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SUMMARY WITH CRITICAL APPRAISAL

Customized or Prefabricated Shoe Inserts for Chronic, Non-Cancer Pain: A Review of Clinical Effectiveness

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Abbreviations

6 MWT	six minute walk time
CI	confidence interval
FFI	foot function index
FHSQ-Br	foot health status questionnaire (Brazilian version)
MCID	minimal clinically important difference
NPRS	numerical pain rating scale
ODI	Oswestry disability index
RA	rheumatoid arthritis
RCT	randomized controlled trial
RCTs	randomized controlled trials
SF-36	36 item short form health survey questionnaire
SMD	standardized mean difference
VAS	visual analog scale

Context and Policy Issues

Chronic pain is generally defined as pain lasting for three months or longer, or persisting beyond the time needed for normal tissue healing.[1] It can impact the individual's quality of life and productivity, and is associated with substantial health care costs.[1,2] Chronic pain is a global problem.[2] It is estimated that one in five Canadians suffer from chronic pain.[3] It is generally more common among older adults, females, Indigenous people, Veterans, and people encountering inequalities and discrimination.[3] According to one report,[4] in Canada during the period 2007 to 2008, the prevalence rates for chronic pain in the age groups 26 years to 35 years, 46 years to 55 years, 56 years to 65 years, and 66 years and older were respectively 17.4%, 23.4%, 28.6% and 31.5% in females and 15.3%, 22.8%, 22.0%, and 22.2% in males.

There are a variety of chronic pain conditions such as chronic back pain, chronic neck pain, chronic tension headache, and chronic arthritic pain.[2,4] Chronic pain can affect various parts of the body such as the lower back, upper back, knee, leg, feet, shoulder, neck, and hip.[4] Lower back pain appears to be the most predominant type, accounting for more than one-third of those suffering from chronic pain.[4]

There are several non-pharmacological treatment options available for chronic pain such as exercise, multidisciplinary rehabilitation, psychological therapies, and physical modalities.[1] Foot orthotics are one example of a non-pharmacological treatment option for chronic pain, and include custom-made shoe inserts or prefabricated shoe inserts (with a treatment intent). These inserts are intended to support or align foot structures or to prevent or correct foot deformaties,[5] and can be of various types such as soft, semi-rigid, and rigid.[6,7] These inserts are sometimes referred to as insoles; however, these are specialized insoles with a treatment intent. It is thought that foot function can affect the kinematics of the knee, hip,

pelvis, and the thorax.[5] Foot orthotics have been used for the management of chronic pain, in individuals with various conditions such as rheumatoid arthritis and low back pain.[5,7] However, there appears to be some uncertainty with respect to its effectiveness in improving pain and disability.[8]

This report is an upgrade from a recent (published in 2020) CADTH Reference List report[9] and with additional restrictions with respect to inclusion criteria. The purpose of the current report is summarize and critically appraise the relevant evidence identified in the previous report[9] regarding the clinical effectiveness of customized foot orthotics or prefabricated shoe inserts (with a therapeutic intent) for chronic non-cancer pain.

Research Question

What is the clinical effectiveness of customized foot orthotics or prefabricated shoe inserts for chronic non-cancer pain?

Key Findings

There were inconsistencies regarding the effectiveness of foot orthoses compared with control (standard insole, placebo, or none) in alleviating pain in adult patients with foot pain based on findings from three systematic reviews and two randomized controlled trials (RCTs); reported results from these studies included statistically significant improvements in pain with foot orthoses compared to control (one systematic review, and two RCTs), no statistically significant between group difference (one systematic review) and inconsistent findings for between group differences (one systematic review describing studies individually).

There were inconsistencies regarding the effectiveness of foot orthoses compared with control (standard insole, placebo, or none) in improving function in adult patients with foot pain based on findings from two systematic reviews and one RCT; reported results from these studies included a statistically significant improvement with foot orthoses compared to control (one RCT) and no statistically significant between group differences (two systematic reviews and one RCT).

Limited evidence (one RCT) showed improvement in pain and function with foot orthoses compared to no foot orthoses, in adult patients with chronic low back pain.

Findings need to be interpreted with caution considering the limitations (such as unclear or variable quality of included studies, small sample size and overlap of studies included in the systematic reviews).

No studies were identified that compared treatments with foot orthoses with pharmacological treatments for non-cancer pain in adults.

Methods

Literature Search Methods

This report is an upgrade of a previously published CADTH report.[9] It makes use of a limited literature search conducted by an information specialist on key resources including Ovid Medline, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health

technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were foot orthotics and chronic pain. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The initial search was also limited to English language documents published between January 1, 2015 and January 20, 2020.

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.

Table 1: Selection Criteria

Population	Adults living with chronic non-cancer pain, excluding pregnant patients (excluding knee osteoarthritis, heel pain, and prevention of lower limb overuse injuries)
Intervention	Customized foot orthotics or prefabricated shoe inserts (i.e., non-custom shoe inserts with therapeutic intent)
Comparator	Pharmacological interventions No treatment (no orthotics) Usual care (if usual care is pharmacological interventions only)
Outcomes	Clinical effectiveness (pain, functional performance, quality of life, disability level, safety, global impression of recovery, adverse events)
Study Designs	Health technology assessments, systematic reviews, and randomized controlled trials

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2015.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by one reviewer using the AMSTAR 2 checklist,[10] and randomized studies were critically appraised using the Downs and Black checklist.[11] Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 228 citations were identified in the literature search. Following screening of titles and abstracts, 215 citations were excluded and 13 potentially relevant reports from the electronic search were retrieved for full-text review. No potentially relevant publications were retrieved from the grey literature search for full text review. Of these 13 potentially relevant articles, seven publications were excluded for various reasons, and six publications met the inclusion criteria and were included in this report. These comprised three

systematic reviews,[6-8] and three RCTs.[5,12,13] Appendix 1 presents the PRISMA[14] flowchart of the study selection.

Summary of Study Characteristics

Study characteristics are summarized and additional details are provided in Appendix 2, Table 2 (systematic reviews) and Table 3 (RCTs). The different outcome measures are described in Appendix 2, Table 4. Three systematic reviews,[6-8] and three RCTs[5,12,13] were included. One systematic review[6] had a broad objective and included studies on both pediatric and adult patients as well as comparisons between different types of orthotics. For this systematic review[6] only the subset of studies that were relevant for this review are described here.

Study Design

Of three systematic reviews[6-8] identified for this report, two systematic reviews[7,8] included meta-analyses. All three systematic reviews included RCTs, the number of relevant RCTs ranged from three to five and were published between 1996 and 2006. There was overlap in the studies included in the systematic reviews (Appendix 5).The literature search periods were until June 2017 in one systematic review,[7] October 2016 in one systematic review,[6] and July 2014 in one systematic review.[8]

Of the three RCTs[5,12,13] included, two RCTs[5,13] were not blinded, and one RCT[12] was double-blinded (patient and assessor were blinded). The RCTs were published between 2016 and 2019.

Country of Origin

The first authors of two systematic reviews[6,7] were from Spain, and the first author of one systematic review[8] was from Brazil. In one systematic review[7] the countries for the included RCTs were mentioned (one each in New Zealand, Slovenia, UK and US), and in two systematic reviews[6,8] the countries for the included RCTs were not mentioned.

