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The Association Between Elevated Foot Skin Temperature and the Incidence of Diabetic Foot Ulcers: A Meta-Analysis

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Abstract

Prior to the appearance of any foot ulcer, there is an increase in the local temperature due to the presence of an underlying inflammatory process. The use of thermometry to identify inflammation could make patients increase preventive measures until the inflammation disappears. We carried out a meta-analysis to determine the effectiveness of the daily measurement of the foot temperature in 6 points to prevent the occurrence of foot ulcers in patients with diabetes. Patients with temperature differences >4°F (2.2°C) between left and right corresponding sites should reduce activity and increase preventive measures until temperature is normalized. We searched the literature in MEDLINE, EMBASE, Cochrane Library, Web of Knowledge, and clinicaltrials.gov. We have only included randomized clinical trials where individuals were assigned to receive enhanced care (temperature measurement and standard care) versus standard care (education, self-care practices, and periodic clinical visits). We found 4 trials comprising 462 patients from the United States and Norway that met our inclusion criteria. The duration of follow-up varied from 4.5 to 15 months. Overall, 18 (7.9%) subjects in the enhanced foot care group and 53 (22.6%) in the standard foot care group developed foot ulcers (pooled risk ratio = 0.37; 95% confidence interval = 0.21-0.66; $P = .0008$; percentage of heterogeneity [I^2], 25%; $P = .26$). The number needed to treat was 7 (95% confidence interval = 5-11). The results were robust after analysis by subgroups according to the potential risk of bias in the studies and the duration of follow-up.

Keywords

foot ulcer, thermometry, wound skin temperature measurements, wound assessment, diabetes

Introduction

The prevalence of foot ulcers in patients with diabetes is between 4% and 10%, and the risk of developing a foot ulcer throughout life can be as high as 25%.[1] The main causes of the appearance of foot ulcers are the presence of diabetic neuropathy accompanied by repeated local trauma.[2,3] With adequate care, which involves skin debridement, pressure discharge, treatment of infection, and vascular reconstruction, if necessary, 77% of ulcers healed after 1 year.[4] Approximately 40% of patients will have a recurrence of the ulcer in the following year after healing.[5] Patient education, daily foot inspection, self-care, and the use of orthopedic material prevent the risk of ulcer recurrence.[6]

Prior to the appearance of any foot ulcer, there is an increase in the local temperature due to the presence of an underlying inflammatory process.[7] The identification of the inflammatory phenomenon, which appears well in advance of the development of the ulcer, allows establishing preventive measures until the inflammation has disappeared. However, the identification of early inflammatory signs by physical examination is difficult for patients and sometimes even for clinicians. The recent commercialization of infrared ray thermometers has facilitated the detection of subtle inflammatory signs such as an increase in temperature in local areas of the feet.[8] The procedure is simple: the tip of the infrared ray thermometer is applied at 6 different points in each foot (first toe, first, third, and fifth metatarsal heads, middle foot, and heel). Temperature readings are compared

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in right and left corresponding sites. Corresponding sites with temperature increase >4°F (2.2°C) denote early local inflammation. In such cases, patients should reduce the mobility of the affected foot and try to achieve a better glucose control until foot temperature returns to normal.

Previous systematic reviews have analyzed the effect of several intervention, such as integrated foot care, self-management, therapeutic footwear, or surgical interventions, but did not assessed the effect of monitoring foot temperature with a rigorous meta-analysis format.[6]

In the present study, we evaluated the effect of enhanced care (temperature monitoring and standard of foot care procedures) compared with standard of foot care (education, self-care practices, and periodic clinical visits) to reduce the incidence of new foot ulcers in patients with diabetes.

Methods

The present systematic review was planned, conducted, and reported in adherence to the recommendations of PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses).[9] The review was registered in PROSPERO (International Prospective Register of Systematic Reviews) with the number CRD42019128070.

Criteria for the Selection of Trials for Review

We included only randomized controlled clinical trials that compared monitoring of foot temperature and standard of care with standard of care. Patients included in the studies had to be individuals with type 2 diabetes at high risk of developing foot ulcers. The high-risk category was defined as either history of neuropathy, deformity of the feet, or previous ulcer. Patients were excluded from the studies if they have active ulcers with or without infection as well as there was evidence of significant peripheral arterial disease. The intervention group was characterized by twice-daily monitoring of the temperature of the sole of the foot in 6 different locations along with the standard of care (use of insoles or orthopedic footwear, education on prevention of diabetic foot, and routine foot care). The control group received standard of care. The main outcome was the proportion of patients who developed a foot ulcer during follow-up.

