentation		
15. The recommendations are specific and unambiguous.	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes	Yes
17. Key recommendations are easily identifiable.	Yes	Yes
Domain 5: Applicability		
18. The guideline describes facilitators and barriers to its application.	Yes	Yes
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	Yes	Yes
20. The potential resource implications of applying the recommendations have been considered.	Yes	Yes
21. The guideline presents monitoring and/or auditing criteria.	No	Yes
Domain 6: Editorial Independence		
22. The views of the funding body have not influenced the content of the guideline.	Yes	Unclear
23. Competing interests of guideline development group members have been recorded and addressed.	Yes	Yes

AGREE II = Appraisal of Guidelines for Research and Evaluation II.

Appendix 4: Main Study Findings and Authors' Conclusions

Note that this appendix has not been copy-edited.

Table 10: Summary of Findings by Outcome – Foot Pain in Adults

Comparison	Study Citation and Study Design	Foot Pain
CMFO vs. prefabricated FO	Gómez-Jurado et al., 2021 ²⁷ SR (1 RCT)	Yurt et al. 2019 Mean VAS score (SD) in people with flatfoot at baseline vs. 8 weeks <ul style="list-style-type: none"> • CADCAM orthoses, n = 22: 59.27 (17.26) vs. 27.84 (18.41); Cohen's d = 0.660 • Conventional FO, n = 22: 60.32 (6.82) vs. 27.05 (16.82); Cohen's d = 0.703 • No statistically significant difference between groups
	Morrissey et al. 2021 ⁸ SR (3 RCTs)	Wrobel et al. 2015 Mean FFI pain score (SD) at 3 months in patients with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 25: 22.4 (9.3) • Prefabricated FO, n = 21: 23.0 (7.68) • SMD (95% CI): -0.07 (-0.65 to 0.51), NSS
		Baldassin et al. 2009 Mean FFI pain score (SD) at 8 weeks in people with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 70: 31.9 (26.0) • Prefabricated FO, n = 72: 34.2 (27.6) • SMD (95% CI): -0.09 (-0.47 to 0.30), NSS
		Landorf et al. 2006 FHSQ pain score at 1 year in people with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 46: -83.1 (21.4) • Prefabricated FO, n = 46: -83.8 (18.0) • SMD (95% CI): 0.04 (-0.38 to 0.45), NSS
Schuitema et al. 2020 ¹ SR (1 RCT)	Martin et al. 2001 ^a VAS score at 12 weeks in patients with plantar fasciitis <ul style="list-style-type: none"> • No statistically significant difference reported by 85 people in CMFO group compared to 85 people in prefabricated FO group 	
CMO vs. placebo / sham FO (i.e., simple flat insoles)	Clarke et al. 2021 ²⁸ SR (1 RCT)	Rome et al. 2017 ^a FFI pain score (SD) at 16 weeks in people with rheumatoid arthritis <ul style="list-style-type: none"> • CMFO, n = 20 • Simple insoles, n = 21 • Between-group differences were not statistically significant • Pain score reduced significantly in both interventions from baseline to follow-up

Comparison	Study Citation and Study Design	Foot Pain
	Gómez-Jurado et al., 2021 ²⁷ SR (1 RCT)	Yurt et al. 2019 Mean VAS score (SD) in people with flatfoot at baseline vs. 8 weeks <ul style="list-style-type: none"> • CADCAM orthoses, n = 22: 59.27 (17.26) vs. 27.84 (18.41); Cohen's d = 0.660 • Flat insoles, n = 23: 58.48 (17.51) vs. 46.39 (20.18); Cohen's d = 0.304 • Statistically significant improvement in pain level in the CADCAM orthoses group compared to flat insole group
	Morrissey et al. 2021 ⁸ Short-term SR and MA (4 RCTs)	VAS or FHSQ pain scores at 3 months in people with plantar fasciitis ^b <ul style="list-style-type: none"> • CMFO, n = 128 • Sham FO, n = 126 • Pooled SMD (95% CI): -0.41 (-0.07 to -0.74), P = 0.02, I² = 42%
	Morrissey et al. 2021 ⁸ Medium- and long-term SR (2 RCTs)	Oliviera et al. 2015 FHSQ pain score at 20.7 weeks in people with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 37: 2.6 (2.5) • Sham FO, n = 37: 4.2 (3.2) • SMD (95% CI): -0.55 (-1.02 to -0.09), P < 0.05 Landorf et al. 2006 FHSQ pain score at 1 year in people with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 46: -83.1 (21.4) • Sham FO, n = 46: -82.3 (18.0) • SMD (95% CI): 0.04 (-0.45 to 0.37), NSS
	Schuitema et al. 2020 ¹ SR (2 RCTs)	Fong et al. 2012 ^a (crossover design) VAS score at single visit in 15 in people with plantar fasciitis <ul style="list-style-type: none"> • No statistically significant difference reported with rocker shoe + CMFO compared to rocker shoe + flat insole • No statistically significant difference reported with normal shoe + CMFO compared to normal shoe + flat insole Pfeffer et al. 1999 ^a FFI pain score at 8 weeks in people with plantar fasciitis <ul style="list-style-type: none"> • No statistically significant difference reported by 34 people in CMFO group compared to 42 people in felt insole group
	Coheña-Jiménez et al. 2021 ³¹ RCT	Mean VAS score (SD) in people with plantar fasciitis at baseline vs. 6 months <ul style="list-style-type: none"> • CMFO, n = 39: 5.73 (1.73) vs. 3.19 (4.26) • Placebo FO, n = 37: 6.31 (1.69) vs. 7.26 (2.77) • Effect size 3.46, P < 0.0001

