

# Prevention, assessment, diagnosis and management of diabetic foot based on clinical practice guidelines

## A systematic review

Alberto J. Pérez-Panero, MSc<sup>a</sup>, María Ruiz-Muñoz, PhD<sup>a,\*</sup>, Antonio I. Cuesta-Vargas, PhD<sup>b</sup>, Manuel González-Sánchez, PhD<sup>b</sup>

### Abstract

**Aim:** Diabetic foot complications are the main reason for hospitalization and amputation in people with diabetes and have a prevalence of up to 25%. Clinical practice guidelines are recommendations based on evidence with the aim of improving health care. The main aim of this study was to carry out a systematic review of the levels of the evaluation and treatment strategies that appear in the clinical practice guidelines focus on diabetic foot or diabetes with diabetic foot section. Another objective of this study was to perform an analysis of the levels of evidence in support of the recommendations made by the selected clinical practice guidelines.

**Methods:** A systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) and a quality assessment by the Appraisal of Guidelines for Research and Evaluation (AGREE II) were performed. The databases checked were "NICE", "Cinahl", "Health Guide", "RNAO", "Sign", "PubMed", "Scopus" and "NCG". The search terms included were "diabetic foot", "guideline(s)", "practice guideline(s)" and "diabetes."

**Results:** Twelve articles were selected after checked inclusion criteria and quality assessment. A summary and classification of the recommendations was completed.

**Conclusions:** The heterogeneity of levels of evidence and grades of recommendation of the CPGs included regarding the management, approach and treatment of DF makes it difficult to interpret and assume them in clinical practice in order to select the most correct procedures. Despite this and according to the detailed study of the guidelines included in this work, it can be concluded that the highly recommendable interventions for DF management are debridement (very high level of evidence and strongly recommended), foot evaluation (moderate level of evidence and fairly recommended) and therapeutic footwear (moderate level of evidence and fairly recommended).

**Abbreviations:** AGREE II = Appraisal of Guidelines for Research and Evaluation, Cinahl = Cumulative Index to Nursing and Allied Health Literature, CPGs = Clinical practice guidelines, DF = Diabetic foot, NCG = National Guideline Centre, NICE = National Institute for Health and Care Excellence, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses, RNAO = Registered Nurses' Association of Ontario.

**Keywords:** diabetes, diabetes complications, evidence, guideline, review

## 1. Introduction

Diabetes is a pathology that affects millions of people worldwide and the global prevalence has increased rapidly in the last thirty

years,<sup>[1]</sup> and the trend is expected to continue increasing in the future from the current 5.1% to 7.7% in 2030.<sup>[2]</sup>

Diabetic neuropathy is a heterogeneous group of complex pathophysiological disorders, which affects both somatic and autonomic components of the nervous system.<sup>[1]</sup> Diabetic foot (DF), one of the clinical manifestations of diabetic neuropathy, is defined as structural or functional alterations of the foot, such as ulceration, infection and/or gangrene, associated with diabetic neuropathy and different degrees of peripheral vascular disease, as a result of the interaction of different factors induced by maintained hyperglycaemia and previous traumatic causes, although the foot does not present lesions.<sup>[3]</sup> DF is described by a decrease in pain and temperature sensation first and later by a decrease in vibratory sensitivity and superficial touch.<sup>[3]</sup> As a result, DF patients may not be able to feel painful mechanical, chemical or thermal stimuli in normal situations.<sup>[3,4]</sup> These pathological processes lead to the development of complications, such as DF ulcer, Charcot osteoarthropathy and subsequently ulceration and amputation as the most complicated evolutions.<sup>[5]</sup> DF complications have a prevalence of up to 25% and are the main reason for hospitalization and amputation in people with

Editor: Daryle Wane.

The authors have no conflicts of interest to disclose.

<sup>a</sup> Department of Nursing and Podiatry, <sup>b</sup> Department of Physiotherapy, University of Málaga, Arquitecto Francisco Peñalosa, s/n. Ampliación campus de Teatinos 29071, Málaga, Spain.