Search Strategy

We conducted a search of the information available until October 2018 in MEDLINE, EMBASE, Cochrane Controlled Trial Register, Web of Knowledge, and clinicaltrials.gov. We used the descriptors "Temperature," "Foot," "Ulcer," "Diabetes," and "Clinical Trial." The search was done by a librarian (CSA) expert in bibliometrics. The results of the search strategy are described in Figure 1. We scanned the references lists of all relevant articles to ensure that all completed trials had been identified.

Review Process

Two reviewers (JC and JCA) considered trials for inclusion in the analysis, and data were collated and checked by both reviewers and were abstracted in a pretested, predefined form. Possible discrepancies were solved by a third reviewer (JE). The quality of the clinical trials was evaluated using the Cochrane Library Risk of Bias Assessment Tool that included the following terms: randomization sequence generation, treatment allocation concealment, blinding, completeness of outcome data, selective outcome reporting, and other sources of bias.[10]

Statistical Analysis

We used the κ statistic to measure the chance-corrected agreement between 2 independent reviewers with regard to trial inclusion and quality assessment. Intervention effects were summarized as risk ratios (RRs) with 95% confidence intervals (CIs), and they were pooled using the DerSimonian and Laird random effect model.[9] The analysis was performed on the intention to treat criterion, that is, all the patients included in the study were analyzed. RR values equal to 1 denote no difference for the outcome.

The heterogeneity between treatment effects between studies was determined using the Cochrane Q test (a χ^2 test for heterogeneity) and the I^2 statistic. "I^2" indicates the percentage of the total variation across the studies that are the results to heterogeneity rather than chance (a value of I^2 of 0% denotes no observed heterogeneity, and greater I^2 values denote increasing heterogeneity).[11] The subgroup analysis planned to explore as possible sources of heterogeneity the trial quality and the duration of follow-up. We have calculated the number of patients needed to treat to prevent the onset of a new foot ulcer.[12] We assessed for the presence of publication bias by the use of using the funnel plot.[13] All the analyses were performed using RevMan version 5.3.

Results

Clinical Trials Included in the Analysis

Of the total articles evaluated in the databases consulted, 5 were initially included for more thorough examination.[14-18] There was a perfect match between the evaluators in the selection of articles for inclusion in the study (κ value = 1). One of the studies, published as congress abstract, was excluded since it lacked from a control group.[14] The present meta-analysis is based on 4 clinical trials that included a total of 462 patients (see the appendix).[15-18] The patients included in the studies were classified as high risk defined