Comparison	Study Citation and Study Design	Foot Pain
	Mendes et al. 2020 ⁷ SR (1 RCT)	Burns et al. 2006 ^a FHSQ pain score in people with cavus foot • Reduction of foot pain was greater with CMFO
	Rasenberg et al. 2021a ³² RCT	NRS score at 26 weeks in patients with plantar fasciitis • Pain at rest: adjusted adj MD (95% CI) -0.33 (-1.0 to 0.34), P = 0.33 • Pain during activity: adj MD (95% CI) 0.07 (-0.46 to 0.60), P = 0.80 • First step pain: adj MD (95% CI) 0.12 (-0.50 to 0.74), P = 0.71 FFI pain scale score at 26 weeks in patients with plantar fasciitis • Adj MD (95% CI) -0.87 (-5.41 to 3.68), P = 0.71
CMFO vs. no FO / standard care	Schuitema et al. 2020 ¹ SR (1 RCT)	Pfeffer et al. 1999 ^a FFI score at 8 weeks in people with plantar fasciitis • No statistically significant difference reported by 34 people in CMFO group compared to 39 people in no FO group
	Gaino et al. 2021 ³⁰ RCT	FFI pain score (SD) in people with rheumatoid arthritis at baseline vs. 4 weeks • CMFO, n = 40: 5.24 (2.60) to 3.69 (2.33), P < 0.0001 • No FO, n = 41: 5.48 (2.97) to 5.39 (2.52), P = 0.6526 • Effect size -0.60, P = 0.0001
	Mendes et al. 2020 ⁷ SR (1 RCT)	Andreasen et al. 2013 ^a Pain (measure NR) in patients with flatfoot • Statistically significant pain reduction in walking within CMFO group and standard care group at short-term and long-term follow-up • No statistically significant differences between groups in any pain parameters at short-term and long-term follow-up
	Rasenberg et al. 2021a ³² RCT	NRS score at 26 weeks in patients with plantar fasciitis • Pain at rest: adjusted adj MD (95% CI) -0.19 (-0.98 to 0.60), P = 0.64 • Pain during activity: adj MD (95% CI) 0.91 (0.20 to 1.62), P = 0.01 • First step pain: adj MD (95% CI) 1.43 (0.61 to 2.26), P = 0.01 FFI pain scale score at 26 weeks in patients with plantar fasciitis • Adj MD (95% CI) 6.50 (0.84 to 12.15), P = 0.03

Comparison	Study Citation and Study Design	Foot Pain
CMFO vs. anterior night splint	Schuitema et al. 2020 ¹ SR (2 RCT)	<ul style="list-style-type: none"> • Roos et al. 2006^a • FAOS pain score at 1 year in 43 people with plantar fasciitis • Statistically significant reduction ($p < 0.01$) in pain in 2 groups using CMFO (CMFO only; CMFO + night splint) compared to anterior night splint only group
		Martin et al. 2001 Pain (VAS) at 12 weeks in people with plantar fasciitis <ul style="list-style-type: none"> • No statistically significant difference reported by 85 people in CMFO group compared to 85 people in posterior night splint group

Adj = adjusted; CADCAM = computer-aided design/computer-aided manufacturing; CMFO = custom-made foot orthotics; FAOS = foot and ankle outcome score; FFI = Foot Function Index; FO = foot orthotics; FFI-R = Foot Function Index - Revised; FHSQ = Foot Health Status Questionnaire; MD = mean difference; NR = not reported; NRS = Numerical Rating Scale; NSS = not statistically significant; RCT = randomized controlled trial; SD = standard deviation; SMD = standardized mean difference; SR = systematic review; VAS = visual analogue scale

a. Raw data, effect sizes, and P values not reported

b. Pooled studies: Landorf et al. 2006, Bishop et al. 2018, Wrobel et al. 2015, Oliveira et al. 2015

Table 11: Summary of Findings by Outcome – Foot Pain in Children

Comparison	Study Citation and Study Design	Foot Pain
CMFO vs. placebo / sham FO (i.e., flat insoles)	Fellas et al. 2021 ²⁹ RCT	Mean VAS score (SD) in children with idiopathic rheumatoid arthritis at baseline vs. 3 months <ul style="list-style-type: none"> • CMFO, n = 33: 48.33 (24.07) vs. 16.87 (14.78) • Placebo FO, n = 33: 42.12 (26.72) vs. 44 (29.71) • Coefficient (95% CI): -28.93 (-40.90 to -16.96), $P < 0.001$ Mean VAS score (SD) in children with idiopathic rheumatoid arthritis at 6 months <ul style="list-style-type: none"> • CMFO, n = 32: 21.77 (21.41) • Placebo FO, n = 29: 29.45 (23.33) • Coefficient (95% CI): -9.66 (-21.72 to 2.39), $P = 0.116$ P = Mean VAS score (SD) in children with idiopathic rheumatoid arthritis at 1 year <ul style="list-style-type: none"> • CMFO, n = 29: 29.11 (28.30) • Placebo FO, n = 27: 37.0 (27.44) • Coefficient (95% CI): -8.37 (-20.81 to 4.07), $P = 0.187$
CMFO vs. prefabricated heel lifts	Alfaro-Santafé et al. 2021 ⁹ RCT	Mean VAS score (SD) in children with calcaneal apophysitis (Sever's disease) at baseline vs. 12 weeks <ul style="list-style-type: none"> • CMFO, n = 100: 80.1 (13.1) vs. 11.6 (17.4) • Heel lifts, n = 99: 81.3, 13.2 vs. 67.3, 21.2 • Beta estimate -68.6 (95% CI -74.5 to -62.7), $P < 0.05$

CI = confidence interval; CMFO = custom-made foot orthotics; FO = foot orthotics; OR = odds ratio; RCT = randomized controlled trial; SD = standard deviation; VAS = visual analogue scale.