\* Correspondence: María Ruiz-Muñoz, Arquitecto Francisco Peñalosa, s/n. Ampliación campus de Teatinos 29071, office 2.14, Málaga, Spain (e-mail: marumu@uma.es).

Copyright © 2019 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Medicine (2019) 98:35(e16877)

Received: 23 April 2019 / Received in final form: 26 July 2019 / Accepted: 25 July 2019

<http://dx.doi.org/10.1097/MD.00000000000016877>

diabetes.<sup>[6]</sup> From 20% to 40% of the resources in diabetes pathology are used for foot problems.<sup>[6]</sup>

Clinical practice guidelines (CPGs) are recommendations based on evidence from systematic reviews and the risks and benefits evaluation of the different alternatives, with the aim of optimizing health care.<sup>[7]</sup>

To our knowledge, a systematic review regarding CPGs focused on diabetic foot or diabetes with diabetic foot section included, which shows an evaluation of their validity and an analysis of the grades of recommendation and the levels of evidence, has not been published.

The main aim of this study was to carry out a systematic review of the levels of the evaluation and treatment strategies that appear in the clinical practice guidelines focus on diabetic foot or diabetes with diabetic foot section. Another objective of this study was to perform an analysis of the levels of evidence in support of the recommendations made by the selected clinical practice guidelines.

## 2. Methods

This systematic review was organized according to the protocol registered in PROSPERO with reference number CRD42018095922 and was submitted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.

### 2.1. Search strategy

The search and selection strategy was developed by two blinded investigators. The databases consulted were: “NICE” (National Institute for Health and Care Excellence), “Cinahl” (Cumulative Index to Nursing and Allied Health Literature), “Health Guide”, “RNAO” (Registered Nurses’ Association of Ontario), “Sign”, “PubMed”, “Scopus” and “NCG” (National Guideline Centre). The search terms used were “diabetic foot”, “guideline(s)”, “practice guideline(s)” and “diabetes”. Any differences in search and selection of the documents were determined by a third external and blinded reviewer.

### 2.2. Eligibility criteria

It was followed PICO method:

- Population: patients with diabetic foot diagnosis.
- Intervention: prevention, assessment, diagnosis and management of diabetic foot.
- Comparison: clinical practice guidelines with high internal validity.
- Outcome: level of evidence and grade of recommendation.

### 2.3. Exclusion criteria

CPGs published until December 2018 were taken in consideration. There were included English documents.

CPGs whose title or summary did not match the current review were excluded, as well as those that did not classify levels of evidence and grades of recommendation.

All the CPGs previous to the last version were excluded.

### 2.4. Quality assessment

Two blinded researchers assessed the quality of the selected CPGs by the Appraisal of Guidelines for Research and Evaluation

(AGREE II)<sup>[8]</sup> which is a scale with 23 items divided within 6 domains followed by 2 global score items (“Overall Assessment”), each domain corresponds to a single dimension of guideline quality and the overall assessment includes the score of the overall guideline quality and whether the guideline is recommended.

For each of the 6 AGREE II domains a quality score is calculated independently. Each domain score is calculated by summing up all the scores of the items included in each domain and by representing the total as a percentage of the maximum score for that domain. Once the 23 items are calculated, it will provide an overall assessments of the guideline rate between 1 (lowest possible quality) and 7 (highest possible quality). “Quality CPGs” were those that achieved an overall score larger than 4. Once the documents were evaluated using the AGREE II tool and selected the definitive ones, the results obtained were synthesized.

### 2.5. Summary of the recommendations

Recommendations were summarized considering each standardized grade of all relevant recommendations. Greater emphasis was placed on guideline recommendations with higher overall quality score (AGREE II).

In order to unify the different levels of evidence shown in the CPGs selected, a simple but complete scale following the literature has been made.<sup>[9]</sup> This scale, shown in Table 1, allows us to compare the different results extracted from each CPG and provide a certain value according to the level of evidence.

