Systematic Review Or Meta-Analysis

Meta-analyses of randomized controlled trials reporting the effect of home foot temperature monitoring, patient education or offloading footwear on the incidence of diabetes-related foot ulcers

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Abstract

Aim The aim of this study was to perform an up-to-date systematic review and meta-analysis of randomized controlled trials (RCTs) examining the efficacy of home foot temperature monitoring, patient education and offloading footwear in reducing the incidence of diabetes-related foot ulcers.

Methods A literature search was performed using MEDLINE, PubMed, CINAHL, Scopus and Cochrane databases to identify relevant original studies. Meta-analyses were performed using intention-to-treat principals for worst (main analysis) and best (sub-analysis) case scenarios. Leave-one-out sensitivity analyses were used to assess the consistency of findings.

Results Of 7575 unique records, 17 RCTs involving 2729 participants were included. Four tested home foot temperature monitoring (n = 468), six examined patient education (n = 823) and seven assessed offloading footwear (n = 1438). Participants who performed home foot temperature monitoring [odds ratio (OR) 0.51, 95% confidence interval (CI) 0.31 to 0.84; n = 468] and those provided offloading footwear (OR 0.48, 95% CI 0.29 to 0.80; n = 1438) were less likely to develop a diabetes-related foot ulcer. Patient education programmes did not significantly reduce diabetes-related foot ulcer incidence (OR 0.59, 95% CI 0.29 to 1.20; n = 823). Sensitivity analyses suggested that offloading footwear findings were consistent, but home foot temperature findings were dependent on the individual inclusion of one trial. All RCTs had either high or unclear risk of bias.

Conclusion This meta-analysis suggests that offloading footwear is effective in reducing the incidence of diabetes-related foot ulcers. Home foot temperature monitoring also appears beneficial but larger trials are needed (PROSPERO registration no.: CRD42019135226).

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Introduction

Diabetes-related foot ulcers are the commonest presentation of diabetes-related foot disease and a leading cause of hospitalization, disability and healthcare costs [1]. A current priority is the identification and implementation of effective ways to reduce the incidence of diabetes-related foot ulcers [1–3]. A number of past systematic reviews [4–7] and meta-analyses [1,8–11] have identified that the most widely investigated approaches to reduce the incidence of diabetes-related foot ulcers are home foot temperature monitoring [12–15], education [16–21] and offloading footwear [22–28]. Past research suggests that high plantar pressures in people with peripheral neuropathy is a key mechanism responsible for diabetes-related foot ulcer development [29–33]. These high plantar pressures can be reduced by offloading footwear [29,30]. Furthermore, the presence of high plantar pressures can be identified by monitoring foot temperature regularly as a warning sign of impending ulceration [34–38]. Hot spots identified in the foot can provide an opportunity for revision
What’s new?

• Diabetes-related foot ulcers are common and precipitated by high plantar pressures that stimulate localized foot inflammation and subsequent ulcer development.
• Previous meta-analyses have suggested that home foot temperature monitoring and offloading footwear, but not patient education, reduce diabetic foot ulcer incidence.
• This meta-analysis incorporated data from 17 randomized clinical trials including two not included in previous pooled data analyses.
• Offloading footwear [odds ratio (OR) 0.48, 95% confidence interval (CI) 0.29 to 0.80; \( n = 1438 \)] and home foot temperature monitoring (OR 0.51, 95% CI 0.31 to 0.84; \( n = 468 \)), but not patient education (OR 0.59, 95% CI 0.29 to 1.20; \( n = 823 \)) reduced the incidence of diabetes-related foot ulcers.
• Findings for offloading footwear, but not home foot temperature monitoring were consistent in sensitivity analyses.
• People at high risk of diabetes-related foot ulcers should be offered offloading footwear. Home foot temperature monitoring appears efficacious but larger trials are needed.

There is therefore a need for an up-to-date and comprehensive meta-analysis to clarify the pooled evidence of benefit for home foot temperature monitoring, education and offloading footwear. The aim was to perform a systematic review and meta-analyses of RCTs examining the efficacy of these three interventions in reducing the incidence of diabetes-related foot ulcers.

Methods

Search strategy and eligibility criteria

This systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement and registered in PROSPERO (registration number: CRD42019135226) [42]. The search was performed on 11 October 2019 using multiple databases (MEDLINE via OvidSP, CINAHL, Scopus, PubMed, Cochrane Central Register of Controlled Trials). These subject headings (MeSH terms) and key words were used: ‘Diabetic foot’ OR ‘Diabetic Peripheral Neuropathy’ AND ‘Nursing care’ OR ‘Patient care’ OR ‘Preventive health services’ OR ‘Health education’ OR ‘Primary prevention’ OR ‘Secondary prevention’ (Doc. S1). No language or date restrictions were used. Reference lists of the studies identified were also searched. Eligibility criteria for inclusion were that studies reported: participants that all had diabetes and were at risk of developing diabetic foot ulcers due to being in IWGDF risk categories 2 or 3 (category 2 includes people with peripheral neuropathy or peripheral arterial disease or foot deformities, whereas category 3 includes people with peripheral neuropathy and a history of foot ulceration or amputation) [29,43]; interventions that were one of the following: home foot temperature monitoring, education of the person with diabetes, or offloading footwear; a control group not receiving the intervention under study; an outcome of the incidence of diabetes-related foot ulcers during follow-up; and was a RCT. Studies including participants with an active diabetes-related foot ulcers were excluded. Home foot temperature monitoring was defined as regular assessment of foot temperature using an objective temperature monitoring device by the participants at home [44]. Patient education was defined as structured education provided to participants aimed at improving their knowledge and foot care [44]. Offloading footwear was defined as any shoes or insoles designed with the intention of relieving mechanical pressure from specific regions of the feet [29]. Diabetes-related foot ulcer was defined as a full thickness wound on the foot of a person with diabetes [1]. Corresponding authors of three trials were contacted to clarify data. Only one responded and provided additional data on the number of participants who were randomized into each group.
Data extraction and analysis

The primary outcome was diabetes-related foot ulcer incidence. Secondary outcomes were minor, major and total amputations (minor and major amputations). Data on adherence to offloading footwear were also extracted. Outcome data were extracted for the latest time point reported. Other data extracted included age, BMI, duration of diabetes, HbA1C and ankle–brachial pressure index [45]. Data were extracted by three authors separately and inconsistencies were resolved through discussion.