Countries where the three RCTs[5,13] were conducted, were Brazil,[12] Turkey,[13] and the US.[5]

Patient Population

The systematic reviews[6-8] included adult patients with rheumatoid arthritis (RA) and foot pain, additionally one systematic review[8] specified the age range as 18 years to 75 years. The total number of included patients in the relevant RCTs ranged between 110 and 318. In one systematic review[6] the proportion of females ranged between 81% and 100%, and in the other two systematic reviews[7,8] the proportions of females were not specified.

Patient populations investigated in the RCTs included adults with painful flexible flatfoot,[13] adults with RA with foot pain[12], and adults with chronic low back pain.[5] The number of included patients ranged between 67 and 110, mean age varied between 22 years and 53 years, and the proportion of females ranged between 19% and 100%. The mean duration of the painful condition was 10 years in one RCT,[5] 13 years in the second RCT,[12] and not reported in the third RCT.[13]

Interventions and Comparators

In the systematic reviews, interventions included custom-made orthoses (soft, semi-rigid, or semi-flexible),[6] customized foot orthoses,[7] functional foot orthoses,[7] and orthotic insoles.[8] Different terminologies were used by the authors of the systematic reviews and descriptions

of interventions and comparators were minimal, hence it was difficult to ascertain what were the differences, if any.

In the RCTs, interventions included computer-aided design/computer-aided manufactured (CAD-CAM) insoles (computer software was used for designing and producing these customized insoles) or conventional insoles (computer software was not used for designing and producing these customized insoles),[13] custom-made leather shoe orthotics,[5] and custom-made insoles.[12]

In the systematic reviews, the comparators included wide-fitting footwear,[6] placebo insoles,[7,8] simple insoles,[7] or no orthoses.[7,8] Description of comparators in the systematic reviews lacked details.

In the RCTs, the comparators included sham or placebo insole (i.e., flat insole),[12,13] or no orthoses.[5]

Outcomes

Outcomes reported included pain;[5-8,12,13] function or disability;[5,7,8,12,13] and adverse events.[5,13] Follow-up was reported for two systematic reviews and all RCTs[5-7,12,13] and varied between four weeks and 12 months; and was not reported[8] for one systematic review.

Measures used include six minute walk time (6 MWT),[12] foot function index (FFI),[12,13] foot health status questionnaire Brazilian version (FHSQ-Br),[12] numerical pain rating scale (NPRS),[5] Oswestry disability index (ODI),[5] 36-item short form health survey (SF-36),[12,13] and visual analog scale (VAS).[12,13] Descriptions of the specific measures are presented in Appendix 2, Table 4.

Summary of Critical Appraisal

The critical appraisal of the included studies is summarized and additional details are provided in Appendix 3, Table 5 (systematic reviews) and Table 6 (RCTs).

Systematic reviews

In all three systematic reviews[6-8] the objective was stated, multiple databases were searched, article selection was described, a list of included articles was presented; and the authors mentioned that they had no conflicts of interest. A list of excluded studies was provided in one systematic review[7] and not in two systematic reviews.[6,8] In two systematic reviews[7,8] article selection was done independently by two reviewers; and in one systematic review[6] article selection was done by two reviewers but it was unclear if it was done independently. In one systematic review[6] data extraction was done by a single reviewer and in two systematic reviews[7,8] the method for data extraction was unclear. In all three systematic reviews quality assessments were conducted and the included studies were found to be of variable quality. In two systematic reviews[7,8] the study characteristics were desribed, and in one systematic review[6] the descriptions of study characteristics such as interventions and comparators were sparse. In all three systematic reviews there was no mention regarding investigation of publication bias. In two systematic reviews, meta-analyses results were presented but appropriateness of pooling is questionable as there was heterogeneity among the included studies. Overall it appears that the findings from these systematic reviews need to be interpreted with caution, considering that the quality of the included primary studies was variable or information regarding quality was lacking and

there was heterogeneity among the studies that were pooled to provide summary estimates.

Randomized controlled trials (RCTs)

In all three included RCTs[5,12,13] the objective; the inclusion and exclusion criteria; and patient characteristics, interventions and outcomes were described. In all three RCTs, randomization was appropriately done; sample size calculations were conducted, and the appropriate number of patients were recruited; and intention to treat analysis was conducted. One RCT[12] was double-blinded, and the other two RCTs[5,13] were not blinded. Lack of blinding has the potential for performance and detection biases. In one RCT[13] it was mentioned that there were no conflicts of interest. In one RCT[12] conflicts of interest were not declared, and in one RCT[5] one of the authors was associated with industry hence potential for bias cannot be ruled out.

Summary of Findings

Relevant study findings are summarized and details of the main study findings and authors' conclusions are presented in Appendix 4, Table 7 (systematic reviews) and Table 8 (RCTs).

Clinical Effectiveness of customized or prefabricated shoe insoles for chronic non-cancer pain

Patients with foot pain

Three systematic reviews[6-8] and two RCTs[12,13] presented results with respect to patients with foot pain.

One systematic review[6] narratively described four RCTs involving patients with RA experiencing foot pain. There were inconsistencies in the findings. One RCT showed that there was a statistically significant decrease in pain with custom-made sole orthosis compared with a standard one (P = 0.001), the follow-up period was 30 weeks. The second RCT showed that there was statistically significant decrease in pain from baseline level with semi-rigid insoles (P = 0.0004), and there was no decrease in pain with standard footwear; the follow-up period was 40 weeks. The third RCT showed custom-made foot orthosis significantly reduced the level of forefoot pain (P = 0.008), and the follow-up period was one month; however, the comparator group was not specified in this systematic review (but was described as "no orthoses" in another systematic review[8] that also included this RCT). The fourth RCT showed that there was no difference in pain with customized semi-rigid orthosis compared with standard footwear; the follow-up period was six months.

The second systematic review[7] included five RCTs involving RA patients with foot pain and presented findings from meta-analyses. It showed that there was no statistically significant difference in pain or disability between customized foot orthosis groups and control (simple insole or placebo) groups (95% confidence interval [CI], -0.58 to 0.65 for pain in the short-term, -0.70 to 0.18 for pain in the long term, and -0.11 to 0.47 for disability in the long-term; expressed in terms of standardized mean difference [SMD]).

The third systematic review[8] included three RCTs involving RA patients, presented findings from meta-analyses. It showed that there was a statistically significant difference in pain between the orthosis group and the control (placebo or none) group (95% CI, -0.67 to -0.13, expressed in terms of SMD), favoring foot orthosis; however there was no statistically significant between group difference in terms of disability (95% CI, -0.54 to 0.04, expressed in terms of SMD).

One RCT[13] involved adult patients with painful flexible flatfoot. This RCT showed that with all three types of insoles (CAD-CAM, conventional and sham), statistically significant improvement was observed with respect to pain intensity, FFI, and SF-36 physical health after treatment compared to before treatment; however the effect size with CAD-CAM insole and conventional insole were greater than the effect size with sham insole. There was a statistically significant between group difference in pain intensity, with CAD-CAM insole compared to sham insole, favoring CAD-CAM insole (P = 0.003) and with conventional insole compared to sham insole, favoring conventional insole (P= 0.001). There was no statistically significant between group difference with CAD-CAM insole compared to conventional insole (P = 0.690). None of the patients experienced adverse events.