In addition, Table 1 shows the grades of recommendation classification.

## 3. Results

### 3.1. Quality assessment

Of the total of 22 guidelines evaluated, 10 were excluded for failing to achieve the minimum score using the AGREE II tool.

RNAO guide<sup>[10]</sup> showed superior quality to the rest of the CPGs. In this line, Kennon<sup>[11]</sup> and NICE<sup>[12]</sup> guides obtained a high score. The results are shown in detail in Table 2.

### 3.2. Summary of the recommendations

The flow diagram shows the initial documents of the search and the final documents included after the exclusion criteria. Twelve articles were selected. A detailed summary and classification of the recommendations included are shown in detail in Table 1.

## 4. Discussion

The objective of this study was to review the current guidelines included in CPGs for DF management. The quality of CPGs was evaluated using the AGREE II tool. It provided a summary of the levels of evidence and grades of recommendation useful for diagnosis, approach and treatment of the DF according to the results provided by the CPGs selected. After analyzing the results, a lack of consistency regarding the levels of evidence and grades of recommendation in most of the guidelines included is observed.

There is a problem that was identified in a previous study, which highlights the variability in the recommendations suggested by the different clinical practice guidelines.<sup>[13]</sup> Clinical

**Table 1**  
Levels of evidence and grades of recommendation of the CPGs selected.

	Barry, P. et al [30]	Teage, L.M. et al [42]	Kennon B. et al [12]	Antón, M. et al [31]	Daza, P. et al [15]	NICE 2015 [13]	RNAO 2015 [16]	Jones N.J. et al [29]	Hingorani MD et al. [19]	Asbury, J. et al [38]	CJD Canada [43]	NHM Indian [39]
<b>VALUATION</b>												
Foot evaluation	Co	B	B	A	B	D	B	A	B	D	A	B
Screening	Co		B	D	B	C	B	B		D	C	B
Charcot's Foot	Co		Co			D	C			D		C
<b>TREATMENT</b>												
Therapeutic footwear			B		B		A	A	B	B		D
Offloading	Co		B		B	D	B	A	B	B	Co	
Debridement	Co				D	A	A	A	A	B	A	C
Dressings	Co				B			A		B	C	
Antibiotherapy	Co		Co		D	D	B	B	B	B		D
Adjuvant treatments	Co		B		B	D		B		B		C
Neuropathic pain	Co		A			C	C	B				
Multidisciplinary team	Co		C	Co		D		A		B	C	D
Education			B		B	Co	D	A	A	D	Co	C
<b>GRADES OF RECOMMENDATION</b>				<b>LEVELS OF EVIDENCE</b>								
				A	B	C	D	Co				
Strongly recommended	Fairly recommended	Little recommended	Nothing recommended	Very high/high	Moderate/half	Low	Very low	Controversial				

practice guidelines being a reference document for the clinical professional, it would be necessary for those who prepare this type of documents to seek the highest methodological quality, so that those recommendations that are made have the most up-to-date level of evidence possible and presented in a way that, in a simple way, can be compared with other CPGs. This would greatly facilitate the process of identifying those assessment and follow-up strategies in patients with diabetic foot, who have a

higher grade of recommendation and the strongest level of evidence.

**4.1. Foot evaluation**

All the guidelines agree on the importance of evaluating the foot and footwear, existence of deformities, gait, ability to perform exercise and determining the patient's risk. Regarding foot