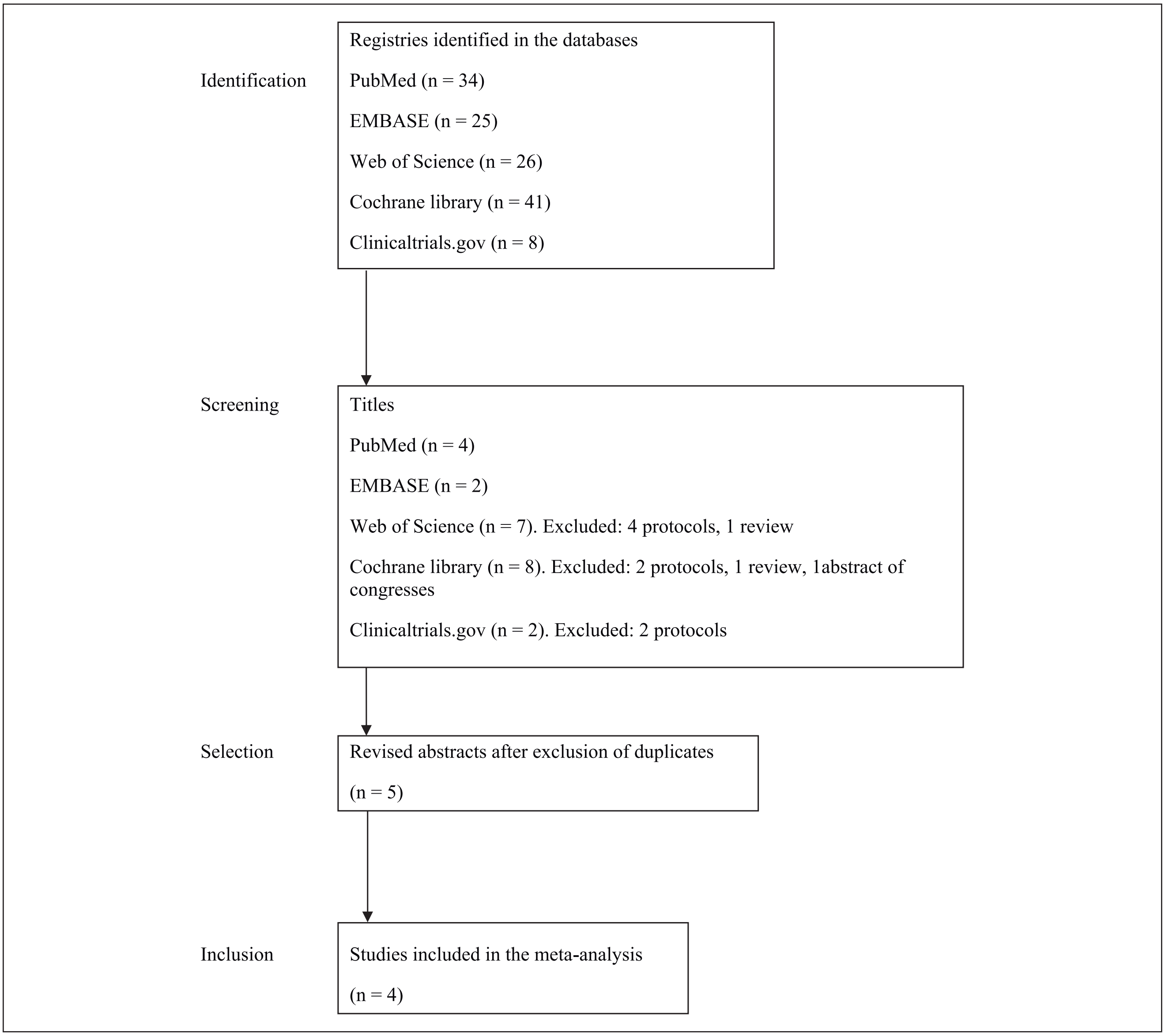


Figure 1. Process of selection of studies included in the meta-analysis.

by groups 2 and 3 of the International Diabetes Foot Risk Classification. The presence of ulcers or active infection was exclusion criteria, as well as having a significant peripheral arterial disease (Table 1). All patients in the intervention group used the same infrared ray device to measure the skin temperature in the sole of the feet (TempTouch, Xilas Medical, San Antonio, TX). Adherence to the recommendations for temperature monitoring was followed in a study by 92% of patients in at least 50% of the prescribed occasions (every 12 hours).[16] In another study, temperature monitoring was followed in 67% of the patients during at least 80% of the prescribed occasions.[18] The remaining 2 studies did not describe the degree of adherence to monitoring and self-care recommendations.

Both the intervention and the control groups received standard of care therapy to prevent the occurrence of foot ulcers. The risk of bias in one of the clinical trials was classified as moderate, since it did not describe the randomization method or the concealment of the randomization sequence[15]; in the other 3 clinical trials, both procedures were described.[14,17,18] Due to the nature of the studies, no clinical trial could be performed as double-blind (Table 2). In each of the studies, the prognostic variables were equally distributed among the groups at the beginning of the study. The evaluation of the outcomes was carried out by the physicians participating in the study. Blinding of outcome assessment was reported in 3 of the studies,[14-16] but not in the study by Skafjeld et al.[18] The clinical follow-up varied

Table 1. Characteristics of Randomized Clinical Trials of Patients With Type 1 or Type 2 Diabetes Included in the Meta-Analysis.