Meta-analyses were performed for any of the primary and secondary outcomes of any of the interventions studied if data were reported for the specific combination of outcome and intervention in at least three RCTs. If one trial included two separate interventions, the two interventions were considered separately divided by the number of participants in the control group into two equal groups to provide consistency with the total number of participants that were recruited to the study. Meta-analyses for different populations and intervention subgroups were also eligible under the same criteria, i.e. at least three RCTs reporting. All analyses used intention-to-treat principles, i.e. participants were assumed to have received the allocated intervention. Missing outcome data from participants who were lost to follow-up were handled using two different approaches. The main analysis approach assumed all participants with missing outcome data had the outcome of interest (worst case scenario) [46]. In a sub-analysis, a second approach assumed that all participants with missing outcome data did not develop the outcome of interest (best case scenario). All meta-analyses were performed using Mantel-Haenszel’s statistical method and random effect models anticipating substantial heterogeneity [47]. The results were reported as odds ratios (OR) and 95% confidence intervals (CI). Relative risks are also reported in Table S1. All statistical tests were two-sided and P-values < 0.05 were considered significant. Heterogeneity was assessed using the I² statistic and interpreted as low (0–49%), moderate (50–74%) or high (75–100%) [48]. Leave-one-out-sensitivity analyses were performed to assess the contribution of each study to the pooled estimates by excluding individual studies one at a time and recalculating the pooled estimates [49]. Publication bias was assessed by funnel plots comparing the summary estimate of each study and its precision (1/standard error) [49]. All analyses were conducted using RevMan 5, version 5.3 (The Cochrane Collaboration, Nordic Cochrane Centre, Copenhagen, Denmark).

Quality assessment

Risk of bias of all included studies was assessed independently by three authors using the Cochrane Collaboration’s tool for assessing risk of bias in randomized trials [41]. Total risk of bias for each study was then defined as: low risk: if low risk of bias was scored for each item; unclear risk: if low or unclear risk of bias was scored for each item; high risk: if high risk of bias was scored on one or more items [41]. Any inconsistencies were resolved through discussion until consensus was reached.

Results

Included trials

A total of 7575 unique records were identified from the initial search and ultimately 17 trials included (Fig. 1). A total of 2729 participants were recruited to four trials testing home foot temperature monitoring (n = 468), six trials examining patient education (n = 823), and seven trials assessing offloading (n = 1438). All trials included participants of diabetes foot risk category 2 or above in the IWGDF grading system [26]. The trials were conducted in Brazil [16], China [18,20], Italy [21,22,25], Netherlands [27], Norway [14], Spain [28], Sweden [17], the UK [19] and the USA [12,13,15,23,24,26]. Tables 1 and 2 display summaries of the participants and outcome data. Details of the inclusion criteria, interventions and controls and outcome measures are shown in Table S1. Table S2 contains details of the quality assessment findings [41].

Risk of bias

Table 3 displays a summary of the findings of the quality assessment. All studies had a total risk of bias score of high or unclear risk of bias, including 14 with high risk of bias [12,13,15–21,23–26,28] and three with unclear risk of bias [14,22,27]. Most high risk of bias was due to a combination of incomplete outcome data because of high dropout rates in seven studies [13,16–18,23,26,28], lack of blinding of participants or personnel in six studies [12,13,15,24,26,28], other biases (significant baseline differences between the intervention and the control groups, participants being assigned to a different group during the study from the initial randomized group or premature termination of studies) in six studies [16,17,19,21,25] and/or lack of intention to treat analyses in four studies [17,18,21,26]. Eight studies did not report blinding of participants and personnel [17–23,25]. Blinding of assessors were not reported in seven studies [14,17,18,20–22,25].

Home foot temperature monitoring

All four trials testing home foot temperature monitoring used a similar infrared thermometer (Temp Touch, Xilas Medical, San Antonio, TX, USA) to monitor temperature at six sites on each foot either once [14,15] or twice [12,13] daily (Table S2). All studies informed the participants to contact a study nurse if they observed a temperature difference of 2.2 °C between either foot on two consecutive days. One
trial instructed the participants to reduce the number of steps taken during the following days until the temperature difference was < 2.2 °C [13]. The action taken when a temperature difference was detected was unclear in the other trials [5,7,8]. All control groups had access to therapeutic footwear, diabetic foot education and regular foot care (Table S2).

Three of the four trials reported that the intervention significantly reduced the incidence of diabetic foot ulcers compared with the control after 6–18 months [12,13,15] (Table 2). Only one trial reported amputation outcomes with no amputations in any groups [13].

The main meta-analysis suggested that infrared thermometry with follow-up preventive care, halved the odds of diabetes-related foot ulcer incidence (OR 0.51, 95% CI 0.31 to 0.84; \( P = 0.009 \)) (Fig. 2; Table S4). There was no heterogeneity between studies (\( I^2 = 0\% \)). Leave-one-out sensitivity analyses showed that these findings were dependent on the inclusion of a single trial [12] (Table S6.1). A sensitivity analysis based on the best-case scenario intention-to-treat analysis showed similar findings to the main analysis (OR 0.30, 95% CI 0.16 to 0.56; \( P < 0.001 \)) (Fig. S1 and Table S4).

**Patient education**

Five of the six patient education trials conducted education sessions in a healthcare centre [16–18,20,21] and the other trial delivered a face-to-face session at participants’ homes (19). Two trials included multiple education sessions [16,18], three trials tested a single session [17,19,21], while one trial did not specify the number of education sessions [20]. The duration of the sessions varied between 60 and 120 min. All programmes contained information on diabetes-related foot ulcer risk factors and preventive footcare. Instructions on footcare and access to regular healthcare services were provided to all control groups (Table S2). The method of delivery of instructions on footcare were markedly different between the studies with some trials offering participants written information or leaflets [17,19,21] and some offering...
Table 1 Baseline characteristics of participants.