**Table 2**  
AGREE II results shown in percentages.

CPGs Domain/CPGs	RNAO 2015 [16]	Asbury J et al [38]	Kennon B et al [12]	NICE 2015 [13]	Barry P et al [30]	NHM Indian [39]	Antón, MA et al [31]	Jones N.J. et al [29]	Teage LM et al [42]	Daza P et al [15]	CJD Canada [43]	Hingorani MD et al [19]
Domain 1 (Scope and Purpose)	77.77%	77.77%	72.22%	55.55%	77.77%	55.55%	72.22%	66.66%	72.22%	72.22%	50%	33.33%
Domain 2 (Stakeholder involvement)	33.33%	61.11%	77.77%	33.33%	61.11%	33.33%	55.55%	27.77%	66.66%	55.55%	50%	22.22%
Domain 3 (Rigour of development)	61.22%	57.17%	51.02%	63.26%	59.18%	51.02%	34.69%	59.18%	48.97%	32.65%	65.30%	46.93%
Domain 4 (Clarity of presentation)	77.77%	72.22%	72.22%	55.55%	72.22%	55.55%	72.22%	50%	55.55%	72.22%	44.44%	44.44%
Domain 5 (Applicability)	45.83%	50%	50%	45.83%	29.16%	45.83%	33.33%	42.85%	20.83%	20.83%	20.83%	20.83%
Domain 6 (Editorial Independence)	83.33%	16.66%	8.33%	83.33%	25%	83.33%	41.66%	75%	8.33%	41.66%	33.33%	66.66%
Global (%)	66.45%	63.32%	62.11%	62.11%	61.49%	59%	58.38%	57.14%	54.65%	53.41%	51.55%	49.68%
Global (1-7)	5	5	5	5	5	5	5	5	4	4	4	4

evaluation, a level of evidence B is found, and the grade of recommendation is highly recommended. In line with this, there is literature that supports the importance of foot evaluation, suggesting that routine foot evaluation is of extreme importance and has a great role in prevention of ulcers and diabetes-related morbidity and mortality.<sup>[14]</sup>

Despite the consensus regarding the importance of foot evaluation, the CPGs consulted do not include Semmes–Weinstein monofilament, tuning fork or temperature monitoring. These are DF assessment systems with a high frequency of clinical use.<sup>[15,16]</sup> A pressure of 10 grams is the pressure able to protect soft tissue as a defense threshold against painful aggressions.<sup>[17,18]</sup> It shows a level of evidence A and a high grade of recommendation.<sup>[16,19]</sup> It measures both deep sensitivity (sensitivity to pressure) and superficial sensitivity (sensitivity to pain). The specificity of this monofilament is higher than 80%, while the sensitivity is higher than 95%.<sup>[17,18]</sup>

There is a study that shows doubts about monofilament sensitivity in neuropathy early detection, and a protocol to perform monofilament tests in patients with diabetes mellitus is being developed.<sup>[20]</sup> Therefore, although monofilament is an important tool based on evidence, more research should be done to establish the relationship between monofilament and lower extremity amputations.<sup>[20–22]</sup>

The tuning fork (Ryder-Seiffer) has a level of evidence B.<sup>[15]</sup> The tuning fork evaluates deep (vibratory) sensitivity and presents markers graduated from 0 to 8 in ascending form starting from the base.<sup>[23,24]</sup>

There is a study that suggests the tuning fork provides a quantitative assessment of DN and can diagnose severe neuropathy, even with a normal result through 10g Semmes–Weinstein monofilament test.<sup>[25]</sup> The risk of foot ulcers is associated with decreased vibratory sensation; therefore, it can be detected earlier and more accurately with the tuning fork.

A meta-analysis and review conclude that evaluation through temperature monitoring is a feasible and relevant method with a wide range of possible applications and an important tool in DF care from subjective evaluation to objective evaluation of high-risk patients.<sup>[26,27]</sup>

## 4.2. Screening

By screening based on sock inspection, feet and legs inspection, hygiene, toenails, pulses, ankle strength, and movement and sensitivity inspection, the risk level can be determined, which helps to identify patients at risk for foot alteration and to initiate protective measures that help prevent lower extremity amputation.<sup>[28]</sup>

The results extracted from the CPGs show disparity regarding screening recommendations. Mostly, the CPGs recommend screening based on a level of evidence B–C and quite a high grade of recommendation.<sup>[11,12,15,16,29]</sup> However, Barry et al<sup>[30]</sup> and Antón et al<sup>[31]</sup> did not find sufficient evidence to support its recommendation.