Study	Number of Patients	Trial Participants	Mean Age in Years; Gender (%); Diabetes Duration (Mean or Median)	Intervention	Outcome
Lavery et al,[15] USA	85	*Inclusion criteria*: Category 2 (59%) or 3 (41%) of the International Risk Classification System *Exclusion criteria*: Patients with presence of active ulcer, active infection, peripheral vascular disease with ankle-brachial index <0.8, absence of pedal pulses, dementia, or use of alcohol or drugs	Mean 55 years; men 50%; diabetes duration 13 years	Measuring the temperature in the soles every 12 hours + standard of care Unknown adherence rate	Incident foot ulcers, infections, Charcot fractures, and amputation after 4.7 months follow-up
Lavery et al,[16] USA	225	*Inclusion criteria*: Category 3 of the International Risk Classification System and ankle-brachial index >0.7 *Exclusion criteria*: Patients with presence of active ulcer, active amputation wound, active Charcot arthropathy, severe peripheral arterial disease, or dementia or impaired cognitive function	Mean 65 years; men 54%; diabetes duration 13 years	Measuring the temperature in the soles every 12 hours + standard of care Adherence rate 50%	Incident foot ulcers at 15 months follow-up
Armstrong et al,[17] USA	115	*Inclusion criteria*: Category 2 (85%) or 3 (15%) of the International Risk Classification System *Exclusion criteria*: Patients with presence of active ulcer, active infection, peripheral vascular disease with ankle-brachial index <0.8, absence of pedal pulses, dementia, use of alcohol or drugs, or severe disability	Mean 69 years; gender not stated; diabetes duration 13 years	Measuring the temperature in the soles every 12 hours + standard of care Unknown adherence rate	Incident foot ulcers at 15 months follow-up
Skafjeld et al,[18] Norway	41	*Inclusion criteria*: Category 3 (100%) of the International Risk Classification System *Exclusion criteria*: Patients with presence of active ulcer, active infection, Charcot arthropathy, or peripheral vascular disease with absence of peripheral pulses or an ankle-brachial index <0.7	Mean 58 years; men 80%; diabetes duration 18 years	Measuring the temperature in the soles every 12 hours + standard of care. Adherence rate 80%	Incident foot ulcers at 12 months follow-up

Table 2. Risk of Bias Assessment for the Clinical Trials Included in the Meta-Analysis.

	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Lavery et al[15]	+	?	−	+	+	+	+
Lavery et al[16]	+	+	−	+	+	+	+
Armstrong et al[17]	+	+	−	+	+	+	+
Skafjeld et al[18]	+	+	−	?	+	+	+

Abbreviations: +, low risk of bias; −, high risk of bias; ?, unclear risk of bias.