| Study                  | Group               | Number of participants randomized | Male (%) | Follow-up (months) | Previous history of diabetic foot ulcer (%) | Previous history of amputations (%) | Duration of diabetes in years | HbA1c (mmol/mol) | HbA1c (%) |
|------------------------|---------------------|-----------------------------------|----------|--------------------|---------------------------------------------|-----------------------------------|---------------------|------------------|------------|
| **Home foot temperature monitoring** |                     |                                   |          |                    |                                             |                                   |                     |                 |            |
| Armstrong *et al.* (2007) [12] | Intervention        | 111                               | 98       | 18                 | 15                                        | NR                                | 13.6 ± 11.6         | 8.1 ± 1.9 |
|                         | Control             | 114                               | 95       | 18                 | 17                                        | NR                                | 12.6 ± 9.1          | 7.4 ± 1.4 |
| Lavery *et al.* (2004) [13] | Intervention        | 41†                               | 49       | 6                  | 11                                        | 2                                 | 14.8 ± 11.5         | NR              |
|                         | Control             | 44†                               | 52       | 6                  | 11                                        | 2                                 | 12.7 ± 10.0         | NR              |
| Lavery *et al.* (2007) [15] | Intervention        | 59                                | 56       | 15                 | 100                                       | 22                                | 12.7 ± 9.7          | NR              |
|                         | Control             | 58                                | 53       | 15                 | 100                                       | 31                                | 13.7 ± 10.3         | NR              |
| Skafjeld *et al.* (2015) [14] | Intervention        | 21                                | 86       | 12                 | 62                                        | 33§                               | 17.0 (NR)*           | 8.3 ± 1.3 |
|                         | Control             | 20                                | 75       | 12                 | 85                                        | 40§                               | 19.5 (NR)*           | 7.9 ± 1.7 |
| **Patient education**   |                     |                                   |          |                    |                                             |                                   |                     |                 |            |
| Castroeros *et al.* (2010) [16] | Intervention        | 30                                | 64       | 24                 | 30                                        | NR                                | 14.0 ± 10.0         | NR              |
|                         | Control             | 23                                | 36       | 24                 | 20                                        | NR                                | 15.0 ± 10.5         | NR              |
| Gershater *et al.* (2011) [17] | Intervention        | 61                                | 75       | 6                  | 100                                       | 26                                | NR                  | 8.1 ± 3.9 |
|                         | Control             | 70                                | 71       | 12                 | 100                                       | 23                                | NR                  | 8.6 ± 3.8 |
| Lincoln *et al.* (2008) [19] | Intervention        | 87                                | 62       | 12                 | 100                                       | 21                                | NR                  | NR              |
|                         | Control             | 85                                | 67       | 6                  | 12                                        | NR                                | 14.2 ± 12.4         | NR              |
| Monami *et al.* (2015) [21] | Intervention        | 61                                | 53       | 6                  | 10                                        | NR                                | 15.9 ± 11.2         | 7.3 ± 1.4 |
|                         | Control             | 60                                | 47       | 24                 | 0                                         | 11.2 (3-26)*                     | 9.7 ± 2.3           |                 |
| Liang *et al.* (2012) [18] | Intervention        | 31                                | 66       | 24                 | 0                                         | 10.1 (5-23)*                     | 9.4 ± 2.5           |                 |
|                         | Control             | 31                                | 64       | 24                 | 0                                         | NR                                | 9.4 ± 2.5           |                 |
| Liu *et al.* (2019) [20] | Intervention        | 142                               | 60       | 24                 | NR                                        | NR                                | 9.1 ± 6.7           | 9.3 ± 2.2 |
|                         | Control             | 142                               | 55       | 24                 | NR                                        | NR                                | 8.7 ± 7.3           | 9.2 ± 2.1 |
| **Offloading footwear** |                     |                                   |          |                    |                                             |                                   |                     |                 |            |
| Bus *et al.* (2013) [27] | Intervention        | 85                                | 82       | 18                 | 100                                       | NR                                | 19.9 ± 15.1§§       | 7.5 ± 1.4 |
|                         | Control             | 86                                | 83       | 18                 | 100                                       | NR                                | 14.7 ± 11.2§§       | 7.6 ± 1.5 |
| Lavery *et al.* (2012) [24] | Intervention        | 149                               | 68       | 18                 | 28                                        | 9                                 | 13.0 ± 8.7          | NR              |
|                         | Control             | 150                               | 78       | 18                 | 25                                        | 9                                 | 12.0 ± 4.9          | NR              |
| Reiber *et al.* (2002) [23] | Intervention 1     | 121                               | 78       | 24                 | NR                                        | NR                                | NR                  | NR              |
|                         | (cork inserts)      |                                   |          |                    |                                             |                                   |                     |                 |            |
|                         | Intervention 2     | 119                               | 77       | 24                 | NR                                        | NR                                | NR                  | NR              |
|                         | (polyurethane inserts) |                                   |          |                    |                                             |                                   |                     |                 |            |
|                         | Control             | 160                               | 77       | 24                 | NR                                        | NR                                | NR                  | NR              |
| Uccioli *et al.* (1995) [22] | Intervention        | 33                                | 61       | 12                 | NR                                        | 0                                 | 16.8 ± 12.7         | NR              |
|                         | Control             | 36                                | 64       | 12                 | NR                                        | 0                                 | 17.5 ± 8.0          | NR              |
| Study                  | Group         | Number of participants randomized | Age (years) | Male (%) | Follow-up (months) | Previous history of diabetic foot ulcer (%) | Previous history of amputations (%) | Duration of diabetes in years | HbA1c (mmol/mol) | HbA1c (%) |
|-----------------------|---------------|-----------------------------------|-------------|----------|--------------------|------------------------------------------|-----------------------------------|-------------------|----------------|-----------|
| Rizzo et al. (2012)   | Intervention  | 148                               | 68.1 ± 14.1 | NR       | 12††               | Overall 20††                             | Overall 25††                      | 18.1 ± 12.1       | 8.6 ± 1.4    |
|                       | Control       | 150                               | 66.2 ± 9.4  | NR       | 12†                | 32                                        | NR                               | 17.4 ± 10.9       | 8.7 ± 1.1    |
| Ulbrecht et al. (2014)| Intervention  | 79                                | 60.5 ± 10.1 | 76       | 15                 | 100                                       | 32                               | NR               | NR          |
|                       | Control       | 71                                | 58.5 ± 10.7 | 81       | 15                 | 100                                       | NR                               | NR               | NR          |
| Lopez-Moral et al. (2019) | Intervention | 26                                | 61.0 ± 8.1  | 92       | 6                  | 100                                       | 50                               | 14.0 ± 8.4       | 7.5 ± 1.2    |
|                       | Control       | 25                                | 60.0 ± 8.6  | 92       | 6                  | 100                                       | 36                               | 17.0 ± 10.0      | 7.5 ± 1.9    |

To convert percentage HbA1c values to mmol HbA1c per mol Hb use the following equation 10.93 × % HbA1c = 23.5 mmol/mol.

Data are shown as numbers or mean ± sd or percentages unless indicated otherwise; *data reported as median (IQR).

NR, not reported.
†Percentage of individuals with a diabetes duration of < 6, 6–24 and > 25 years.
‡Based on the data presented in results in contrast to the numbers presented in the abstract.
§Included participants with a history of toe amputations.
¶Interim analysis at 6 months.
All data from this study were reported only for the those who completed the study; 30 in the intervention group and 29 in the control group.
*This study had two intervention groups (intervention 1: custom cork-insert group; intervention 2: polyurethane insert group). For the meta-analyses the control group was divided equally into two groups to be consistent with the total number of participants included in the study.
††Data reported for 12-month outcomes only.
‡‡Only reported a combined value for both groups.
§§Indicates studies with significant differences between the intervention and the control groups.
Offloading footwear

Six trials tested either custom-made orthoses (pressure or shape based) or custom-made footwear [22–27]. The remaining trial tested prefabricated therapeutic footwear with rigid rocker soles in the intervention arm against prefabricated therapeutic footwear with semi-rigid soles in the control arm [28]. Management of the control groups varied between trials with some prescribing off-the-shelf footwear [22,23,25], some prescribing therapeutic footwear [24,26,28] and one prescribing custom-made footwear without plantar pressure-guided modifications [27]. Four trials provided footcare education to all participants [22,24–26] (Table S2). Six trials monitored adherence to footwear [22–24,26–28] (Tables 2 and S8.1). Four trials reported that offloading footwear significantly reduced diabetes-related foot ulcer incidence [22,25,26,28] (Table 2). Three trials reported no benefit of offloading footwear [23,24,27] (Table 2). One trial reported the incidence of major and minor amputations, with no significant differences found between groups [23] (Table 2).