One of the main disadvantages in foot screening is neglect/forgetfulness on the part of patients. Omission of the annual foot exam for people with diabetes is attributed to the nature of foot problems related to diabetes, people with diabetes, health professionals and health care system structure.<sup>[32]</sup>

The existing literature does not help to consolidate neither levels of evidence nor grades of recommendation.<sup>[13]</sup>

## 4.3. Charcot's foot

Charcot's foot is associated with reduced quality of life and even increased mortality.<sup>[33]</sup> In addition, the costs of treatment of the comorbidities associated with Charcot's foot are 17.2% higher compared to the costs of treatment for peripheral DN only. It often appears without warning and progresses rapidly, becoming a serious and irreversible foot deformity that leads to ulceration or even amputation.<sup>[33]</sup>

The incidence of DF ulceration is 17% per year, and the amputation of lower extremity risk is 12 times higher in patients with Charcot's foot deformity and ulcer compared with Charcot's foot only.<sup>[33]</sup>

The majority of the CPGs analyzed do not show data regarding this pathology; CPGs that show information about their management have a level of evidence C–D and a low grade of recommendation.<sup>[12,17,34,35]</sup>

The only proven treatment that is considered a gold standard is the total contact cast (TCC). Recent pharmacological therapies used in Charcot's foot treatment have not demonstrated efficacy and are not recommended for clinical practice. New therapeutic approaches are needed to prevent bone destruction of Charcot's foot in an acute stage.<sup>[36]</sup>

## 4.4. Therapeutic footwear

Most guides agree on therapeutic footwear recommendation with a level of evidence B, although with a moderate grade of recommendation. Astbury et al<sup>[37]</sup> and Daza et al<sup>[15]</sup> recommend the use of therapeutic shoes only in patients with foot deformities, while Kennon et al<sup>[11]</sup> recommend its use for all people with diabetes in order to reduce recurrence of foot pathologies and ulcerations.

Literature suggests using therapeutic shoes for all people with diabetes to protect and accommodate the foot in order to reduce the incidence of pathologies and even ulcerations. This is thought to avoid shearing and friction of the footwear although always under health professional supervision.<sup>[39,40]</sup>

## 4.5. Offloading

Pressure offloading is a therapeutic procedure focused on reducing the pressure on the affected area. There is a certain discrepancy between those who advise its use to reduce pressure ulcers<sup>[11,15,19,29,41]</sup> and those who advise against it because they do not find enough evidence for its effectiveness.<sup>[30,42]</sup>

Astbury et al,<sup>[37]</sup> Daza et al<sup>[15]</sup>, and Kennon et al<sup>[11]</sup> agree that, for successful offloading, there should be total contact splints with level of evidence B and a moderate–high grade of recommendation. In turn, Daza et al<sup>[15]</sup> and Kennon et al<sup>[11]</sup> suggest that immovable glass splints are an alternative to TCC, with a level of evidence B and a moderate grade of recommendation.

Barry et al<sup>[30]</sup> and Diabetes Canada Clinical Practice Guidelines Expert Committee (DCPGEC)<sup>[42]</sup> do not rule out its use, but they affirm it does not have enough indication to prove its effectiveness or evidence for its recommendation.

## 4.6. Debridement

Debridement is a technique that removes slough or necrotic tissue from a wound. This necrotic tissue acts as a barrier that prevents

the approximation of wound edges, removing it allows wound healing.<sup>[15,30,43,44]</sup>

The majority of CPGs analyzed support the use of debridement with level of evidence A and high grade of recommendation.<sup>[12,16,19,29,42]</sup> Debridement is considered one of the most recommended DF action techniques.

Of the selected CPGs, only Barry et al<sup>[30]</sup> affirms that there is controversy regarding its use due to the inconclusive evidence but does not indicate specific techniques, although it does recognize its usefulness beyond the evidence. However, Daza et al<sup>[15]</sup> recommends necrotic tissue removal by surgery and suggests the use of hydrogel as debridement.