Table 12: Summary of Findings by Outcome – Foot Function in Adults

Comparison	Study Citation and Study Design	Foot Function
CMFO vs. prefabricated FO	Morrissey et al. 2021 ⁸ SR (3 RCTs)	Wrobel et al. 2015 Mean FFI function score (SD) at 3 months in patients with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 25: 2.6 (2.4) • Prefabricated FO, n = 21: 2.5 (2.1) • SMD (95% CI): -0.02 (-0.57 to 0.53), NSS Baldassin et al. 2009 Mean FFI total score (SD) at 8 weeks in people with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 70: 22.9 (21.3) • Prefabricated FO, n = 72: 27.9 (24.6) • SMD (95% CI): -0.22 (-0.55 to 0.11), NSS Landorf et al. 2006 FHSQ function score at 1 year in people with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 46: 90.2 (17.8) • Prefabricated FO, n = 46: 89.5 (19.0) • SMD (95% CI): 0.04 (-0.38 to 0.45), NSS
	Coheña-Jiménez et al. 2021 ³¹ RCT	RM rating in people with plantar fasciitis at 6 months <ul style="list-style-type: none"> • Custom-made orthotics, n = 39: Acceptable 2.5%, Excellent 97.5% • Flat insoles, n = 37: Poor 81.3%, Acceptable 3.1%, Excellent 15.6% • Effect size 0.875, P < 0.0001
	CMFO vs. placebo / sham FO (i.e., simple flat insoles)	Morrissey et al. 2021 ⁸ Short-term SR and MA (3 RCTs)
Morrissey et al. 2021 ⁸ Medium- and long-term SR (2 RCTs)		Oliviera et al. 2015 FHSQ function score at 20.7 weeks in people with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 37: -86.0 (14.9) • Sham FO, n = 37: -78.5 (22.8) • SMD (95% CI): -0.39 (-0.85 to 0.07), NSS
		Landorf et al. 2006 Mean FHSQ function score (SD) at 1 year in people with plantar fasciitis <ul style="list-style-type: none"> • CMFO, n = 46: -90.2 (17.8) • Sham FO, n = 46: -87.8 (20.6) • SMD (95% CI): -0.12 (-0.54 to 0.29), NSS

Comparison	Study Citation and Study Design	Foot Function
CMFO vs. placebo / sham FO (i.e., simple flat insoles) (continued)	Mendes et al. 2020 ⁷ SR (2 RCTs)	Munteanu et al. 2015 ^b Function (measure NR) at in people with Achilles tendinopathy • CMFO were not better than placebo at improving function
		Burns et al. 2006 ^b Function (measure NR) in people with cavus foot • Function scores improved more with CMFO
	Rasenberg et al. 2021a ³² RCT	FFI function score at 26 weeks in patients with plantar fasciitis • Adj MD 1.89 (95% CI -3.54 to 7.32), P = 0.49
CMFO vs. no FO / standard care	Gaino et al. 2021 ³⁰ RCT	FFI total score (SD) in people with rheumatoid arthritis at baseline vs. 4 weeks • CMFO, n = 40: 4.08 (2.43) to 2.66 (1.67), p<0.0001 • No FO, n = 41: 4.22 (2.31) to 4.00 (2.21), P = 0.4390 • Effect size -0.57, P = 0.0029
	Rasenberg et al. 2021a ³² RCT	FFI function score at 26 weeks in patients with plantar fasciitis • Adj MD 7.07 (95% CI 1.01 to 13.13), P = 0.02
CMFO vs. anterior night splint	Schuitema et al. 2020 ¹ SR (1 RCT)	Roos et al. 2006 ^b FAOS ADL score at 52 weeks in 34 people with plantar fasciitis • No statistically significant difference reported between CMFO only group, CMFO + night splint group, and night splint only group

CMFO = custom-made foot orthotics; FAOS ADL = Foot and Ankle Outcome score – Activities of Daily Living; FFI = Foot Function Index; FFI-R = Foot Function Index - Revised; FHSQ = Foot Health Status Questionnaire; FO = foot orthotics; MA = meta-analysis; MD = mean difference; NR = not reported; NNS = not statistically significant; NR = not reported; RCT = randomized controlled trial; RM = Roles and Maudsley scale; SD = standard deviation; SF-36 = 36-Item Short Form Health Survey; SMD = standardized mean difference; SR = systematic review

a. Pooled studies: Landorf et al. 2006, Wrobel et al. 2015, Oliveira et al. 2015

b. Raw data, effect sizes, and P values not reported in systematic review

Table 13: Summary of Findings by Outcome – Disability in Adults

Comparison	Study Citation and Study Design	Disability
CMFO vs. placebo / sham FO (i.e., simple flat insoles)	Clarke et al. 2021 ²⁸ SR (1 RCT)	Rome et al. 2017 ^a FFI disability score at 16 weeks in 41 people with rheumatoid arthritis • Reduced significantly in the CMFO group (P < 0.000) from baseline to 16 weeks, but not in the simple insoles group (P = 0.40)
CMFO vs. no FO	Gaino et al. 2021 ³⁰ RCT	FFI disability score (SD) in people with rheumatoid arthritis at baseline vs. 4 weeks • CMFO, n=40: 4.46 (2.50) to 3.60 (2.48), P = 0.0014 • No FO, n=41: 4.91 (2.85) to 4.72 (2.71), 0.3121 • Effect size -0.28, P = 0.0501