The main meta-analysis suggested that offloading footwear reduced the incidence of diabetes-related foot ulcers (OR 0.48, 95% CI 0.29 to 0.80; P = 0.005) (Fig. 4 and Table S4). Heterogeneity among studies was moderate (I² = 72%). Leave-one-out sensitivity analyses showed similar findings to the main analysis (OR 0.47, 95% CI 0.27 to 0.82; P = 0.008) despite moderate heterogeneity (I² = 70%) (Fig. S7) [22–27]. Leave-one-out sensitivity analyses showed that these findings were consistent (Table S8.3).

Publication bias

The funnel plots (Figs S8–S10) based on the primary analyses showed asymmetry suggesting the possibility of publication bias.

Discussion

This meta-analysis suggests that offloading footwear is effective at reducing the incidence of diabetes-related foot ulcers. The main analysis also suggested that home foot temperature monitoring reduced the incidence of foot ulcers, however, the findings were not robust in all sensitivity analyses. The meta-analysis suggested that previously tested patient education programmes are not effective in reducing the incidence of diabetes-related foot ulcers, but again findings were not robust in sensitivity analyses.

Superficially, the findings of this meta-analysis are similar to a recently published systematic review [9] but a number of important differences should be noted. First, the current meta-analysis employed a strict and clearly stated way of handling missing data not present in past systematic reviews. Intention-to-treat is an established cornerstone of analysis of data from RCTs [41]. Missing data has an important impact on such analyses. In order to include all participants randomized, we performed analyses to assess both the worst (where the participant with missing data was assumed to have developed an ulcer) and best (where the participant with missing data was assumed not to have developed an ulcer) case scenarios, as we have previously described [46]. Second, in order to further assess the robustness of findings, leave-one-out sensitivity analyses were performed, as recommended by the PRISMA guidelines [42]. As a result of these further analyses, it was evident that the findings for home foot temperature monitoring were not completely robust as they were dependent on the inclusion of a single trial [12]. Similarly, the findings for the patient education programmes...
Table 2 Outcome data from individual studies

| Study                        | Incidence of diabetic foot ulcers (reported per number initially randomized) | Incidence of major amputations | Incidence of minor amputations | Adherence to offloading footwear (%) |
|------------------------------|--------------------------------------------------------------------------------|--------------------------------|--------------------------------|-------------------------------------|
|                             |                                                                                |                                 |                                |                                     |
|                             | 5 of 111 (4.5%)**                                                            | NR                             | NR                             | NA                                  |
|                             | 14 of 114 (12.2%)**                                                          | NR                             | NR                             | NA                                  |
| Armstrong et al. (2007) [12] |                                                                                |                                 |                                |                                     |
| Lavery et al. (2004) [13]*   | 1 of 41 (2.4%)**                                                              | 0 of 41 (0.0%)                 | 0 of 41 (0.0%)                 | NA                                  |
|                             | 7 of 44 (15.9%)**                                                             | 0 of 44 (0.0%)                 | 0 of 44 (0.0%)                 | NA                                  |
| Lavery et al. (2007) [15]    |                                                                                |                                 |                                |                                     |
|                             | 5 of 39 (8.3%)**                                                              | NR                             | NR                             | NA                                  |
|                             | 17 of 58 (29.3%)**                                                            | NR                             | NR                             | NA                                  |
| Skafeld et al. (2015) [14]   |                                                                                |                                 |                                |                                     |
|                             | 7 of 21 (33.3%)                                                               | NR                             | NR                             | NA                                  |
|                             | 10 of 20 (50.0%)                                                              | NR                             | NR                             | NA                                  |
|                             |                                                                                |                                 |                                |                                     |
| Home foot temperature monitoring |                                                                                |                                 |                                |                                     |
|                             |                                                                                |                                 |                                |                                     |
|                             | 8 of 30 (26.7%)                                                               | NR                             | NR                             | NA                                  |
|                             | 8 of 23 (34.8%)                                                               | NR                             | NR                             | NA                                  |
|                             | 19 of 61 (31.1%)                                                              | NR                             | NR                             | NA                                  |
|                             | 22 of 70 (31.4%)                                                              | NR                             | NR                             | NA                                  |
|                             |                                                                                |                                 |                                |                                     |
|                             | 36 of 87 (41.4%)                                                              | 1 of 87 (1.4%)                 | 8 of 87 (9.2%)                 | NA                                  |
|                             | 35 of 85 (41.2%)                                                              | 1 of 85 (1.2%)                 | 8 of 85 (9.4%)                 | NA                                  |
|                             | 0 of 61 (0.0%)                                                               | 0 of 61 (0.0%)                 | 0 of 61 (0.0%)                 | NA                                  |
|                             | 6 of 60 (10.0%)                                                               | 0 of 60 (0.0%)                 | 0 of 60 (0.0%)                 | NA                                  |
|                             | 1 of 31 (3.2%)**                                                              | 0 of 31 (0.0%)                 | 0 of 31 (0.0%)                 | NA                                  |
|                             | 7 of 31 (22.5%)**                                                             | 0 of 31 (0.0%)                 | 2 of 31 (6.4%)                 | NA                                  |
|                             |                                                                                |                                 |                                |                                     |
|                             | 16 of 142 (11.3%)**                                                           | Overall 0 of 142 (0.0%)†       | NA                             |                                     |
|                             | 33 of 142 (23.3%)**                                                           | Overall 4 of 142 (2.8%)†       | NA                             |                                     |
| Patient education |                                                                                |                                 |                                |                                     |
|                             |                                                                                |                                 |                                |                                     |
|                             | 33 of 85 (38.8%)                                                              | NR                             | NR                             | 41.2%**                            |
|                             | 38 of 86 (44.2%)                                                              | NR                             | NR                             | 51.2%**                            |
|                             | 3 of 149 (2.0%)                                                               | NR                             | NR                             | 4 h: 15.5%                          |
|                             |                                                                                |                                 |                                | 4–8 h: 52.0%                       |
|                             |                                                                                |                                 |                                | 8–12 h: 25.7%                      |
|                             |                                                                                |                                 |                                | 12–16 h: 6.8%                      |
|                             |                                                                                |                                 |                                | 4 h: 10.6%                         |
|                             |                                                                                |                                 |                                | 4–8 h: 55.0%                       |
|                             |                                                                                |                                 |                                | 8–12 h: 30.5%                      |
|                             |                                                                                |                                 |                                | 12–16 h: 3.9%                      |
|                             |                                                                                |                                 |                                |                                     |
|                             | 18 of 121 (14.9%)                                                             | Overall 5 of 400 (1.0%)‖       | Overall 6 of 400 (1.5%)‖       | 83.0%                              |
|                             | 17 of 119 (14.3%)                                                             |                                 |                                |                                     |
|                             | 27 of 160 (16.8%)                                                             | NR                             | NR                             | 100% adhered either frequently or occasionally |
|                             | 9 of 33 (27.7%)**                                                             | NR                             | NR                             |                                     |
|                             |                                                                                |                                 |                                |                                     |
|                             | 21 of 36 (58.3%)**                                                            | NR                             | NR                             | NR                                  |
|                             | 17 of 148 (11.5%)**                                                           | NR                             | NR                             | NR                                  |
|                             | 58 of 150 (38.7%)**                                                           | NR                             | NR                             | NR                                  |
|                             | 6 of 79 (7.6%)**                                                              | NR                             | NR                             | NR                                  |
|                             | 16 of 71 (22.5%)**                                                            | NR                             | NR                             | NR                                  |
|                             | 6 of 26 (23.1%)**                                                             | NR                             | NR                             | 88.4%**                            |
|                             | 16 of 25 (64.0%)**                                                            | NR                             | NR                             | 92.0%**                            |

NR, not reported; NA, not applicable.