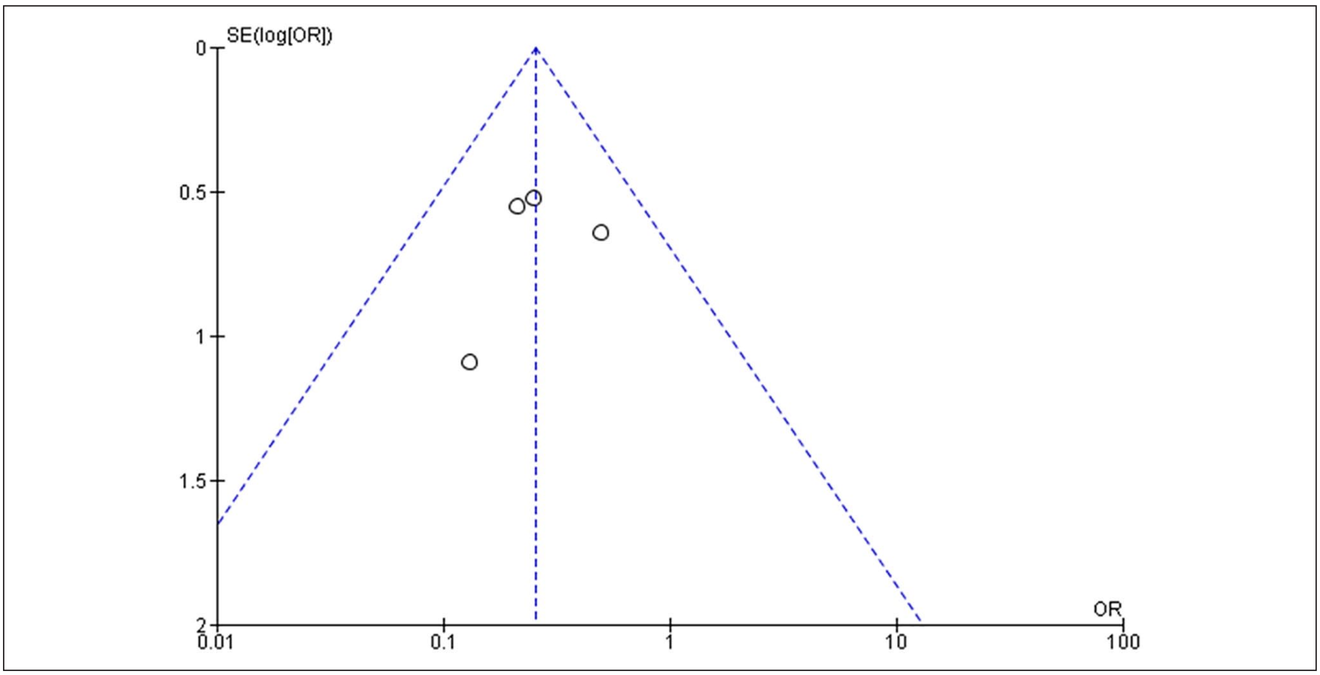


Figure 2. Funnel test showing the absence of publication bias.

from 4.5 months in one study[14] to 12 to 15 months in the remaining studies.[15-17] The funnel test ruled out the possibility of publication bias (Figure 2).

Incidence of Foot Ulcers

A total of 18 (7.9%) patients in the intervention group developed foot ulcers compared with 53 (22.6%) in the control group. The random effect model showed a significant reduction in the risk of ulceration in the intervention group compared with the control group (pooled RR = 0.37, 95% CI = 0.21-0.66; P = .0008; Figure 3). The percentage of the total variation between studies that was the result of heterogeneity over chance was I^2 = 25% (P = .26). The number of patients needed to treat to prevent the appearance of a new ulcer was 7 (95% CI = 5-11).

We carried out subgroup analyses to confirm that our results were valid and robust. In the first subgroup analysis, we compared the effect of temperature measurement on the reduction of foot ulcers in studies with high potential risk of bias[14] compared with others with a lower potential risk of bias.[15-17] In the study with a high potential risk of bias, the RR was 0.15 (95% CI = 0.02-1.19), and in the studies with low potential risk of bias, the pooled RR was 0.37 (95% CI = 0.22-0.61). The comparison between both RRs showed a value of P = .18. As a second subgroup analysis, we compared the effect of temperature measurement in studies with short follow-up period (≤12 months)[14,17] with regard to those with longer duration (>12 months).[15,16] The RRs observed were 0.46 (95% CI = 0.23-0.95) versus 0.28 (95% CI = 0.15-0.55). The comparison between both RRs showed a value of P = .16. These analyses confirmed a significant source of heterogeneity across the studies.

Discussion

The present meta-analysis shows that daily measurement of the skin temperature of the foot, using a handheld infrared

	Experimental		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Armstrong, 2007	5	106	19	115	27.1%	0.29 [0.11, 0.74]
Lavery, 2004	1	41	7	44	7.4%	0.15 [0.02, 1.19]
Lavery, 2007	5	59	17	56	28.0%	0.28 [0.11, 0.71]
Skafjeld, 2015	7	21	10	20	37.5%	0.67 [0.32, 1.41]
Total (95% CI)		**227**		**235**	**100.0%**	**0.37 [0.21, 0.66]**
Total events	18		53			

Heterogeneity: Tau² = 0.09; Chi² = 4.00, df = 3 (P = 0.26); I² = 25%
Test for overall effect: Z = 3.34 (P = 0.0008)

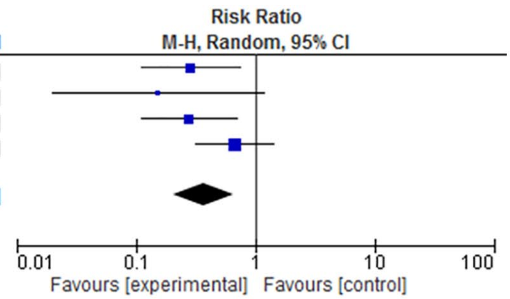


Figure 3. Meta-analysis of the effect of the use of cutaneous thermometry of the foot together with standard care compared with standard care to reduce the occurrence of foot ulcers in patients with diabetes mellitus and foot risk.

thermometer added to the standard of care, reduces the appearance of new foot ulcers in patients at risk. The risk of bias in the studies included in the analysis was low and there was no significant heterogeneity across the studies. The number of patients needed to treat to avoid the appearance of a new skin ulcer was 7.