One RCT[12] involving RA patients with foot pain was identified. This RCT showed that with repeated measures over a time duration of 180 days, there was a statistically significant between group difference in pain while walking (based on VAS scores), with custom-made insole compared to flat insole, favoring custom-made insole (P < 0.001). However, there was no statistically significant between group differences with respect to other measures (6 MWT, FFI, FHSQ-Br, SF-36) with P values ranging between 0.092 to 0.793.

None of the systematic reviews or RCTs reported on what would be considered a clinically important difference for any of the outcomes.

Patients with chronic low back pain

One RCT[5] presented results with respect to patients with chronic low back pain. This RCT found that low back pain and disability improved after care with shoe orthotics. This RCT showed that at 6 weeks, there was a statistically significant between group difference in pain (based on NPRS scores) in the orthotic group compared with the waitlist group, favoring orthotics (95% confidence interval [CI], 0.7 to 1.9; P < 0.0001). Also, at 6 weeks, there was a statistically significant between group difference in disability (based on ODI scores) in the orthotic group compared with the waitlist group, favoring orthotics (95% CI, 0.6 to 3.9; P = 0.0068). After 6 weeks, the waitlist group were also given orthotics and both groups were followed up to 12 months; at the 12-week, 3-month, 6-month and 12-month assessments there were no statistically significant differences between the groups with respect to pain or disability. This study reported that ≥30% decrease in disability (ODI) from baseline, was considered to be a minimal clinically important difference (MCID). It reported that at week 6, the proportions of patients with a MCID with respect to decrease in disability were 38.4% in the orthotic group and 20.3% in the waitlist group. None of the patients experienced adverse events.

Limitations

There was overlap in the studies included in the selected systematic reviews, hence the findings are not exclusive. Two systematic reviews[7,8] reported summary estimates for disability using the same two RCTs (i.e., complete overlap) and showed that there was no statistically significant difference between the intervention and control. The numerical values of the summary estimates differed and the reason for this was unclear

One systematic review[6] had several methodological limitations. The other two systematic reviews[7,8] had few methodological limitations, but the included primary studies were of variable quality or quality was unclear. One systematic review[7] reported that the included studies were small and did not have sufficient statistical power to detect a difference in outcomes between the groups.

The intervention and comparator (control) were described differently for one study that was included in two systematic reviews,[7,8] which gives rise to some ambiguity. Hence it was difficult to ascertain the specifics of the intervention and control. Description of foot orthoses devices and comparators in the systematic reviews[6-8] lacked details. In one systematic review (Arias-Martin)[6] there was discrepancy in the number of patients reported in the table and text, so it was unclear which number was accurate. We have reported the number from the table.

None of the studies involving patients with RA or flexible flat foot with pain reported on what would be considered a clinically important difference for the particular outcome investigated.

The majority of the primary studies were of small sample size (less than 100 patients).

Findings need to be interpreted with caution considering the limitations (such as unclear or variable quality of included studies, small sample size, discrepancies in data)

No studies were identified that compared treatments with customized foot orthotics or prefabricated shoe inserts (with a therapeutic intent) with pharmacological treatments for non-cancer pain (excluding knee osteoarthritis, heel pain, and prevention of lower limb overuse injuries) in adults. The selected studies involved patients with RA or flexible flat foot with pain, and chronic low back pain. No evidence was identified regarding the impact of foot orthoses in case of pain associated with other conditions.

The countries where the studies were conducted were not always specified. None of the studies (which specified the country) were conducted in Canada, hence generalizability of the findings to the Canadian setting is unclear. Additionally, it was unclear if the products investigated are available in Canada.

Conclusions and Implications for Decision or Policy Making

Three systematic reviews[6-8] and three RCTs[5,12,13] regarding the clinical effectiveness of foot orthotics for patients with chronic non-cancer pain were identified for this report.

Findings from three systematic reviews[6-8] and two RCTs[12,13] involving patients with RA or flexible flatfoot with foot pain showed there were inconsistencies regarding effectiveness of foot orthoses compared with control (standard insole [no therapeutic intent], placebo, or none) in alleviating pain. One systematic review[6] described individual primary studies and reported statistically significant between group differences in pain, favoring foot orthoses in some studies, and no between group differences in others. Of the other two systematic reviews[7,8] with meta-analysis, one systematic review[8] reported a statistically significant between group difference in pain, favoring foot orthoses and one systematic review[7] reported no statistically significant between group difference in pain. Two RCTs[12,13] reported statistically significant between group differences in pain, favoring foot orthoses. Findings from two systematic reviews[7,8] and two RCTs[12,13] showed there were inconsistencies regarding effectiveness of foot orthoses compared with control (standard insole, placebo, or none) in improving function; these results included a statistically significant between group difference in function, favoring foot orthoses (one RCT[13]) and no statistically significant between group difference (two systematic reviews[7,8] [including the same two RCTs; i.e., complete overlap] and one RCT[12]).

One RCT[5] involving patients with chronic low back pain showed statistically significant between group differences at 6 weeks in pain and disability, in the orthotic group compared with the waitlist group, favoring orthotics.

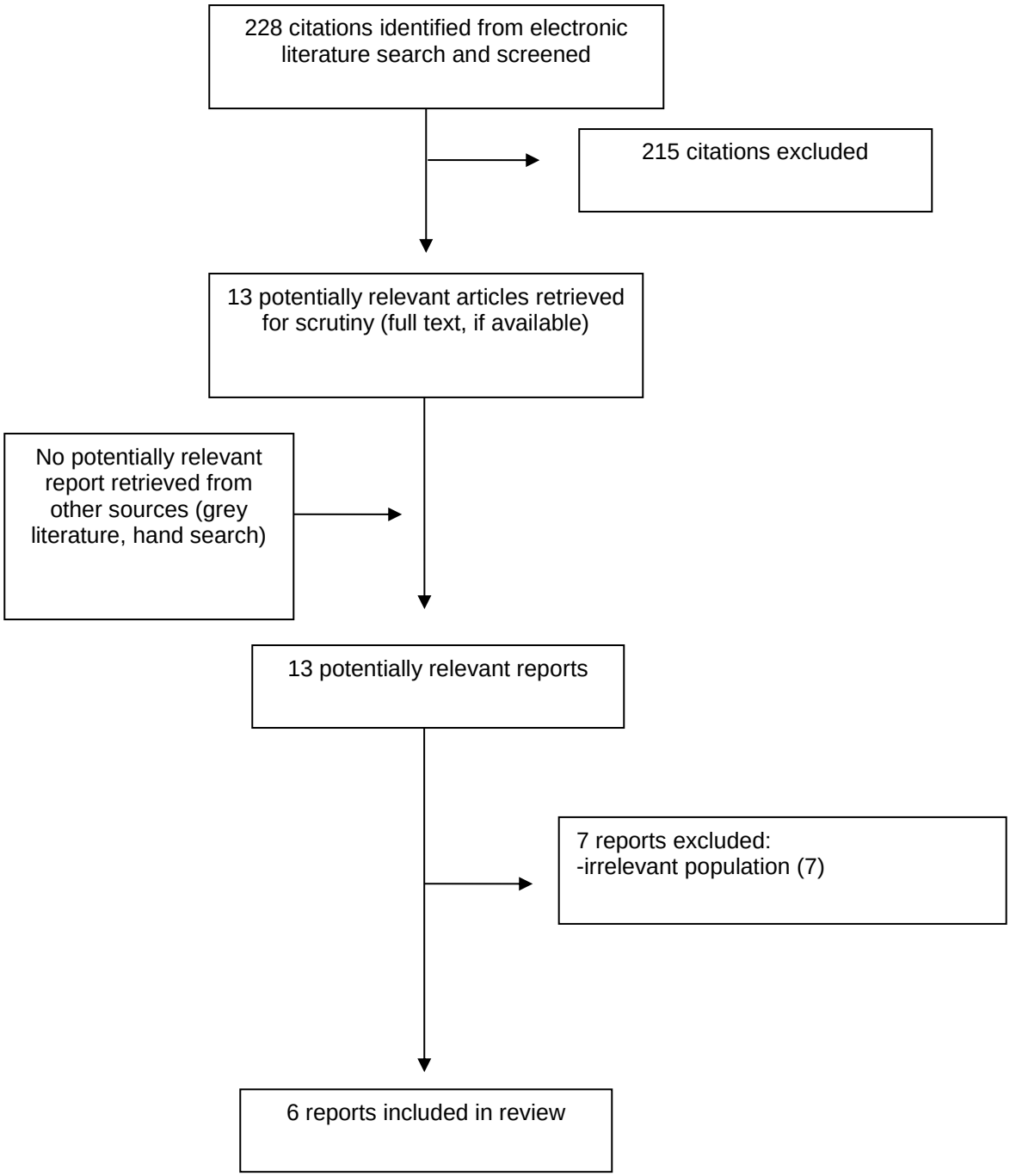
No studies were identified that compared treatments with customized foot orthotics or prefabricated shoe inserts (with a therapeutic intent) with pharmacological treatments for non-cancer pain (excluding knee osteoarthritis, heel pain, and prevention of lower limb overuse injuries) in adults.