*Based on the data presented in results of the study as opposed to conflicting data presented in the abstract

†Based on data presented in the results as opposed to conflicting data presented in a table from the study

‡Data reported as total amputations

§Adherence data reported as the percentage of patients who adhered to offloading footwear <4, 4-8, 8-12 and 12-16 hours

¶This study had two intervention groups (intervention 1: custom cork-insert group, intervention 2: polyurethane insert group). For the meta analyses the control group was divided equally into two groups to be consistent with the total number of patients included in the study

Data reported as total number of minor and major amputations in the entire study

Indicates studies with significant differences between the intervention and the control groups

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also changed in one of the sensitivity analyses. By contrast, the findings for offloading footwear were consistent in all sensitivity analyses. Our interpretation of these findings is that there is robust evidence on the benefit of offloading footwear. By contrast, the current evidence for home foot temperature and against patient education programmes is

**Table 3** Quality assessment summary

| Study                          | Random sequence generation | Blinding of participants/personnel | Blinding of assessors | Sample size estimate | Incomplete outcome data (>10% loss) | Clear primary outcome | Intention to treat analysis | Other biases | Total risk of bias |
|-------------------------------|---------------------------|-----------------------------------|-----------------------|----------------------|--------------------------------------|-----------------------|---------------------------|--------------|-------------------|
| **Home foot temperature monitoring** |                           |                                   |                       |                      |                                      |                       |                           |              |                   |
| Armstrong et al. (2007) [12]  | (+)                       | (-)                               | (+)                   | (+)                  | (?)                                  | (+)                   | (?)                       | (?           | High              |
| Lavery et al. (2004) [13]     | (?                        | (-)                               | (+)                   | (?)                  | (+)                                  | (-)                   | (+)                       | (?           | High              |
| Lavery et al. (2007) [15]     | (+)                       | (-)                               | (+)                   | (+)                  | (-)                                  | (+)                   | (+)                       | (+)          | High              |
| Skafjeld et al. (2015) [14]   | (+)                       | (+)                               | (?)                   | (?)                  | (+)                                  | (+)                   | (+)                       | (?           | Unclear           |
| **Patient education**         |                           |                                   |                       |                      |                                      |                       |                           |              |                   |
| Cisneros et al. (2010) [16]   | (?                        | (+)                               | (+)                   | (-)                  | (-)                                  | (+)                   | (?)                       | (?           | High              |
| Gershater et al. (2011) [17]  | (+)                       | (?)                               | (+)                   | (-)                  | (-)                                  | (+)                   | (-)                       | (-)          | High              |
| Lincoln et al. (2008) [19]    | (+)                       | (?)                               | (+)                   | (+)                  | (-)                                  | (+)                   | (+)                       | (-)          | High              |
| Monami et al. (2015) [21]     | (+)                       | (?)                               | (+)                   | (+)                  | (+)                                  | (+)                   | (-)                       | (-)          | High              |
| Lang et al. (2012) [18]       | (?)                       | (?)                               | (?)                   | (?)                  | (+)                                  | (-)                   | (-)                       | (?)          | High              |
| Liu et al. (2019) [20]        | (?                        | (?)                               | (?)                   | (?)                  | (?)                                  | (+)                   | (?)                       | (?)          | High              |
| **Offloading footwear**       |                           |                                   |                       |                      |                                      |                       |                           |              |                   |
| Bus et al. (2013) [27]        | (+)                       | (+)                               | (+)                   | (?)                  | (+)                                  | (+)                   | (+)                       | (+)          | Unclear           |
| Lavery et al. (2012) [24]     | (?                        | (-)                               | (+)                   | (?)                  | (+)                                  | (+)                   | (?           | (?)            |
| Reiber et al. (2002) [23]     | (+)                       | (?)                               | (+)                   | (+)                  | (-)                                  | (+)                   | (+)                       | (?           | High              |
| Uccioli et al. (1995) [22]    | (?                        | (?)                               | (?)                   | (?)                  | (?)                                  | (+)                   | (?)                       | (?)          | Unclear           |
| Rizzo et al. (2012) [25]      | (+)                       | (?)                               | (?)                   | (?)                  | (?)                                  | (+)                   | (?)                       | (?)          | High              |
| Ulbrecht et al. (2014) [26]   | (+)                       | (-)                               | (+)                   | (+)                  | (+)                                  | (+)                   | (-)                       | (-)          | High              |
| Lopez-Moral et al. (2019) [28]| (+)                       | (-)                               | (+)                   | (+)                  | (+)                                  | (+)                   | (?)                       | (?)          | High              |

(+): Low risk of bias; (−): high risk of bias; (?): unclear risk of bias.

*Other biases include significant baseline differences between the intervention and the control groups, participants being assigned to a different group during the study from the initial randomized group or premature termination of studies.

**FIGURE 2** Effect of home foot temperature monitoring with infrared thermometry in prevention of diabetic foot ulcers.
less robust. Third, in the meta-analysis reported by Crawford and colleagues, data were handled differently from the current study [9]. Crawford et al. combined data from two different offloading interventions [23] into one group. They also extracted data on ulcer incidence per participant years from one trial [23] mixed with actual ulcer incidence from other trials. By contrast, in the current meta-analysis all data were allocated to individual groups as actual ulcer numbers. Finally, Crawford and colleagues reported relative risk rather than OR as reported in the current meta-analysis. These differences likely explain the disparity in reported effect sizes and 95% CIs between the current and previous meta-analyses.

The findings of this meta-analysis for home foot temperature may be reflective of the relatively small number of past RCTs and the small sample sizes included in these trials [12–15]. A larger RCT testing home foot temperature monitoring is currently ongoing [35] and the addition of these data to the current meta-analysis is expected to have an important effect on interpretation. It should also be noted that this ongoing RCT and the prior trials included in this review all used the same hand-held infrared thermometer [12–15,35]. This approach may not be feasible for widespread use and a number of alternative ways of assessing foot temperature have been developed [50–55]. A recent RCT tested the use of an infrared camera used by clinicians to assess people attending out-patient clinics. Assessments were performed at monthly intervals rather than on a daily basis. This trial reported no benefit of the intervention studied, suggesting that much more frequent assessment of foot temperature is needed for this approach to be effective [56]. Recently, a temperature assessment mat (Podometrics Inc., Somerville, MA, USA) has been developed for easy participant use within the home [55]. This is marketed within the USA and has been reported to be sensitive at identifying hot spots that predict ulcers [57]. RCTs employing this and other easy-to-use home foot temperature monitoring techniques [52,55,58] are needed to thoroughly examine the potential of this intervention in preventing foot ulcers.