CMFO = custom-made foot orthotics; FFI = Foot Function Index; FO = foot orthotics; RCT = randomized controlled trial; SR = systematic review

a. Raw data, effect sizes, and P values not reported

Table 14: Summary of Findings by Outcome – Disability in Children

Comparison	Study Citation and Study Design	Pain
CMFO vs. placebo / sham FO (i.e., simple flat insoles)	Fellas et al. 2021 ²⁹ RCT	<p>Mean JAFI-Imp score (SD) in children with idiopathic rheumatoid arthritis at baseline vs. 3 months</p> <ul style="list-style-type: none"> • CMFO, n = 33: 14.76 (7.04) to 9.87 (5.38) • Placebo FO, n = 33: 16.85 (7.55) to 13.73 (8.09) • Coefficient (95% CI) -2.59 (-5.63 to 0.45) P = 0.095 <p>Mean JAFI-Imp score (SD) in children with idiopathic rheumatoid arthritis at 6 months</p> <ul style="list-style-type: none"> • CMFO, n = 32: 9.23 (6.28) • Placebo FO, n = 27: 12.52 (6.29) • Coefficient (95% CI) -1.97 (-5.04 to 1.09) P = 0.207 <p>Mean JAFI-Imp score (SD) in children with idiopathic rheumatoid arthritis at 1 year</p> <ul style="list-style-type: none"> • CMFO, n = 29: 11.96 (7.21) • Placebo FO, n = 27: 11.64 (7.42) • Coefficient (95% CI) 2.36 (-0.83 to 5.55) P = 0.147

CMFO = custom-made foot orthotics; JAFI-Imp = juvenile arthritis foot disability index – impairment; RCT = randomized controlled trial; SD = standard deviation

Table 15: Summary of Findings by Outcome – Quality of Life in Adults

Comparison	Study Citation and Study Design	Quality of life
CMFO vs. placebo / sham FO (i.e., simple flat insoles)	Rasenberg et al. 2021a ³² RCT	<p>SF-12-MCS at 26 weeks in patients with plantar fasciitis</p> <ul style="list-style-type: none"> • Adj MD (95%CI) -3.00 (-5.71 to 0.29), P = 0.03
CMFO vs. standard care	Rasenberg et al. 2021a ³² RCT	<p>SF-12-MCS at 26 weeks in patients with plantar fasciitis</p> <ul style="list-style-type: none"> • Adj MD (95% CI) -2.99 (-5.96 to -0.03), P = 0.05
CMFO vs. anterior night splint	Schuitema et al. 2020 ¹ SR (1 RCT)	<p>Roos et al. 2006^a</p> <p>FAOS QoL score at 52 weeks in people with plantar fasciitis</p> <ul style="list-style-type: none"> • No statistically significant difference reported between CMFO only group, CMFO + night splint group, and night splint only group

CMFO = custom-made foot orthotics; FAOS = Foot and Ankle Outcome score; FO = foot orthotics; MD = mean difference; QoL = Quality of Life; RCT = randomized controlled trial; SF-12-MCS = 12-Item Short Form Health Survey - Mental Component Score Mental Component Score; SR = systematic review

a. Raw data, effect sizes, and P values not reported

Table 16: Summary of Findings by Outcome – Quality of Life in Children

Comparison	Study Citation and Study Design	Quality of Life
CMFO vs. placebo / sham FO (i.e., simple flat insoles)	Fellas et al. 2021 ²⁹ RCT	<p>Self-reported mean PedsQL score (SD) in children with idiopathic rheumatoid arthritis at baseline vs. 3 months</p> <ul style="list-style-type: none"> • CMFO, n = 33: 71.11(16.06) 73.94 (12.19) • Placebo FO, n = 33: 64.78 (15.04) to 67.42 (18.27) • Coefficient 1.21 (-4.09 to 7.11), P = 0.598 <p>Self-reported mean PedsQL score (SD) in children with idiopathic rheumatoid arthritis at 6 months</p> <ul style="list-style-type: none"> • CMFO, n = 32: 73.26 (14.80) • Placebo FO, n = 29: 71.54 (17.85) • Coefficient -2.66 (95% CI -8.29 to 2.97), P = 0.355 <p>Self-reported mean PedsQL score (SD) in children with idiopathic rheumatoid arthritis at 1 year</p> <ul style="list-style-type: none"> • CMFO, n = 29: 71.76 (16.94) • Placebo FO, n = 33: 69.89 (19.55) • Coefficient -5.23 (95% CI -11.07 to 0.62), P = 0.08 <hr/> <p>Parent reported mean PedsQL score (SD) at baseline vs. 3 months</p> <ul style="list-style-type: none"> • CMFO, n = 33: 64.03 (14.71) to 72.05 (14.41) • Placebo FO, n = 33: 59.97 (17.93) to 66.94 (20.63) • Coefficient 2.14 (-4.23 to 8.52), P = 0.510 <p>Parent reported mean PedsQL score (SD) at 6 months</p> <ul style="list-style-type: none"> • CMFO, n = 32: 69.73 (17.36) • Placebo FO, n = 29: 71.28 (18.09) • Coefficient -3.76 (-10.25 to 2.74), P =0.257 <p>Parent reported mean PedsQL score (SD) at 1 year</p> <ul style="list-style-type: none"> • CMFO, n = 29: 69.32 (18.71) • Placebo FO, n = 27: 72.77 (17.93) Coefficient -7.48 (95% CI -14.15 to -0.81), P = 0.028