Well-designed, and adequately powered studies are needed to decrease the level of uncertainty with respect to the clinical effectiveness of foot orthoses compared to no treatment or placebo. Future studies are needed to investigate treatments with foot orthoses as compared with pharmacological treatments for non-cancer pain.

References

1. Skelly AC, Chou R, Dettori JR, et al. AHRQ comparative effectiveness reviews. *Noninvasive nonpharmacological treatment for chronic pain: a systematic review*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2018.
2. Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. *Cochrane Database Syst Rev.* 2017;4:Cd011279.
3. Canadian Pain Task Force. Chronic pain in Canada: laying a foundation for action. 2019; https://www.canada.ca/en/health-canada/corporate/about-health-canada/public-engagement/external-advisory-bodies/canadian-pain-task-force/report-2019.html#a1. Accessed 2020 Apr 13.
4. Schopflocher D, Taenzer P, Jovey R. The prevalence of chronic pain in Canada. *Pain Res Manag.* 2011;16(6):445-450.
5. Cambron JA, Dexheimer JM, Duarte M, Freels S. Shoe orthotics for the treatment of chronic low back pain: a randomized controlled trial. *Arch Phys Med Rehabil.* 2017;98(9):1752-1762.
6. 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.
7. 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.
8. Conceicao CS, Gomes Neto M, Mendes SM, Sa KN, Baptista AF. Systematic review and meta-analysis of effects of foot orthoses on pain and disability in rheumatoid arthritis patients. *Disabil Rehabil.* 2015;37(14):1209-1213.
9. Customized or pre-fabricated shoe inserts for chronic non-cancer pain: clinical effectiveness and guidelines. *(CADTH Rapid response report: reference list)*. Ottawa (ON): CADTH; 2020: https://www.cadth.ca/customized-or-prefabricated-shoe-inserts-chronic-non-cancer-pain-clinical-effectiveness-and. Accessed 2020 Apr 7.
10. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ.* 2017;358:j4008. http://www.bmj.com/content/bmj/358/bmj.j4008.full.pdf. Accessed 2020 Apr 13.
11. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health.* 1998;52(6):377-384. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf. Accessed 202 Apr 13.
12. Moreira E, Jones A, Oliveira HA, Jennings F, Fernandes A, Natour J. Effectiveness of insole use in rheumatoid feet: a randomized controlled trial. *Scand J Rheumatol.* 2016;45(5):363-370.
13. Yurt Y, Sener G, Yakut Y. The effect of different foot orthoses on pain and health related quality of life in painful flexible flat foot: a randomized controlled trial. *Eur J Phys Rehabil Med.* 2019;55(1):95-102.
14. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol.* 2009;62(10):e1-e34.
15. Haefeli M, Elfering A. Pain assessment. *Eur Spine J.* 2006;15(Suppl 1):S17-S24.
16. Mehra A, Baker D, Dysney S, Pynsent PB. Oswestry disability index scoring made easy. *Ann R Coll Surg Engl.* 2008;90(6):497-499.
17. Chalmers AC, Busby C, Goyert J, Porter B, Schulzer M. Metatarsalgia and rheumatoid arthritis--a randomized, single blind, sequential trial comparing 2 types of foot orthoses and supportive shoes. *J Rheumatol.* 2000;27(7):1643-1647.
18. Cho NS, Hwang JH, Chang HJ, Koh EM, Park HS. Randomized controlled trial for clinical effects of varying types of insoles combined with specialized shoes in patients with rheumatoid arthritis of the foot. *Clin Rehabil.* 2009;23(6):512-521.
19. Conrad KJ, Budiman-Mak E, Roach KE, et al. Impacts of foot orthoses on pain and disability in rheumatoid arthritics. *J Clin Epidemiol.* 1996;49(1):1-7.
20. Mejjad O, Vittecoq O, Pouplin S, Grassin-Delyle L, Weber J, Le Loet X. Foot orthotics decrease pain but do not improve gait in rheumatoid arthritis patients. *Joint Bone Spine.* 2004;71(6):542-545.
21. Novak P, Burger H, Tomsic M, Marincek C, Vidmar G. Influence of foot orthoses on plantar pressures, foot pain and walking ability of rheumatoid arthritis patients--a randomised controlled study. *Disabil Rehabil.* 2009;31(8):638-645.
22. Postema K, Burm PE, Zande ME, Limbeek J. Primary metatarsalgia: the influence of a custom moulded insole and a rockerbar on plantar pressure. *Prosthet Orthot Int.* 1998;22(1):35-44.
23. Rome K, Clark H, Gray J, McMeekin P, Plant M, Dixon J. Clinical effectiveness and cost-effectiveness of foot orthoses for people with established rheumatoid arthritis: an exploratory clinical trial. *Scand J Rheumatol.* 2017;46(3):187-193.
24. Woodburn J, Barker S, Helliwell PS. A randomized controlled trial of foot orthoses in rheumatoid arthritis. *J Rheumatol.* 2002;29(7):1377-1383.

Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Arias-Martin,[6] 2018, Spain	Systematic review (Includes 4 relevant RCTs published between 1998 and 2014, countries where the RCTs were conducted were not reported) (Note: Of the 9 studies included in the systematic review, 4 studies were relevant for this report) Aim: To assess effectiveness of custom-made foot orthoses for treating forefoot pain.	Adults with forefoot pain (3 RCTs – rheumatoid arthritis, 1 RCT - metatarsalgia); No of patients = 110 and size range for individual RCTs, 16 to 42 Mean age (years) for the individual RCTs ranged between 49 to 60 % Female: 92% and range 81% to 100%	Intervention: Custom made orthoses (soft and semi-rigid [1 RCT], semi-rigid [1RCT], semi-flexible [1 RCT], thermoplastic: type of orthosis unknown [1 RCT]. Comparators: wide fitting footwear (3 RCTs) and unclear (1 RCT)	Pain, function (Details of measures used were not presented) Follow-up: 1 month to 40 weeks
Gijon-Nogueron,[7] 2018, Spain	Systematic review with meta-analysis (included 5 RCTs [all relevant to this report] published from 1996 to 2016, one each from Korea, New Zealand, Slovenia, UK and US) Aim: To assess effectiveness of custom-made foot orthoses for treating patients with RA	Adult patients with RA and having foot pain N = 318, size range for individual RCTs 40 to 102 Age: adult (age details not reported) % Female: not reported	Intervention: customized foot orthoses (3 RCTs), functional foot orthoses (2 RCTs). Comparator: simple insoles (2 RCTs), placebo orthoses (1 RCT), unshaped material (1 RCT), and none unless prescribed under medical are (1 RCT)	Pain, disability (Measures used included VAS, FFI, 6MWT, AIMS. Results were expressed in terms of SMD) Follow up: 4 months to 36 months
Conceição,[8] 2015, Brazil	Systematic review with meta-analyses (included 3 RCTs [all relevant to this report]published between 1996 and 2004; countries where the RCTs were conducted were not stated)	Adult patients with RA and having foot pain (had not received foot orthoses in at least the previous 4 weeks) N = 218, size range for individual RCTs 32 to 98) Mean age (years) in the individual RCTs	Intervention: Foot orthoses (defined as orthotic devices [insoles], placed between the plantar surface and the sole of the shoe, with the intention to support or align foot structures or to prevent or correct foot abnormalities.	Pain, disability (Measures used included FFI, VAS, AIMS. Results were expressed as SMD) Follow up: not reported

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
	Aim: To assess effectiveness of custom-made foot orthoses for treating patients with RA	ranged between 18 to 75 % Female: not reported	Control: no orthoses or placebo	

6MWT = 6-minute walk time; AIMS = American impact measurement scale; FFI = foot function index; RA = rheumatoid arthritis; RCT = randomized controlled trial; SMD = standardized mean difference; UK = United Kingdom; US = United States of America; VAS = visual analog scale.

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Yurt,[13] 2019, Turkey	RCT, no blinding (with 3 arms) Patients recruited between January 2014 and September 2015, last follow-up ended in January 2016) Setting: Outpatient rehabilitation clinic Patients were recruited between January 2014 and January 2016. Eligibility criteria: adults with a minimum of +6 points on FPI, no foot treatment for ≤ 6 months, no leg length discrepancy ≥ 1 cm, no lower extremity surgery, and no disease likely to impact lower extremity biomechanics.	Adult patients with foot pain (for at least one month) due to flexible flatfoot deformity. N = 67 (22 in CAD-CAM; 22 in conventional; and 23 in sham) Age (years) (mean ± SD): 21.73 ± 2.89 in CAD-CAM; 23.05 ± 5.53 in conventional; and 21 .09 ± 1.95 in sham. % Female:19.4% in CAD-CAM; 17.9% in conventional; and 20.9% in sham BMI (kg/m2) (mean ± SD): 23.03 ± 3.48 in CAD-CAM; 24.11 ± 4.15 in conventional; and 23.32 ± 3.28 in sham. Disease duration: not reported Groups were also well balanced with respect	CAD-CAM insole (computer software was used in designing these) versus conventional insole (computer software was not used in designing these) versus sham insole In addition, all groups underwent home-based exercises.	Pain (using VAS), FFI, Qol (using SF-36). Adverse event (deterioration of pain using VAS). Follow-up: 2 months

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
		to factors such as foot posture index, foot pain localization, and calcaneal valgus angle		
Cambron,[5] 2017, US	RCT, no blinding (Of the 3 treatment arms, the two arms that were relevant for this report are included here [the third arm that include orthotics plus chiropractor care is not relevant for this report and is not discussed here]) Patients were recruited between Spring 2014 and Fall 2015, via media advertising in a midwestern suburban region in US Exclusion criteria: use of custom-made orthotics or undergoing other treatment for LBP in the last 6 months, chronic pain other than LBP, other conditions such as brain disorder, bleeding disorder, peripheral neuropathy, severe skeletal deformity of the foot, arterial aneurysm, and pregnancy.	Adult patients with chronic LBP N = 150 (75 in orthotic group [A], and 75 in the waitlist group [B]) Age (years) (mean ± SD): 52 ± 15 in A, and 53 ± 15 in B. % Female: 40% in A, and 47% in B. BMI: not reported Duration of back pain (years) (mean ± SD): 9.6 ± 10.0 in A, and 10.0 ± 9.0 in B Groups were also well balanced with respect to other factors such as status of back pain, ODI total score	Foot Levelers custom-made leather shoe orthotics versus no treatment (waitlist) (Note: The waitlist group was given the same Foot Levelers custom-made leather shoe orthotics after the 6-week wait period.)	Pain, disability (NPRS, ODI). Adverse events Follow-up: 12 months
Moreira,[12] 2016, Brazil	RCT, double blinded (2 arms) Setting: outpatient clinic in Brazil (study conducted between 2011 and 2012) Exclusion criteria: received injection in foot or ankle, or used insoles in the previous 3 months; history of foot surgery; mental	Adult RA patients with foot pain N = 80 (39 in EG, 41 in CG) Age (years) (mean ± SD): 53.3 ± 8.0 in EG, and 52.2 ± 9.0 in CG. % Female: 100% BMI (kg/m2) (mean ± SD):	Experimental group (EG): custom made insoles from ethylene vinyl acetate (EVCA) with a metatarsal support and a medial arch support Control group (CG): custom made placebo insole (flat insole) of the same material. All patients received the same instructions	Primary outcome: Foot pain while walking (VAS); Secondary outcomes: foot pain at rest (VAS), global function (HAQ), foot function (FFI, FHSQ-Br), walking ability (6MWT), general health status (SF-36) Follow-up: 180 days

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
	disability; accessibility issue; nervous system disease; diabetes; or inability to walk	25.8 ± 4.6 in EG; 26.6 ± 5.0 in CG Disease duration (years) (mean ± SD): 12.7 ± 8.5 in EG, and 12.6 ± 7.7 in CG	for insole use: 2 hours on day 1, with gradual increase of I hour per day until continuous use was reached. All patients were provided standardized special doll shoe so as to avoid possible influence that may arise from use of different types of shoes	

BMI = body mass index; CAD-CAM = computer-aided design/ computer-aided manufacturing; cm centimeter; FFI = foot function index; FHSQ-Br = FHSQ-Br = foot health status questionnaire (Brazilian version); FPI = foot posture index; HAQ = health assessment questionnaire; LBP = low back pain; NPRS = numerical pain rating scale; ODI = Owestry disability index; QoL = quality of life; RCT = randomized controlled trial; SD = standard deviation; SF-36 = short form 36; VAS = visual analog scale

Table 4: Details of Outcome Measures

Outcome measure	Explanation
FFI	Scores range from 0 to 100, with higher scores indicating greater impact from foot disability.[12]
FHSQ-Br	Scores range from 0 to 100, with higher scores indicating better foot health status.[12]
HAQ	Scores range from 0 to 3, with higher scores indicating poorer functional capacity.[12]
NPRS	Scores out of 10,[5] with higher scores indicating greater pain.[15]
ODI	Scores out of 50,[5] with higher scores indicating greater disability.[16]
SF-36	Scores range from 0 to 100, with higher scores indicating better overall health status.[12]
VAS	Scores range from 0 to 10, with higher scores indicating greater pain.[12,13]

FFI = foot function index; FHSQ-Br = foot health status questionnaire (Brazilian version); HAQ = Health assessment questionnaire; NPRS = numerical pain rating scale; ODI =Owestry disability index; SF-36 = 36-item short form; VAS = visual analog scale.