Despite a strong recommendation in the IWGDF guidelines that at-risk people should receive structured patient education programmes, previous meta-analyses and systematic reviews [6,8,9] have suggested no benefit of patient education programmes in reducing diabetes-related foot ulcer incidence. The current meta-analysis supports these prior findings with the addition of a recent trial to the pooled estimate [20]. The main analysis showed no benefit of the programmes tested [8]. A leave-one-out sensitivity analysis, however, suggested findings were not completed robust. There was noted to be a high percentage of people who were lost to follow-up among three trials [16,17,19]. The current meta-analyses suggested no benefit of the previously tested education programmes in reducing the number of total, minor or major amputations. This result was dependent on one study that reported only an interim analysis with a high drop-out rate [17]. The patient education programmes tested varied considerably in terms of their design, such as the number of sessions, group or one-on-one programmes and their content. The education programmes in the three trials that showed benefit included discussions with participants that encouraged them to ask questions [16,17,19], was delivered to the participant at their own home using an individualized approach [19] and included games and teaching aids not typical of commonly used education sessions [16,17]. Most programmes only included one education session [17,19,21,59] and it is possible that a more effective outcome might have been achieved with more intensive education or through combining education with behaviour change support interventions, such as motivational interviewing [60]. Further trials are needed to test well-designed patient education programmes.

This meta-analysis provides robust evidence that use of offloading footwear reduces the incidence of diabetes-related foot ulcers, which is consistent with a previous meta-analysis [9]. There was a high heterogeneity noted within the included trials that may reflect the different types of footwear tested, the variation in footwear in the control groups and the variable footwear adherence rates reported in the trials [24,27]. A sub-analysis suggested the benefit of custom-made orthoses or footwear, which supports the recommendations of the IWGDF guidelines about prescribing shoes that uniquely address each person’s problem [2]. Bus et al.
reported that participants who adhered to their offloading shoes had significantly lower recurrence rates of diabetes-related foot ulcers compared with the control group [27]. Combining offloading with methods to improve adherence may provide further benefit, although this remains to be demonstrated. Methods that have been reported to improve footwear adherence include behaviour change support systems [60–62] such as motivational interviewing and coaching [63,64], regular monitoring [63] and individualized education [64].

A number of limitations of the included trials and this meta-analysis should be acknowledged. The risk of bias of the included RCTs was considered to be either high or unclear using the Cochrane Collaborative tool. Other risk of bias assessments are available and using another tool may have led to different findings. Identified deficiencies of the trials included lack of reporting of sample size calculations [13,14,16,18,22,25,59], absence of outcome assessor blinding [14,17,18,21,22,59,63], large drop-out rates [15–17,19,23,26,59] and failure to comment on the method of randomization [13,16,18,24]. There was also heterogeneity in follow-up frequency and in reporting participant characteristics. Furthermore, funnel plots suggested a risk of publication bias. Therefore, well-designed trials are still needed to clearly define the best combination of interventions in preventing diabetes-related foot ulcers.

In conclusion, this meta-analyses provides robust evidence that offloading footwear reduces the incidence of diabetes-related foot ulcers in high-risk people [44]. The meta-analyses also suggests that there may be benefit for home foot temperature monitoring but that further trials are needed. The value of patient education programmes in preventing diabetes-related foot ulcers is currently unclear despite strong recommendations given by the IWGDF.

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### Competing interests

None declared.

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### References

1. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. *N Engl J Med* 2017; 376: 2367–2375.
2. Bus SA, Lavery LA, Monteiro Soares M, Rasmussen A, Raspovic A, Sacco IC *et al*. IWGDF Guideline on the Prevention of Foot Ulcers in Persons with Diabetes, 2019. Available at www.iwgdfguidelines.org Last accessed 24 May 2020.
3. Barshes NR, Saedi S, Wrobel J, Kougias P, Kundakcioglu OE, Armstrong DG. A model to estimate cost-savings in diabetic foot ulcer prevention efforts. *J Diabetes Complicat* 2017; 31: 700–707.
4. van Netten JJ, Raspovic A, Lavery LA, Monteiro-Soares M, Rasmussen A, Sacco ICN *et al*. Prevention of foot ulcers in the at-risk patient with diabetes: a systematic review. *Diabetes Metab Res Rev* 2020; 36(Suppl 1): e3270.
5. van Netten JJ, Price PE, Lavery LA, Monteiro-Soares M, Rasmussen A, Jubiz Y *et al*. Prevention of foot ulcers in the at-risk patient with diabetes: a systematic review. *Diabetes Metab Res Rev* 2016; 32: 84–98.
6. Doresteijn JA, Kriegsman DM, Assendelft WJ, Valk GD. Patient education for preventing diabetic foot ulceration. *Cochrane Database System Rev* 2014; (12):CD001488.
7. Arad Y, Fonseca V, Peters A, Vinik A. Beyond the monofilament for the insensate diabetic foot: a systematic review of randomized