CI = confidence interval; CMFO = custom-made foot orthotics; FO = foot orthotics; PedsQL: pediatric quality of life questionnaire rheumatology scale; RCT = randomized controlled trial; SD = standard deviation

Table 17: Summary of Findings by Outcome – DFU Recurrence

Comparison	Study Citation and Study Design	DFU Recurrence
CMFO vs. prefabricated FO	Crawford et al. 2020 ⁵ SR (2 RCTs)	Reiber et al. 2002 Recurrent DFU at 2 years in patients with diabetes <ul style="list-style-type: none"> • 3 pairs therapeutic shoes + customized cork inserts, n = 121: 15% • 3 pairs of therapeutic shoes + prefabricated polyurethane inserts, n = 119: 14% • No statistically significant difference
		Ulbrecht et al. 2014 Recurrent DFU at 15 months in people with diabetes <ul style="list-style-type: none"> • CMFO: 6/79 (8%) • Prefabricated FO: 16/71 (23%) • RR (95% CI) 0.34 (0.13 to 0.82)
CMFO vs. no FO / standard care	Crawford et al. 2020 ⁵ SR (3 RCTs)	Rizzo et al. 2012 Recurrent DFU at 1 year in people with diabetes <ul style="list-style-type: none"> • CMFO + shoes: 17/148 (12%) • Usual care: 58/150 (39%) • RR (95% CI) 0.3 (0.18 to 0.49)
		Reiber et al. 2002 Recurrent DFU at 2 years in patients with diabetes <ul style="list-style-type: none"> • 3 pairs of therapeutic shoes + customized cork inserts, n = 121: 15% • Own usual footwear, n = 160: 17% • No statistically significant difference
		Uccioli et al. 1995 Recurrent DFU at 1 year in patients with diabetes <ul style="list-style-type: none"> • Therapeutic shoes with CMFO: 6/33 (18%) • Own usual footwear: 21/36 (58%) • RR (95% CI) 0.47 (0.25 to 0.88)

CMFO = custom-made foot orthotics; DFU = diabetic foot ulcer; FO = foot orthotics; RR = relative risk; RCT = randomized controlled trial; SR = systematic review

Table 18: Summary of Findings of Included Economic Evaluations

Main study findings	Authors' conclusion
Clarke et al. 2021 ²⁸	
SR (2 economic evaluations)	
<p>Rome et al. 2017 Cost-utility and cost-effectiveness analysis of CMFO vs. SI in people with rheumatoid arthritis Benefits (HR QoL on EQ-5D) from baseline to 16 weeks</p> <ul style="list-style-type: none"> • CMFO 0.02 reduction • SI 0.07 increase <p>Total cost (Euros) to NHS</p> <ul style="list-style-type: none"> • CMFO 76.56 • SI 67.66 <p>Total cost to participants</p> <ul style="list-style-type: none"> • CMFO 31.45 • SI 16.86 <p>Incremental cost to NHS: 8.90 Incremental cost to participants: 14.62 Incremental QALY: -0.03, NSS ICUR: Not reported as the SI group is dominant, having an incremental gain in QALY at a lower cost compared to the CMFO group ICER: The results of the FFI are not brought together to establish an ICER</p>	<p>“Both CMFO and SI had statistically significant effects from baseline to 16 weeks in pain, and the CFMO had statistically significant effect on foot disability score. These results are not brought together with the costs. The cost-utility analysis indicates the SI as more cost-effective than the CMFO with a greater impact on HR-QoL at a lower cost.” (SR supplemental excel file)²⁸</p>
<p>Ring and Otter 2014 Cost-effectiveness analysis of prefabricated FO vs CMFO in people with heel pain Cost analysis (Euros)</p> <ul style="list-style-type: none"> • Prefabricated FO <ul style="list-style-type: none"> ◦ Mid-scale practitioner 23.97 ◦ Mid-scale specialist 26.05 • CMFO <ul style="list-style-type: none"> ◦ Mid-scale practitioner 33.95 ◦ Mid-point specialist 39.76. • Prefabricated FO had an approximate saving of 8.78 or a 38% cost saving per participant 	<p>“The cost of achieving the outcome was substantially lower in the pre-fabricated intervention compared to the custom-made intervention.” (SR supplemental excel file)²⁸</p>

Main study findings	Authors' conclusion
Rasenberg et al. 2021b³³	
<p>Cost-utility analysis of CMFO vs. GP-led usual care in people with plantar fasciitis</p> <p>Total health care costs (Euros): mean (SE) at 26 weeks</p> <ul style="list-style-type: none"> • CMFO 375 (55) • Usual care 135 (32) • MD (95% CI) 240 (159 to 427) <p>Total non-health care costs (i.e., lost productivity; Euros): mean (SE) at 26 weeks</p> <ul style="list-style-type: none"> • CMFO 2590 (517) • Usual care 2453 (905) • MD (95% CI) 137 (-1775 to 2038) <p>Total societal costs (Euros): mean (SE) at 26 weeks</p> <ul style="list-style-type: none"> • CMFO 2,965 (520) • Usual care 2,588 (909) • MD (95% CI) 376 (-1,775 to 3,038) <p>Cost-effectiveness analysis, health care payer perspective</p> <ul style="list-style-type: none"> • Difference in costs between 2 groups: 240 (146 to 389) • Difference in effectiveness outcome between 2 groups: -0.0015 (-0.027 to 0.024) • ICER –150,548 per QALY • Probability that CMFO intervention is dominated by control increased to 41% for pain at rest, 55% for QALYs, 70% for SF-12-PCS, 98% for SF-12-MCS, and 100% for pain during activity 	<p>“Our findings show that custom-made insoles are not cost-effective in comparison to GP-led usual care.” (p. 7)</p> <p>“The cost-effectiveness analyses showed that treatment with custom-made insoles was dominated by GP-led usual care (i.e., more expensive and less effective) for pain during activity and quality of life outcomes. For the outcome pain at rest, treatment with custom-made insoles was also more expensive, but more effective than GP-led usual care. However, the maximum probability of cost-effectiveness was only 0.59 at very high ceiling ratios.” (p. 7)</p>