Appendix 3: Critical Appraisal of Included Publications

Table 5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR 2 checklist[10]

Strengths	Limitations
Arias-Martin,[6] 2018, Spain	
• The objective was clearly stated • Multiple databases (CINAHL, Medline, PEDro and Cochrane library) were searched until October 2016. • Study selection was described, and a flow chart was presented • A list of included studies was provided • Article selection was done independently by two reviewers • It was mentioned that the authors had no conflicts of interest • Quality assessment (risk of bias) was conducted. Quality of the included studies varied	• A list of excluded studies was not provided • Data extraction was done by one reviewer not independently by two reviewers • Unclear if quality assessment was done in duplicate • Unclear if publication bias was examined • Description of characteristics of the studies lacked details or were unclear. Additionally, there were some discrepancies in the information reported in the table and in the text.
Gijon-Nogueron,[7] 2018, Spain	
• The objective was clearly stated • Multiple databases (SCOPUS, Cuiden Plus, EMBASE, CINAHL, Medline and Cochrane library) were searched until June 2017. Also, reference list of include studies were searched. • Study selection was described, and a flow chart was presented • A list of included studies was provided • A list of excluded studies was provided • Article selection was done independently by two reviewers • Quality assessment (risk of bias) was conducted two reviewers using the Cochrane risk of bias tool. Quality of the included studies varied. • Characteristics of the included studies were presented • Meta-analysis was conducted and appeared to be appropriate • It was mentioned that the authors had no conflicts of interest	• Unclear if data extraction was done independently by two reviewers • Unclear if publication bias was examined
Conceição,[8] 2015, Brazil	
• The objective was clearly stated • Study selection was described, and a flow chart was presented • Multiple databases (Medline [from 1950 to July 2014] LILACS (to July 2014), CINAHL [from 1982 to July 2014], EMBASE [from 1980 to July 2014], PEDro, and Cochrane) Also, reference list of include studies were searched. • Study selection was described, and a flow chart was presented • A list of included studies was provided • Quality assessment was conducted using the Physiotherapy Evidence Database (PEDro) scale. The authors mentioned that randomization and allocation	• List of excluded studies was not presented • Unclear if data extraction was done independently by two reviewers. • As explained in the adjacent column, assessment of bias was not possible • Unclear if publication bias was examined • Meta-analysis was conducted. However, a fixed effect model was used, although there was considerable heterogeneity and no justification for choosing the fixed effects model was presented

Strengths	Limitations
concealment were poorly reported in the studies, hence assessment of potential risk of bias was difficult. • Article selection was done by two reviewers • Characteristics of the included studies were presented • It was mentioned that the authors had no conflicts of interest	

Table 6: Strengths and Limitations of Clinical Studies using Downs and Black checklist[11]

Strengths	Limitations
Yurt,[13] 2019, Turkey	
• The objective was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, intervention and outcomes were described. • Randomized study and the randomization method appeared appropriate (computer-generated random numbers were used, and each number was placed in an opaque unmarked envelope). Enrollment of patients was done by an independent researcher • Sample size calculation was conducted, and the appropriate number of patients were recruited. • Discontinuation and the associated reason were reported; 4.5%, 4.5% and 8.7% in CAD-CAM, con, and sham groups respectively. • ITT analysis was conducted • P values were reported • The authors mentioned that there were no conflicts of interest with any financial organization with respect to the material discussed	• The study was not blinded
Cambron,[5] 2017, US	
• The objective was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, intervention and outcomes were described. • Randomized study and the randomization method appeared appropriate (random numbers table, and random allocation) • Sample size calculation was conducted, and the appropriate number of patients were recruited. • ITT analysis was conducted • P values were reported • It was mentioned that of the four authors, one author had association with the manufacturer and the remaining three authors had no conflicts of interest	• The study was not blinded • Missed clinic visits during the duration of the study, were reported but reasons were not provided. Proportions of patients missing visits were 4% in both groups at 6-week and may not be an issue being a small percentage and equal in both groups. However, for later time points (such as 3, 6, and 12 months), the missing visits were substantial, ranging between 13% and 32% in the orthotic group and 16% to 29% in the waitlist group, and could have an impact on findings.

Strengths	Limitations
Moreira,[12] 2016, Brazil	
• The objective was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, intervention and outcomes were described. • Randomized study and the randomization method appeared appropriate (electronically generated randomization numbers, concealed allocation) • Double blinded (patients and assessor/investigator were blinded) • Sample size calculation was conducted, and the appropriate number of patients were recruited. • Missing clinic visits and associated reasons were reported for each time point (proportions missing visits ranged between 2.6% and 5.1% in the experimental group (EG) and 2.4% and 7.3% in the control group (CG). • ITT analysis was conducted • P values were reported	• Conflicts of interest of the authors were not presented

CAD-CAM = computer-aided design/ computer-aided manufacturing; con = conventional; ITT = intention-to-treat.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 7: Summary of Findings Included Systematic Reviews and Meta-Analyses

<table>
<tr><th>Main Study Findings</th><th>Authors' Conclusion</th></tr>
<tr><td colspan="2">Arias-Martin,[6] 2018, Spain</td></tr>
<tr><td>Findings from the systematic review involving patients with RA and forefoot pain and comparing intervention group (customized foot orthoses) with control group. The relevant included RCTs (4) were described individually.
<table>
<tr><th>Primary study</th><th>Study design</th><th>No. of patients</th><th>Findings</th></tr>
<tr><td>Cho, 2009</td><td>CCT</td><td>28</td><td>The study compared custom made semi-rigid orthoses with standard soles. Both groups had decreased pain from baseline. No between group difference was observed. The follow-up period was six months.</td></tr>
<tr><td>Mejjad, 2004</td><td>Study (details not reported)</td><td>16</td><td>The use of custom-made foot orthosis significantly reduced the level of forefoot pain in RA patients, when walking (P = 0.008). Comparator group was unclear. The follow-up period was 1 month</td></tr>
<tr><td>Chalmers, 2000</td><td>Cross-over study</td><td>24</td><td>The study compared semi-rigid orthoses with only footwear or soft orthoses in RA patients with foot pain. With the semi-rigid orthoses, there was significant improvement in pain compared with baseline (P = 0.0004). There was no decrease in symptoms with only footwear or soft orthoses. The follow-up period was 40 weeks</td></tr>
<tr><td>Postema, 1998</td><td>Study (details not reported)</td><td>42</td><td>The study compared custom-made sole orthoses with a standard one in patients with metatarsalgia (rheumatoid forefoot pain). It showed that pain level was significantly reduced with custom-made sole compared to a standard one, irrespective of whether the shoe used a rocker or not (P = 0.001). The follow-up period was 30 weeks.</td></tr>
</table>
</td><td>The authors concluded that "The use of custom-made foot orthoses improved the level of forefoot pain in rheumatoid arthritis, hallux abductus valgus and secondary metatarsalgia as it increases sole pressures." p.1865</td></tr>
<tr><td colspan="2">Gijon-Nogueron,[7] 2018, Spain</td></tr>
<tr><td>Findings from the systematic review and meta-analysis involving patients with RA and comparing intervention group (customized foot orthoses) with control group (simple insoles or placebo).</td><td>The authors concluded that "Foot orthoses can relieve pain and disability and enhance patients, but no significant differences were found between control and intervention groups." p. 3059</td></tr>
</table>