The available literature is in line with most of the CPGs selected and supports the effectiveness of several debridement methods, such as surgical, autolytic and larval debridement.<sup>[43,44]</sup>

A Cochrane systematic review (evidence level A) published in 2010<sup>[44]</sup> states that there is evidence to suggest hydrogel increases the cure rate of DF ulcers compared to gauze dressings or standard care and that larval debridement resulted in a significantly greater reduction in wound area than hydrogel<sup>[44]</sup>; therefore, these techniques should be included in CPGs for their recommendation based on published evidence.

#### 4.7. Dressings

The use of this technique has slight evidence to support or reject it. However, both Daza et al,<sup>[15]</sup> Astbury et al<sup>[37]</sup> and DCPGEC<sup>[42]</sup> recommend its use with level of evidence B<sup>[15,37]</sup> and C,<sup>[42]</sup> respectively, and low grade of recommendation. Astbury et al<sup>[37]</sup> and Barry et al<sup>[30]</sup> agree on the fact that dressing choice depends on cost-effectiveness, professional experience and wound assessment as well as patient preference.

A Cochrane systematic review (evidence level A) published in 2015<sup>[45]</sup> states that currently there is no solid evidence regarding differences between dressings for any outcome in DF ulcers treated in any environment.

The available evidence regarding dressings is inconclusive to make specific recommendations for its use and, therefore, more research is needed to evaluate its effects and usefulness.<sup>[37,42,45]</sup>

#### 4.8. Antibiotherapy

Concerning antibiotics, no guide makes specific recommendations on which is the one to be used in each case. Although there is some controversy regarding their level of evidence and grade of recommendation, in the CPGs selected for this review, level of evidence B and high grade of recommendation prevails. Most CPGs recommend controlling infection without referring to a specific antibiotic. Daza et al<sup>[15]</sup> and Barry et al<sup>[30]</sup> advise these drugs when ulcers are progressive, do not heal and have signs of infection. Choice of treatment should be selected taking into account microorganism resistance.

Because high-quality evidence studies do not find evidence to show that one type of antibiotic is more effective than another, Kennon et al<sup>[11]</sup> advise to start antibiotic treatment if there is infection or osteomyelitis and to modify the treatment according to the response to it and the bacteriological references.

Barry et al<sup>[30]</sup> advise for mild infections, oral antibiotics with activity against Gram-positive microorganisms,<sup>[46]</sup> and for moderate and severe infections, antibiotics with activity against Gram-positive and Gram-negative microorganisms, including anaerobic bacteria. Administration route is orally or intrave-

nously for moderate infections and intravenously exclusively for severe infections. Because the evidence is limited, it is advisable to carry out future research studies to achieve conclusive results.

Different studies,<sup>[47,48]</sup> among which there is a Cochrane systematic review,<sup>[47]</sup> suggest that more research is needed to evaluate antibiotic effectiveness for treatment of foot infections, because there are not enough studies with high-quality evidence; largely due to trial design limitations and differences between the existing literature regarding the diversity of antibiotics evaluated, duration of the treatments and time points in which results were evaluated.<sup>[47,48]</sup>

#### 4.9. Adjuvant treatments

The levels of evidence regarding adjuvant treatments range from level B<sup>[11,15,29,37]</sup> to level C.<sup>[30]</sup> The grade of recommendation ranges from strongly recommended<sup>[11,14]</sup> to not recommended.<sup>[12,29,30,39]</sup>

Barry et al<sup>[30]</sup> and Astbury et al<sup>[37]</sup> agree that, because they are very expensive, adjuvant treatments are not offered routinely and should only be used as part of a clinical trial.