CI = confidence interval; CMFO = custom-made foot orthotics; EQ-5D = European Quality of Live - Five Dimension; FFI = Foot Function Index; FO = foot orthotics; HR QoL = Health-related quality of life; ICER = incremental cost-effectiveness ratio; ICUR = incremental cost-utility ratio; MCS = Mental Component Score; MD = mean difference; NHS = National Health Service; NSS = not statistically significant; PCS = physical component score; QALY = quality-adjusted life-year; SE = standard error; SF-12 = 12-Item Short Form Health Survey; SR = systematic review

Table 19: Summary of Recommendations in Included Guidelines

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
IWGDF, 2019 Update³⁵	
<p>Recommendation 7: “Instruct a person with diabetes who is at moderate risk for foot ulceration (IWGDF risk 2) or who has healed from a non-plantar foot ulcer (IWGDF risk 3) to wear therapeutic footwear that accommodates the shape of the feet and that fits properly, to reduce plantar pressure, and help prevent a foot ulcer. When a foot deformity or a preulcerative sign is present, consider prescribing custom-made footwear, custom-made insoles, or toe orthoses.” (p. 7)</p> <p>Supporting evidence: Based on 3 RCTs, therapeutic footwear, including shoes, insoles, or orthoses may reduce the risk of a first-ever foot ulcer in a person at moderate risk for foot ulceration (IWGDF risk 2). Additionally, such footwear can reduce the plantar pressure during walking.</p>	<p>Strength of recommendation: Strong Quality of evidence: Low</p>
<p>Recommendation 9: “In a person with diabetes who has a healed plantar foot ulcer (IWGDF risk 3), prescribe therapeutic footwear that has a demonstrated plantar pressure relieving effect during walking, to help prevent a recurrent plantar foot ulcer; furthermore, encourage the patient to consistently wear this footwear.” (p. 8)</p> <p>Supporting evidence: Two RCTs with very low risk of bias have demonstrated a reduction in ulcer risk with custom-made orthopedic footwear or custom-made insoles that were demonstrably optimized for pressure reduction, provided the patient wears the footwear.</p>	<p>Strength of recommendation: Strong Quality of evidence: Moderate</p>
Diabetic Foot Australia, 2018³⁴	
<p>Evidence-based guideline regarding footwear for people with diabetes</p> <p>Recommendation 7: “For people with a foot deformity or pre-ulcerative lesion, consider prescribing medical grade footwear, which may include custom-made in-shoe orthoses or insoles.” (p. 7)</p> <p>Supporting evidence: Based on footwear requirements algorithms for prescription and footwear modifications in the literature.</p>	<p>Strength of recommendation: Not provided Quality of evidence: Not provided</p>
<p>Recommendation 8: “For people with a healed plantar foot ulcer, prescribe medical grade footwear with custom-made in-shoe orthoses or insoles with a demonstrated plantar pressure relieving effect at the high-risk areas.” (p. 7)</p> <p>Supporting evidence: 2 RCTs demonstrated > 30% reduction at the area of the highest plantar pressure with new medical-grade footwear with orthosis or insole compared to the patient’s current footwear. One of these RCTs reported that the risk of re-ulceration is smaller with medical-grade footwear. This aligns with the IWGDF recommendation.</p>	<p>Strength of recommendation: Not provided Quality of evidence: Not provided</p>

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
<p>Recommendation 9: “Review prescribed footwear [and custom-made orthoses or insoles] every three months to ensure it still fits, protects, and supports the foot.” (p. 9)</p> <p>Supporting evidence: One RCT that used a 3-month interval to ensure prescribed footwear remained appropriate, on expert opinion from seeing wear and tear in footwear in daily clinical practice, and aligns with the regular foot-screening interval for people at intermediate- or high-risk of foot ulceration as recommended in the Australian NHMRC diabetic foot guideline.</p>	<p>Strength of recommendation: Not provided</p> <p>Quality of evidence: Not provided</p>

IWGDF = International Working Group on the Diabetic Foot; NHMRC = National Health and Medical Research Council; RCT = randomized controlled trial

Appendix 5: Overlap Between Included Systematic Reviews

Note that this appendix has not been copy-edited.