Main Study Findings	Authors' Conclusion

Outcome	No of studies	No. of patients	SMD (95% CI)	Heterogeneity, I^2
Pain (FU: short term)	3	87	0.03 (-0.58 to 0.65) (-0.70 to 0.65)	50%
Pain (FU: long term)	2	186	-0.26 (-0.70 to 0.18)	57%
Disability (FU: long term)	2	186	0.18 (-0.11 to 0.47)	78%

Disability (FU: short term): One study with 41 patients showed there was no statistically significant difference between the intervention and the control groups (P = 0.12)

No statistically significant differences were found between the intervention and control groups. The systematic review authors mentioned that the included studies did not have sufficient statistical power to detect a difference in outcomes between the groups.

Conceição,[8] 2015, Brazil

Findings from the systematic review and meta-analysis involving RA patients and comparing intervention group (foot orthoses) with control group (placebo or none).

All studies

Outcome	No of studies	No. of patients	SMD (95% CI)	Heterogeneity, I^2
Pain	3	218	-0.40 (-0.67 to -0.13)	84%
Disability	2	186	-0.25 (-0.54 to 0.04)	50%

The authors concluded that "FO may improve pain in RA patients, but their impact on disability remains undetermined. Additional large RCTs are needed to investigate the effects of these devices in RA patients." P. 1209

CCT = controlled clinical trial; CI = confidence interval; FO = foot orthoses; NA = not applicable; RA = rheumatoid arthritis; SMD = standardized mean difference;

Table 8: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion

Yurt,[13] 2019, Turkey

Findings from RCT comparing CAM-CAD insoles, conventional insoles and sham insoles for treating adults with flexible flatfoot (additionally all patients underwent home-based exercise)

Pain intensity (VAS, mm)

Group	Findings
CAD-CAM group	Before treatment: 59.27 ± 17.26 After treatment: 27.84 ± 18.41 Change between before and after: Effect size, 0.660; P <0.001
Conventional	Before treatment: 60.32 ± 16.82 After treatment: 27.05 ± 16.82 Change before and after: Effect size, 0.703; P <0.001
Sham	Before treatment: 58.48 ± 17.51X After treatment: 46.39 ± 20.18 Change before and after: Effect size, 0.304; P <0.001

The authors concluded that "CAM-CAD and conventionally designed insoles in con-junction with a home-based exercise program are both more effective in controlling pain compared with sham insole and exercise in flexible flatfoot." p. 101

Main Study Findings	Authors' Conclusion

Foot function index

Group	Findings
CAD-CAM group	Before treatment: 29.95 ± 14.47 After treatment: 21.81 ± 11.94 Change between before and after: Effect size, 0.293; P = 0.016
Conventional	Before treatment: 37.62 ± 17.35 After treatment: 24.11 ± 11.70 Change before and after: Effect size, 0.415; P <0.001
Sham	Before treatment: 30.09 ± 13.34 After treatment: 26.50 ± 13.91 Change before and after: Effect size, 0.130; P = 0.017

SF-36 physical health

Group	Findings
CAD-CAM group	Before treatment: 44.76 ± 7.24 After treatment: 50.14 ± 5.44 Change between before and after: Effect size, 0.387; P = 0.001
Conventional	Before treatment: 43.49 ± 6.85 After treatment: 50.17 ± 6.70 Change before and after: Effect size, 0.442; P <0.001
Sham	Before treatment: 45.60 ± 7.16 After treatment: 47.55 ± 7.21 Change before and after: Effect size, 0.134; P = 0.015

SF-36 mental health

Group	Findings
CAD-CAM group	Before treatment: 46.82 ± 10.90 After treatment: 46.13 ± 10.29 Change between before and after: Effect size, NR; P =0.433
Conventional	Before treatment: 48.91 ± 10.30 After treatment: 47.54 ± 9.05 Change before and after: Effect size, NR; P = 0.409
Sham	Before treatment: 47.91 ± 10.14 After treatment: 45.65 ± 9.17 Change before and after: Effect size, NR; P = 0.917

(Note:
Before treatment there were no statistically significant differences between the three groups with respect to pain intensity, foot function index, and QoL [SF-36 physical and SF 36 mental].
Effect size (Cohen's d) was calculated. Effect size between 0.2 to 0.5 indicates small effect, from 0.5 to 0.8 indicates medium effect, and > 0.8 indicates large effect)

Main Study Findings	Authors' Conclusion

Post-hoc analyses (Bonferroni correction)

Comparison	P values with respect to	
	Pain intensity	Insole satisfaction
CAD-CAM versus sham	0.003	0.182
Conventional versus sham	0.001	0.002
CAD-CAM versus conventional	0.690	0.020

Deteriorating foot pain (measured using VAS) was considered as an adverse event. None of patients reported such adverse events.

Cambron,[5] 2017, US

Findings from RCT comparing foot levelers shoe orthotics group with waitlist group for adult patients with chronic low back pain

Pain

Change in NPRS scores (out of 10) at various time points compared with baseline scores (Baseline values [mean, 95% CI] on NPRS were 5.5 [95% CI, 5.1 to 5.9] for orthotics group and 5.6 [5.2 to 6.0] for the wait-list group)

Time point	Change in NPRS score from baseline			
	Orthotics group		Waitlist group	
	Mean (95% CI)	P value (intra group)	Mean (95% CI)	P value (intra group)
Week 6	-1.9 (-2.4 to -1.4)	< 0.0001	-0.7 (-1.1 to -0.3)	0.0012
Week 12	-2.4 (-2.9 to -1.8)	< 0.0001	-2.2 (-2.7 to -1.8)	< 0.0001
3 months	-2.2 (-2.8 to -1.5)	< 0.0001	-2.2 (-2.9 to -1.6)	< 0.0001
6 months	-2.4 (-3.1 to -1.7)	< 0.0001	-1.9 (-2.6 to -1.2)	< 0.0001
12 months	-2.5 (-3.2 to -1.8)	< 0.0001	-2.2 (-3.0 to -1.4)	< 0.0001
NPRS scores: out of 10. Note: After week 12, patients were followed up for an additional 3, 6, and 12 months.				