![FIGURE 4 Effect of offloading footwear in prevention of diabetic foot ulcers.](image-url)
trials to prevent the occurrence of plantar foot ulcers in patients with diabetes. *Diabetes Care* 2011; 34: 1041–1046.
8 Adewere P, Gillis RB, Inman Jwani S, Meal A, Shaw I, Adams GG. A systematic review and meta-analysis of patient education in preventing and reducing the incidence or recurrence of adult diabetes foot ulcers (DFU). *Helyon* 2018; 4: e00614.
9 Crawford F, Nicolson DJ, Amana AE, Martin A, Gupta S, Leese GP et al. Preventing foot ulceration in diabetes: systematic review and meta-analyses of RCT data. *Diabetologia* 2020; 63: 49–64.
10 Houghton VJ, Bower VM, Chant DC. Is an increase in skin temperature predictive of neuropathic foot ulceration in people with diabetes? A systematic review and meta-analysis. *J Foot Ankle Res* 2013; 6: 31.
11 Ena J, Carretero-Gomez J, Arevalo-Lorido JC, Sanchez-Ardila C, Zapatero-Gaviria A, Gomez-Huelgas R. The association between elevated foot skin temperature and the incidence of diabetic foot ulcers: a meta-analysis. *Int J Lower Extrem Wounds* 2020; https://doi.org/10.1177/1534734619897501 [Epub ahead of print].
12 Armstrong DG, Holtz-Neiderer K, Wendel C, Mohler MJ, Kimbriel HR, Lavery LA. Skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients. *Am J Med* 2007; 120: 1042–1046.
13 Lavery LA, Higgins KR, Lancot DR, Constantinides GP, Zamorano RG, Armstrong DG et al. Preventing diabetic foot ulcer recurrence in high-risk patients: use of temperature monitoring as a self-assessment tool. *Diabetes Care* 2004; 27: 2642–2647.
14 Skafjeld A, Iversen MM, Holme I, Ribu L, Hvaal K, Kilhovd BK. A pilot study testing the feasibility of skin temperature monitoring to reduce recurrent foot ulcers in patients with diabetes—a randomized controlled trial. *BMJ Endoc mobs Disord* 2015; 15: 55.
15 Lavery LA, Higgins KR, Lancot DR, Constantinides GP, Zamorano RG, Athanasiou KA et al. Preventing diabetic foot ulcer recurrence in high-risk patients: use of temperature monitoring as a self-assessment tool. *Diabetes Care* 2007; 30: 14–20.
16 Cisneros LL. Evaluation of a neuropathic ulcers prevention program for patients with diabetes. *Rev Bras Fisioter* 2010; 14: 31–37.
17 Gershater MA, Pilhammar E, Apleqvist J, Alm-Roijer C. Patient education for the prevention of diabetic foot ulcers: interim analysis of a randomised controlled trial due to morbidity and mortality of participants. *Eur Diabetes Nurs* 2011; 8: 102–107.
18 Liang R, Dai X, Zuoie L, Zhou A, Meiquan C. Two-year foot care program for minority patients with type 2 diabetes mellitus of Zhaung Tribe in Guaxx, China. *Can J Diabetes* 2012; 36: 15–18.
19 Lincoln NB, Radford KA, Game FL, Jeffcoate WJ. Education for secondary prevention of foot ulcers in people with diabetes: a randomised controlled trial. *Diabetologia* 2008; 51: 1954–1961.
20 Liu J, Chen T, Wang S, Liu H. The effect of transitional care on the prevention of diabetic foot ulcers in patients at high risk for diabetic foot. *Int J Diabetes Dev Countries* 2019; 39: 659–666.
21 Monami M, Zannoni S, Gaias M, Nreu B, Marchionni N, Mannucci E. Effects of a short educational program for the prevention of foot ulcers in high-risk patients: a randomized controlled trial. *Int J Endocrinol* 2015; 2015: 615680.
22 Uccioi L, Faglia E, Monticone G, Favale F, Durola L, Aldeghe A et al. Manufactured shoes in the prevention of diabetic foot ulcers. *Diabetes Care* 1995; 18: 1376–1378.
23 Reiber GE, Smith DG, Wallace C, Sullivan K, Hayes S, Vath C et al. Effect of therapeutic footwear on foot ulceration in patients with diabetes: a randomized controlled trial. *JAMA* 2002; 287: 2552–2558.
24 Lavery LA, Lafontaine J, Higgins KR, Lancot DR, Constantinides G. Shear-reducing insoles to prevent foot ulceration in high-risk diabetic patients. *Adv Skin Wound Care* 2012; 25: 519–526.
25 Rizzo I, Tedeschi A, Fallani E, Cappelli A, Vallini V, Iacopi E et al. Custom-made orthosis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. *Int J Lower Extrem Wounds* 2012; 11: 59–64.
26 Ullbrecht JS, Hurley T, Mauger DT, Cavanagh PR. Prevention of recurrent foot ulcers with plantar pressure-based in-shoe orthoses: the CareFUL prevention multicenter randomized controlled trial. *Diabetes Care* 2014; 37: 1982–1989.
27 Bus SA, Waaismman R, Arts M, de Haart M, Busch-Westbroek T, van Baal J et al. Effect of custom-made footwear on foot ulcer recurrence in diabetes: a multicenter randomized controlled trial. *Diabetes Care* 2013; 36: 4109–4106.
28 Lopez-Moral M, Lazarro-Martinez JL, Garcia-Morales M, Garcia-Alvarez Y, Alvaro-Afonso FJ, Molines-Barroso RJ. Clinical efficacy of therapeutic footwear with a rigid rocker sole in the prevention of recurrence in patients with diabetes mellitus and diabetic polyneuropathy: a randomized clinical trial. *PLoS One* 2019; 14: e0219537.
29 Bus SA, Armstrong D, Gooday C, Jarl G, Caravaggi C, Viswanathan V et al. IWGDF Guideline on Offloading Foot Ulcers in Persons with Diabetes, 2019. Available at www.iwgdf guidelines.org Last accessed 24 May 2020.
30 Bus SA. Priorities in offloading the diabetic foot. *Diabetes Metab Res Rev* 2012; 28: 54–59.
31 Bus SA. Innovations in plantar pressure and foot temperature measurements in diabetes. *Diabetes Metab Res Rev* 2016; 32: 221–226.
32 Bus SA, van Netten JJ, Kottink AI, Manning EA, Spraul M, Woittiez AJ et al. The efficacy of removable devices to offload and heal neuropathic plantar forefoot ulcers in people with diabetes: a single-blinded multicentre randomised controlled trial. *Int Wound J* 2018; 15: 65–74.
33 Lavery LA, Vela SA, Lavery DC, Quebedeaux TL. Reducing dynamic foot pressures in high-risk diabetic subjects with foot ulcers: a comparison of treatments. *Diabetes Care* 1996; 19: 818–821.
34 Armstrong DG. Infrared dermal thermometry: the foot and ankle stethoscope. *J Foot Ankle Surg* 1998; 37: 75–76.
35 van de Stegge WB, Meijari N, van Netten JJ, Djikgraaf MGW, van Baal JG, Busch-Westbroek TE et al. The cost-effectiveness and cost-utility of at-home infrared temperature monitoring in reducing the incidence of foot ulcer recurrence in patients with diabetes (DIATEMP): study protocol for a randomized controlled trial. *Trials* 2018; 19: 520.
36 Alper BS, Brown C. Evidence-based medicine. Foot-temperature monitoring may reduce diabetic ulcers. *Clin Advisor* 2008; 11: 109–110.
37 Armstrong DG. Tips, quips and pearls. Infrared dermal thermometry: the foot and ankle stethoscope? *J Foot Ankle Surg* 1998; 37: 75–83.
38 Armstrong DG, Lavery LA. Predicting neuropathic ulceration with infrared dermal thermometry. *J Am Podiatr Med Ass* 1997; 87(7): 336–7.
39 Armstrong DG, Sangalang MB, Jolley D, Maben F, Kimbriel HR, Nixon BP et al. Cooling the foot to prevent diabetic foot wounds: a proof-of-concept trial. *J Am Podiatr Med Assoc* 2005; 95: 103–107.
40 Bakker K, Apleqvist J, Lipsky BA, Van Netten JJ, Schaper NC. The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. *Diabetes Metab Res Rev* 2016; 32: 2–6.
41 Higgins JP, Altman DG, Ghotzsche PC, Juni P, Moher D, Oxman AD et al. The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. *BMJ* 2011; 343: d5928.
DIABETIC Medicine

42 Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP 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: e1–e34.