Granulocyte colony stimulating factor (G-CSF) increases the release of neutrophil endothelial progenitor cells from the bone marrow and improves neutrophil function, which is often affected in people with diabetes; so G-CSF could be used as adjuvant therapy for DF infections.<sup>[3,49]</sup>

The available evidence regarding G-CSF is low, but it suggests G-CSF treatment in patients with DF infection, including infected ulcers, does not increase the likelihood of infection resolution or foot ulcer cure.<sup>[49]</sup> However, it seems to reduce surgical interventions, especially amputations, and hospitalization length.<sup>[49]</sup> Clinicians may consider adding G-CSF to the usual treatment of DF infections, especially in patients with an infection that threatens the limb, but it is not clear which patients would be suitable.

As for negative pressure therapy (NPT), there is contradictory information. On the one hand, with a level of evidence B and a strong grade of recommendation, Kennon et al<sup>[11]</sup> advises using this therapy on all patients with DF ulcers, while Barry et al<sup>[29]</sup> advises that its use should be limited to clinical trials or as a last alternative.

There is a 2017 review and meta-analysis that analyses the effectiveness of NPT in the treatment of DF ulcers. The results affirmed NPT is effective, safe and profitable in the treatment of DF ulcers, so CPGs should include this information for knowledge and application by professionals.<sup>[50]</sup>

#### 4.10. Neuropathic pain

Less than half of the CPGs included in this review have information about neuropathic pain. The treatment of neuropathic pain presents a level of evidence that ranges between A and C,<sup>[11,12,16]</sup> while it is strongly recommended by Kennon et al<sup>[11]</sup> and NICE<sup>[12]</sup> and moderately recommended by RNAO.<sup>[16]</sup> Barry et al<sup>[30]</sup> suggests there is controversy regarding its evidence, and Teage et al<sup>[41]</sup> advises the treatment of neuropathic pain is not recommendable.

Kennon et al<sup>[11]</sup> suggests that antidepressants (including venlafaxine, duloxetine, and tricyclics), anticonvulsants (including pregabalin and gabapentin) and opioids combined with gabapentin can be used for neuropathic pain.



Only duloxetine and pregabalin are officially approved by the Food and Drug Administration; tricyclic antidepressants have been effective in clinical trials for the treatment of neuropathic pain.<sup>[51–53]</sup>

#### 4.11. Multidisciplinary team

Recommendations from the CPGs consulted for treatment of DF through a multidisciplinary team show a certain disparity. Astbury et al,<sup>[37]</sup> Kennon et al<sup>[11]</sup>, and NICE<sup>[12]</sup> suggest a multidisciplinary intervention, although its level of evidence ranges between B<sup>[37]</sup> and D.<sup>[12,38]</sup> Barry et al<sup>[30]</sup> states there is controversy in the grade of recommendation, which varies between highly recommendable<sup>[12,38]</sup> and little/nothing recommended.<sup>[30,42]</sup>

However, there is literature that suggests a multidisciplinary team to evaluate patients with diabetes mellitus can provide favorable results<sup>[19,54–56]</sup> and even reduce frequency of amputations.<sup>[57]</sup> However, due to the lack of evidence and heterogeneity in published studies, these results should be interpreted with caution.<sup>[58,59]</sup>

#### 4.12. Education

Most of the CPGs analyzed agree that foot care education is an essential part of ulcer risk prevention and, more specifically, Teage et al<sup>[41]</sup> includes a section for education in ulcer care. Levels of evidence range between A (very strong) by Hingorani et al<sup>[19]</sup> and D (low) by RNAO,<sup>[17]</sup> Jones et al<sup>[29]</sup> and Astbury et al.<sup>[37]</sup> It must be taken into account that the grade of preferential recommendations is strongly recommended by some of the CPGs<sup>[15,37,41]</sup> and not recommended by others.<sup>[19,23,33]</sup> In addition, there are 2 CPGs which do not recommend education in DF intervention,<sup>[12,42]</sup> although they show controversy in the evidence that supports this recommendation. Therefore, concerning patient education, there is controversy in its grade of recommendation.