Disability

Change in ODI scores at various time points compared with baseline scores (Baseline values [mean, 95% CI] on ODI were 12.6 [95% CI, 11.2 to 14.0] for orthotics group and 12.4 [11.1 to 13.7] for the wait-list group)

Time point	Change in ODI score from baseline			
	Orthotics group		Waitlist group	
	Mean (95% CI)	P value (intra group)	Mean (95% CI)	P value (intra group)
Week 6	-2.3 (-3.4 to -1.1)	0.0002	-0.05 (-1.2 to 1.1)	0.9230
Week 12	-3.6 (-4.9 to -2.3)	< 0.0001	-3.1 (-4.4 to -1.8)	< 0.0001
3 months	-3.5 (-4.9 to -2.2)	< 0.0001	-2.1 (-3.8 to -0.4)	0.0189
6 months	-3.5 (-5.1 to -1.9)	< 0.0001	-3.4 (-5.4 to -1.4)	0.0016
12 months	-3.7 (-5.3 to -2.2)	< 0.0001	-2.9 (-5.4 to -0.5)	0.0192
ODI score: out of 50. Note: After week 12, patients were followed up for an additional 3, 6, and 12 months				

The authors concluded "This large-scale clinical trial demonstrated that LBP and disability were significantly improved after 6 weeks of Foot Levelers shoe orthotics care compared with a waitlist group. [….] The within-group change scores from baseline to every follow-up through 12 months were statistically significant. However, there were no significant between-group differences at week 12 or later." P. 1760

Main Study Findings	Authors' Conclusion

Pain and disability (between group differences; waitlist group compared to orthotics group as reference group)

Time point	Outcome			
	Pain (NPRS)[a]		Disability (ODI)[a]	
	Between group difference[b]	P value	Between group difference[b]	P value
Week 6	1.3	<0.0001	2.3	0.0068
Week 12	0.2	0.4655	0.6	0.5355
3 months	-0.04	0.9269	1.4	0.2197
6 months	0.6	0.2150	0.04	0.9731
12 months	0.6	0.1725	0.8	0.5282

[a]Positive values indicate a higher level of pain or disability
[b]Waitlist group is compared to orthotics group as reference group. The waitlist group was given the shoe orthotics after the 6-week wait period.
Note: After week 12, patients were followed up for an additional 3, 6, and 12 months.

MCID (≥30% decrease in disability [ODI])

Time point	Percentage of patients achieving MCID compared with baseline			
	Pain (NPRS)		Disability (ODI)	
	Orthotics group	Waitlist group	Orthotics group	Waitlist group
Week 6	57.5	21.6	38.4	20.3
Week 12	67.7	52.4	51.6	41.0
3 months	58.7	60.4	52.4	44.2
6 months	72.5	49.0	56.9	53.1
12 months	62.3	54.2	56.6	50.0
Note: After week 12, patients were followed up for an additional 3, 6, and 12 months.				

Adverse events
It was reported that no patients experienced adverse events.

Moreira,[12] 2016, Brazil

Findings from RCT comparing experimental group (EG: orthotic custom made insole with metatarsal support and medial arch support) with control group (CG: flat insole) for adult RA patients with foot pain

Pain while walking
Comparison of VAS scores between EG and CG, at the various time points (Baseline scores [mean ± SD] on VAS for right foot were 6.9 ± 1.1 for EG and 6.8 ± 1.3 for CG; and for left foot were 7.0 ± 1.3 for EG and 6.2 ± 1.6 for CG)

Time point	Between group difference in VAS score			
	Right foot		Left foot	
	Mean difference	P value (ANOVA)	Mean difference	P value (ANOVA)
Day 45	-3.2	< 0.001	-2.5	< 0.001
Day 90	-2.9		-2.9	
Day 180	-2.2		-2.1	
Negative value indicates greater improvement in EG compared to CG				

The authors concluded that "In conclusion, insoles with medial arch and metatarsal supports for patients with RA can be used to diminish foot pain while walking and at rest. Duration of insole use was correlated with improvements in pain and function." p. 369

Main Study Findings	Authors' Conclusion

Pain while at rest

Comparison of VAS scores between EG and CG, at the various time points (Baseline scores [mean ± SD] on VAS for right foot were 5.3 ± 2.5 for EG and 4.8 ± 2.7 for CG; and for left foot were 5.1 ± 2.6 for EG and 4.5 ± 2.7 for CG)

Time point	Between group difference in VAS score			
	Right foot		Left foot	
	Mean difference	P value (ANOVA)	Mean difference	P value (ANOVA)
Day 45	-2.4	< 0.001	-0.3	< 0.001
Day 90	-1.6		-1.7	
Day 180	-0.3		-0.5	
Negative value indicates greater improvement in EG compared to CG				

SF-36

Comparison of SF-36 scores between EG and CG, at the various time points

Time point	Physical functioning		General health status		Mental health	
	Mean difference	P value (ANOVA)	Mean difference	P value (ANOVA)	Mean difference	P value (ANOVA)
Day 45	3.9	0.447	4.9	0.793	5.7	0.675
Day 90	0.0		4.4		4.6	
Day 180	0.1		1.0		1.1	
Positive value indicates greater improvement in EG compared to CG						

FHSQ-Br

Comparison of FHSQ-Br scores between EG and CG, at the various time points

Time point	Foot pain		General health		Physical activity	
	Mean difference	P value (ANOVA)	Mean difference	P value (ANOVA)	Mean difference	P value (ANOVA)
Day 45	1.1	0.593	5.7	0.319	3.9	0.163
Day 90	7.2		1.3		-1.6	
Day 180	5.4		-1.6		2.2	
Positive value indicates greater improvement in EG compared to CG						

6MWT, HAQ, and FFI

Time point	6MWT		HAQ		FFI	
	Mean difference	P value (ANOVA)	Mean difference	P value (ANOVA)	Mean difference	P value (ANOVA)
Day 45	27.2	0.293	-0.09	0.349	-6.1	0.789
Day 90	13.1		0.02		-5.6	
Day 180	13.6		-0.15		-6.5	
For 6MWT, positive value indicates greater improvement in EG compared to CG. For HAQ, negative value indicates greater improvement in EG compared to CG. For FFI, negative value indicates greater improvement in EG compared to CG.						

Main Study Findings	Authors' Conclusion
Insole use Comparison of insole use between EG and CG, at the various time points Time point / Insole use (h/day): Mean difference / P value (ANOVA) Day 45: 1.1 / 0.200 Day 90: 2.0 Day 180: 2.0	

6MWT = 6-minute walk test; ANOVA = analysis of variance; CAD-CAM = computer-aided design/computer aided manufacturing; CG = control group; EG = experimental group; FFI = foot function index; FHSQ-Br = foot health status questionnaire (Brazilian version); HAQ = health assessment questionnaire; MCID = minimal clinically important difference; NPRS = numerical pain rating scale; ODI = Oswestry disability index; RA = rheumatoid arthritis; SF-36 = 36-item short form health survey; VAS = visual analog scale.

Appendix 5: Overlap between Included Systematic Reviews

Table 9: Primary Study Overlap between Included Systematic Reviews

Primary Study Citation	Systematic Review Citation		
	Arias-Martin,[6] 2018, Spain	Gijon-Nogueron,[7] 2018, Spain	Conceição,[8] 2015, Brazil
Chalmers,[17] 2000	x		
Cho,[18] 2009	x	x	
Conrad,[19] 1996		x	x
Mejjad,[20] 2004	x		x
Novak,[21] 2009		x	
Postema,[22] 1998	x		
Rome,[23] 2017		x	
Woodburn,[24] 2002		x	x