Education has a positive impact on foot care knowledge and self-reported patient behavior at least in the short term. Nevertheless, there were only 2 sufficiently powered clinical trials to support the effect of patient education and there were no clinically important reductions in the incidence of foot ulcer or amputation to provide a strong recommendation.[19] Another meta-analysis on the effect of patient education in preventing and reducing the incidence or recurrence of adult diabetes foot ulcers also found a positive effect of education, but with significant heterogeneity among studies to provide a robust recommendation.[20]

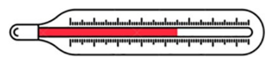
On the other hand, our study provides robust evidence that thermometry of the soles added to the standard of care is effective to reduce the incidence of new foot ulcers. Due to the small number of studies, we selected the random effects model in the analysis. The random effects model provides a more conservative approach to the analysis than a fixed effect model to find statistical significance. In addition, the strengths of the present analyses include the explicit definition of the inclusion and exclusion criteria of the studies (only randomized clinical trials were included), a broad search of the literature, and sufficient sample size to detect significant differences. The intervention evaluated was the measurement of skin temperature in 6 points of the sole of each foot. The infrared ray thermometer used to measure skin temperature was the same in all studies. The alarm sign was to confirm a difference of temperature $>$4°F (2.2°C) between the same corresponding sites in the left and right foot. In such a case, the patient should reduce the physical activity and make efforts to improve glucose control and foot care. The presence of a new ulcer was an objective and robust outcome since we did not observe differences in the effect of the intervention across studies in the subgroup analysis we carried out.

There are some limitations in the present study that deserves to be highlighted. Studies collecting information showed a high degree of patients' adherence to self-monitoring and foot care recommendations. In the real world, adherence to self-care recommendations, especially when they must be carried out throughout life, may be lower than those recorded in the present analysis. In other published studies, adherence to self-care for at least 5 days a week was followed by 32% to 39% of patients.[21,22] There is a clear association between socioeconomic level and participation in research studies,[23] which limits the generalization of our results to other populations with fewer resources. On the other hand, some patients will need assistance due to visual difficulties, physical limitations, or cognitive disorders that prevent them from examining the foot and starting care measures.

Other important outcomes, such as the appearance of infections or amputations, were not included in all the studies. Only one study included the appearance of amputations as a variable outcome.[15] However, the appearance of foot ulcers is an objective outcome with a great clinical impact since it is directly related to the presence of other complication, such as infections, amputations, and death.

In conclusion, daily monitoring of skin temperature of the sole of the foot in patients with diabetes mellitus added to self-care of foot reduces the appearance of new foot ulcers. As implications for the practice of our study, it should be noted that the financing of infrared ray thermometers should be facilitated in order to reduce the high cost and disability caused by diabetic foot problems. In terms of research, the development of devices that allow a thermal image of the feet on domestic scales would be a great step forward in improving adherence to self-monitoring of the temperature.[24] Likewise, it would be useful to know the effect of interventions to reduce the temperature in the feet for the prevention of new ulcers.[25]

Appendix

Monitoring Feet Temperature and Incidence of Foot Ulcers in Patients at Risk		
4 Randomized controlled trials N= 462 patients with diabetes at risk of foot ulcer	Standard of care (N = 227)  + 6 areas checking feet temperature (twice daily)  Temperature difference between feet >4°F (2.2°C) → Foot rest and better glucose control	Standard of care (N = 235) 
Incidence of new foot ulcers	8% Risk ratio: 0.37 (95% CI = 0.21-0.66) NNT = 7 (95% CI = 5-11).	23%

Abbreviations: CI, confidence interval; NNT, number needed to treat.

Author Contributions

JE, CSA, JCG, JCAL, AZG, and RGH contributed to data interpretation and writing. JE, CSA, and AZG designed the study. JE analyzed the data. JE wrote the first draft manuscript. JCG and JCAL supervised the data quality control. JE, CSA, JCG, and JCAL are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: American Diabetes Association provided permission to reproduce foot care vignettes of the Appendix.

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Ethical Approval

Since this study is a pooled analysis of published articles, additional ethical approval is not required.

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