Table 20: Overlap in Relevant Primary Studies Between Included Systematic Reviews

Primary study citation	Clarke et al. 2021 ²⁸	Gomez-Jurado et al. 2021 ²⁷	Morrissey et al. 2021 ⁸	Crawford et al. 2020 ⁵	Mendes et al. 2020 ⁷	Schuiterna et al. 2020 ¹
Yurt et al. Eur J Phys Rehabil Med. 2019;55(1): 95–102.	No	Yes	No	No	No	No
Bishop et al. BMC Musculoskelet Disord. 2018;19:222.	No	No	Yes	No	No	No
Rome et al. J Am Podiatr Med Assoc. 2004;94:229-38.	Yes	No	No	No	No	No
Munteanu et al. Br J Sports Med. 2015;49(15):989-94.	No	No	No	No	Yes	No
Wrobel et al. J Am Podiatr Med Assoc. 2015;105:281-94.	No	No	Yes	No	No	Yes
Oliviera et al. J Rheumatol. 2015;42:870–8.	No	No	Yes	No	Yes	Yes
Ring & Otter. Musculoskelet. 2014;12:1-10.	Yes	No	No	No	No	No
Ulbrecht et al. Diabetes Care. 2014;37(7):1982-9.	No	No	No	Yes	No	No
Andreasen et al. Foot. 2013;23(1):22-8.	No	No	No	No	Yes	No
Fong et al. Clin Biomech. 2012;27(10):1072-77.	No	No	No	No	No	Yes
Rizzo et al. Int J Low Extrem Wounds. 2012;11(1);59-64.	No	No	No	Yes	No	No
Baldassin et al. Arch Phys Med Rehabil. 2009;90:701-6.	No	No	Yes	No	No	Yes
Burns et al. J. Am. Podiatr. Med. Assoc. 2006; 96(3):205-11.	No	No	No	No	Yes	No
Landorf et al. Arch Intern Med. 2006;166(12):1305-10.	No	No	Yes	No	Yes	Yes

Primary study citation	Clarke et al. 2021 ²⁸	Gomez-Jurado et al. 2021 ²⁷	Morrissey et al. 2021 ⁸	Crawford et al. 2020 ⁵	Mendes et al. 2020 ⁷	Schuitema et al. 2020 ¹
Roos et al. Foot Ankle Int. 2006;27(8):606-11.	No	No	No	No	No	Yes
Reiber et al. JAMA. 2002; 287(19):2552-8.	No	No	No	Yes	No	No
Martin et al. J Am Podiatr Med Assoc. 2001;91(2):55-62.	No	No	No	No	No	Yes
Pfeffer et al. Foot Ankle Int. 1999;20(4):214-21.	No	No	No	No	No	Yes
Uccioli et al. Diabetes Care. 1995;18(10):1376-8.	No	No	No	Yes	No	No

Appendix 6: References of Potential Interest

Previous CADTH Reports

- Customized or Prefabricated Shoe Inserts for Chronic, Non-Cancer Pain: A Review of Clinical Effectiveness. Ottawa (ON): CADTH; 2020 Apr. <https://www.cadth.ca/sites/default/files/pdf/htis/2020/RC1259%20Orthotics%20Pain%20Final.pdf> Accessed 2022 Feb 4.
- Customized or pre-fabricated shoe inserts for chronic non-cancer pain: clinical effectiveness and guidelines. Ottawa (ON): CADTH; 2020: <https://www.cadth.ca/sites/default/files/pdf/htis/2020/RA1087%20Orthotics%20Pain%20Final.pdf> Accessed 2022 Feb 4.
- Custom-Made Foot Orthoses versus Prefabricated Foot Orthoses: A Review of Clinical Effectiveness and Cost-Effectiveness. Ottawa (ON): CADTH; 2019 Sep. https://www.cadth.ca/sites/default/files/pdf/htis/2019/RC1169%20Custom%20made%20orthotics%20versus%20prefabricated%20orthotics_Final.pdf Accessed 2022 Feb 4.
- Orthotics material for patients requiring foot orthotics: a review of clinical effectiveness and cost effectiveness. Ottawa (ON): CADTH; 2019 Aug. <https://www.cadth.ca/orthotics-material-patients-requiring-foot-orthotics-clinical-effectiveness-and-cost-effectiveness> Accessed 2022 Feb 4.
- Prevention of plantar ulcers in people with diabetic peripheral neuropathy using pressure-sensing shoe insoles. Ottawa (ON): CADTH; 2017 Jun. <https://www.cadth.ca/prevention-plantar-ulcers-people-diabetic-peripheral-neuropathy-using-pressure-sensing-shoe-insoles> Accessed 2022 Feb 4.

Systematic Reviews – Published Before 2020

- Tenten-Diepenmaat M, Dekker J, Heymans MW, Roorda LD, Vliet Vlieland TPM, van der Leeden M. Systematic review on the comparative effectiveness of foot orthoses in patients with rheumatoid arthritis. *J Foot Ankle Res.* 2019;12:32. [PubMed](#)
- Arias-Martin I, Reina-Bueno M, Munuera-Martinez PV. Effectiveness of custom-made foot orthoses for treating forefoot pain: a systematic review. *Int Orthop.* 2018;42(8):1865-1875. [PubMed](#)
- Frecklington M, Dalbeth N, McNair P, et al. Footwear interventions for foot pain, function, impairment and disability for people with foot and ankle arthritis: A literature review. *Semin Arthritis Rheum.* 2018;47(6):814-824. [PubMed](#)
- Gijon-Nogueron G, Ramos-Petersen L, Ortega-Avila AB, Morales-Asencio JM, Garcia-Mayor S. Effectiveness of foot orthoses in patients with rheumatoid arthritis related to disability and pain: a systematic review and meta-analysis. *Qual Life Res.* 2018;27(12):3059-3069. [PubMed](#)
- Healy A, Farmer S, Pandyan A, Chockalingam N. A systematic review of randomised controlled trials assessing effectiveness of prosthetic and orthotic interventions. *PLoS ONE.* 2018;13(3):e0192094. [PubMed](#)
- Fellas A, Coda A, Hawke F. Physical and Mechanical Therapies for Lower-Limb Problems in Juvenile Idiopathic Arthritis: A Systematic Review with Meta-Analysis. *J Am Podiatr Med Assoc.* 2017;107(5):399-412. [PubMed](#)