43 Jeffcoate WJ, Bus SA, Game FL, Hinchliffe RJ, Price PE, Schaper NC. Reporting standards of studies and papers on the prevention and management of foot ulcers in diabetes: required details and markers of good quality. Lancet Diabetes Endocrinol 2016; 4: 781–788.

44 Bus SA, Lavery LA, Monteiro-Soares M, Rasmussen A, Raspovic A, Sacco ICM, Netten JJ, International Working Group on the Diabetic Foot. Guidelines on the prevention of foot ulcers in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020; 36(Suppl 1): e3269.

45 Lavery LA, Peters EJ, Williams JR, Murdoch DP, Hudson A, Lavery DC. Reevaluating the way we classify the diabetic foot: restructuring the diabetic foot risk classification system of the International Working Group on the Diabetic Foot. Diabetes Care 2008; 31: 154–156.

46 Golldeje J, Singh TP. Systematic review and meta-analysis of clinical trials examining the effect of hyperbaric oxygen therapy in people with diabetes-related lower limb ulcers. Diabet Med 2019; 36: 813–826.

47 Kulinskaya E, Morgenthaler S, Staudte RG. Combining statistical evidence. Int Stat Rev 2014; 82: 214–242.

48 Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002; 21: 1539–1558.

49 Sterne JA, Gavaghan D, Egger M. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. J Clin Epidemiol 2000; 53: 1119–1129.

50 Armstrong DG, Giovinco NA. Diagnostics, theragnostics, and the personal health server: fundamental milestones in technology with revolutionary changes in diabetic foot and wound care to come. Foot Ankle Spec 2011; 4: 54–60.

51 Lazo-Porras M, Bernabe-Ortiz A, Sacksteder KA, Gilman RH, Malaga G, Armstrong DG et al. Implementation of foot thermometry plus mHealth to prevent diabetic foot ulcers: study protocol for a randomized controlled trial. Trials 2016; 17: 206.

52 Killeen AL, Walters JL. Remote temperature monitoring in diabetic foot ulcer detection. Wounds 2018; 30: E44–E48.

53 van Doremalen RFM, van Netten JJ, van Baal JG, Vollenbroek-Hutten MMR, van der Heijden F. Validation of low-cost smartphone-based thermal camera for diabetic foot assessment. Diabetes Res Clin Pract 2019; 149: 132–139.

54 van Doremalen RFM, van Netten JJ, van Baal JG, Vollenbroek-Hutten MMR, van der Heijden F. Infrared 3D thermography for inflammation detection in diabetic foot disease: a proof of concept. J Diabetes Sci Technol 2019; 14: 46–54.

55 Frykberg RG, Gordon IL, Reyzelman AM, Cazzell SM, Fitzgerald RH, Rothenberg GM et al. Feasibility and efficacy of a smart mat technology to predict development of diabetic plantar ulcers. Diabetes Care 2017; 40: 973–980.

56 Petrova NL, Donaldson NK, Tang W, MacDonald A, Allen J, Lomas C et al. Infrared thermography and ulcer prevention in the high-risk diabetic foot: data from a single-blind multicentre controlled clinical trial. Diabet Med 2020; 37: 95–104.

57 Gordon IL, Rothenberg GM, Lepow BD, Petersen BJ, Linders DR, Bloom JD et al. Accuracy of a foot temperature monitoring mat for predicting diabetic foot ulcers in patients with recent wounds or partial foot amputation. Diabetes Res Clin Pract 2020; 108074.

58 Killeen AL, Brock KM, Dancho JF, Walters JL. Remote temperature monitoring in patients with visual impairment due to diabetes mellitus: a proposed improvement to current standard of care for prevention of diabetic foot ulcers. J Diabetes Sci Technol 2020; 14: 37–45.

59 Malone JM, Snyder M, Anderson G, Bernhard VM, Holloway Jr GA, Bunt TJ. Prevention of amputation by diabetic education. Am J Surg 1989; 158: 520–524.

60 Binning J, Woodburn J, Bus SA, Barn R. Motivational interviewing to improve adherence behaviours for the prevention of diabetic foot ulceration. Diabetes Metab Res Rev 2019; 35: e3105.

61 Formosa C, Borg A, Papanas N, Mizzi S. Adherence to therapeutic footwear in type 2 diabetes in Malta. Exp Clin Endocrinol Diabetes 2020; 128: 244–245.

62 Keukenkamp R, Merkx MJ, Busch-Westbroek TE, Bus SA. An explorative study on the efficacy and feasibility of the use of motivational interviewing to improve footwear adherence in persons with diabetes at high risk for foot ulceration. J Am Podiatr Med Assoc 2018; 108: 90–99.

63 Barwick AL, Hurn SE, van Netten JJ, Reed LF, Lazzarini PA. Factors associated with wearing inadequate outdoor footwear in populations at risk of foot ulceration: a cross-sectional study. PLoS One 2019; 14: e0211140.

64 Waaajman R, Keukenkamp R, de Haart M, Polomski WP, Nollet F, Bus SA. Adherence to wearing prescription custom-made footwear in patients with diabetes at high risk for plantar foot ulceration. Diabetes Care 2013; 36: 1613–1618.

65 Westphal C, Neame JM, Harrison JC, Bower VM, Gurr JM. A diabetic foot ulcer pilot study: does silicone gel sheeting reduce the incidence of reulceration? J Am Podiatr Med Assoc 2011; 101: 116–123.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Doc S1. Search terms.

Figure S1. Forest plot of studies looking at home foot temperature monitoring in prevention of diabetic foot ulcers (best case scenario).

Figure S2. Forest plot of studies looking at patient education in prevention of diabetic foot ulcers (best case scenario).

Figure S3. Forest plot of studies looking at patient education in prevention of total amputations (minor + major amputations) (worst case scenario).

Figure S4. Forest plot of studies looking at patient education in prevention of major amputations (worst case scenario).

Figure S5. Forest plot of studies looking at patient education in prevention of minor amputations (worst case scenario).

Figure S6. Forest plot of studies looking at offloading footwear in prevention of diabetic foot ulcers (best case scenario).

Figure S7. Forest plot of subgroup analysis of studies looking at custom made offloading orthoses/footwear in prevention of diabetic foot ulcers (worst case scenario).

Figure S8. Funnel plot of studies looking at home foot temperature monitoring in prevention of diabetic foot ulcers (worst case scenario).

Figure S9. Funnel plot of studies looking at patient education in prevention of diabetic foot ulcers (worst case scenario).

Figure S10. Funnel plot of studies looking at offloading footwear in prevention of diabetic foot ulcers (worst case scenario).
Table S1. Relative risks of the meta-analyses.
Table S2. Study characteristics.
Table S3. Quality assessment using the Cochrane tool.
Table S4. Best-case and worst-case data extraction of diabetic foot ulcers.
Table S5. Best-case and worst-case data extraction of amputation data (minor/major/total amputations) from patient education trials.
Table S6. Home monitoring of foot temperature.
Table S7. Patient education.
Table S8. Offloading footwear.