Randomized Controlled Trials – Published Before 2020

- de Oliveira HAV, Natour J, Vassalli M, Rosenfeld A, Jennings F, Jones A. Effectiveness of customized insoles in patients with Morton's neuroma: a randomized, controlled, double-blind clinical trial. *Clin Rehabil.* 2019;33(12):1898-1907. [PubMed](#)
- Grim C, Kramer R, Engelhardt M, John SM, Hotfiel T, Hoppe MW. Effectiveness of Manual Therapy, Customised Foot Orthoses and Combined Therapy in the Management of Plantar Fasciitis-a RCT. *Sports.* 2019;7(6):28. [PubMed](#)
- Reina-Bueno M, Vazquez-Bautista MDC, Perez-Garcia S, Rosende-Bautista C, Saez-Diaz A, Munuera-Martinez PV. Effectiveness of custom-made foot orthoses in patients with rheumatoid arthritis: a randomized controlled trial. *Clin Rehabil.* 2019;33(4):661-669. [PubMed](#)
- Hsieh RL, Peng HL, Lee WC. Short-term effects of customized arch support insoles on symptomatic flexible flatfoot in children: A randomized controlled trial. *Medicine.* 2018;97(20):e10655. [PubMed](#)
- Linberg BH, Mengshoel AM. Effect of a thin customized insole on pain and walking ability in rheumatoid arthritis: A randomized study. *Musculoskeletal Care.* 2018;16(1):32-38. [PubMed](#)

Non-Randomized Studies

- Albano D, Bonifacini C, Zannoni S, et al. Plantar forefoot pain: ultrasound findings before and after treatment with custom-made foot orthoses. *Radiol Med.* 2021;126(7):963-970. [PubMed](#)
- Feyzioğlu Ö, Ozturk O, Mugarbi S. Effects of custom-made insoles on foot pressure redistribution, gait parameters, and pain in calcaneal apophysitis-a pretest and posttest study. *Prosthet Orthot Int.* 2021;45(6):532-537. [PubMed](#)
- Reina-Bueno M, Vazquez-Bautista C, Palomo-Toucedo IC, Dominguez-Maldonado G, Castillo-Lopez JM, Munuera-Martinez PV. Custom-Made Foot Orthoses Reduce Pain and Fatigue in Patients with Ehlers-Danlos Syndrome. A Pilot Study. *Int J Environ Res Public Health.* 2020;17(4):20. [PubMed](#)
- Tenten-Diepenmaat M, Dekker J, Twisk JWR, Huijbrechts E, Roorda LD, van der Leeden M. Outcomes and potential mechanism of a protocol to optimize foot orthoses in patients with rheumatoid arthritis. *BMC Musculoskelet Disord.* 2020;21(1):348. [PubMed](#)
- Wang K, Lu C, Ye R, et al. Research and development of 3D printing orthotic insoles and preliminary treatment of leg length discrepancy patients. *Technol Health Care.* 2020;28(6):615-624. [PubMed](#)

De la Corte-Rodriguez H, Rodriguez-Merchan EC, Alvarez-Roman MT, Martin-Salces M, Jimenez-Yuste V. Hindfoot malalignment in adults with haemophilic ankle arthropathy: The importance of early detection and orthotic treatment. *Haemophilia*. 2019;25(3):500-508. [PubMed](#)

Molines-Barroso RJ, Lazaro-Martinez JL, Beneit-Montesinos JV, Alvaro-Afonso FJ, Garcia-Morales E, Garcia-Alvarez Y. Predictors of Diabetic Foot Reulceration beneath the Hallux. *J Diabetes Res*. 2019;2019:9038171. [PubMed](#)

Jarl G, Tranberg R. An innovative sealed shoe to off-load and heal diabetic forefoot ulcers - a feasibility study. *Diabet Foot Ankle*. 2017;8(1):1348178. [PubMed](#)

Guidance Documents — Methodology Not Reported

Professional Guideline Custom Orthotics. Vancouver (BC): The Board of the College of Physicians and Surgeons of British Columbia. 2020. <https://www.cpsbc.ca/files/pdf/PSG-Custom-Orthotics.pdf> Accessed 2022 Feb 4.

Ambulatory Adult Management of Type 2 Diabetes Mellitus Guideline. Ann Arbor (MI): University of Michigan. 2021 <https://michmed-public.policystat.com/policy/10636439/latest/> Accessed 2022 Feb 4.

Alternative Interventions and Comparators

Dissaneewate T, Na Rungsri T, Cheunchokasan P, Leelasamran W. Comparison between the plantar pressure effects of toe separators and insoles in patients with hallux valgus at a one-month follow-up. *Foot Ankle Surg*. 2022;28:12. [PubMed](#)

Seligman DAR, Dawson D, Streiner DL, Seligman DJ, Davis A. Treating Heel Pain in Adults: A Randomized Controlled Trial of Hard vs Modified Soft Custom Orthotics and Heel Pads. *Arch Phys Med Rehabil*. 2021;102(3):363-370. [PubMed](#)

Costa ARA, de Almeida Silva HJ, Mendes A, Scattone Silva R, de Almeida Lins CA, de Souza MC. Effects of insoles adapted in flip-flop sandals in people with plantar fasciopathy: a randomized, double-blind clinical, controlled study. *Clin Rehabil*. 2020;34(3):334-344. [PubMed](#)

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