The literature supports education as part of DF interventions. There are 2 systematic reviews that suggest patient education is an important component<sup>[60]</sup> and plays an essential role in this disease, improving self-care and helping to reduce chronic complications.<sup>[61]</sup> However, a Cochrane systematic review<sup>[62]</sup> points out that knowledge about foot care and self-reported outcomes from patients seem to be positively influenced by short-term education, but, based on the few studies that report the effect of patient education, it concludes that there is not enough solid evidence to confirm that education limited to the patient is effective in achieving clinically relevant reductions in ulcers and incidence of amputations.<sup>[62]</sup>

Therefore, more research is needed to evaluate, with quality and reliability, the effects of patient education and the influence of health professionals trained in education promotion.<sup>[62–64]</sup>

Diabetic foot is one of the costliest consequences of diabetes. Although the role of the podiatrist is crucial for the correct resolution of the problem, it is essential not to forget that in pathology of systemic origin, thus, the treatment must be global and multidisciplinary.<sup>[65]</sup> This approach, which is so evident, is not recommended, nor suggested nor integrated into the clinical practice guidelines that have been consulted. Addressing the consequence of a systemic problem locally seems a short-term solution but one that is difficult to achieve in medium and long term.<sup>[65]</sup> It would be necessary to design future studies of the

highest quality, by means of multimodal interventions so that the diagnosis and treatment of diabetic foot is approached integrating different considerations: people suffering from systemic pathologies may suffer mechanical alterations in the foot as a result of mismanagement of the pathology globally.<sup>[13]</sup> In addition, problems in the foot may recur even after clinical remission of the local problem.<sup>[13]</sup>

To summarize, DF best management is based on evaluation and screening on one hand and treatment approach on the other. In terms of interventions fairly or strongly recommended, the first one includes evaluating foot, footwear, deformities, gait, physical activity, hygiene, toenails, pulses, ankle strength and movement, sensitivity inspection and patient's risk. The second one includes debridement to allow wound healing, off loading to reduce the pressure on the affected area, therapeutic footwear to reduce the risk of ulceration and antibiotherapy if there is infection or osteomyelitis.

#### 4.13. Limitations and strengths

In the present study, all the recommendations based on the evidence published in the clinical practice guidelines for the evaluation and treatment of the diabetic foot were collected. Given the heterogeneity in the different classification systems, both of the levels of evidence and of the degrees of recommendation, we have tried to unify the criterion to favor the comparison and facilitating the identification of the convergence and divergences between the different clinical practice guidelines included in this study.

On the other hand, the diabetic foot is the local consequence of different factors, both local and systemic. This study has focused on the role of the podiatrist in the assessment and treatment of diabetic foot. However, this professional presents a limited field of action from an anatomical point of view, which should be taken into account in order to properly evaluate the results presented in this study to offer the patient with diabetic foot the best alternative therapy.

## 5. Conclusion

The heterogeneity of levels of evidence and grades of recommendation of the CPGs included regarding the management, approach and treatment of DF makes it difficult to interpret and assume them in clinical practice in order to select the most correct procedures. Despite this and according to the detailed study of the guidelines included in this work, it can be concluded that the highly recommendable interventions for DF management are debridement (very high level of evidence and strongly recommended), foot evaluation (moderate level of evidence and fairly recommended) and therapeutic footwear (moderate level of evidence and fairly recommended).

## References

- [1] Singh Randhir , Lalit Kishore , Navpreet Kaur . Diabetic peripheral neuropathy: current perspective and future directions. *Pharmacol Res* 2014;80:21–35.
- [2] Faruque LI, Wiebe N, Ehteshami-Afshar A, et al. Effect of telemedicine on glycated hemoglobin in diabetes: a systematic review and meta-analysis of randomized trials. *Can Med Assoc J* 2017;189: E341–64.
- [3] Cruciani M, Lipsky BA, Mengoli C, et al. Granulocyte-colony stimulating factors as adjunctive therapy for diabetic foot infections. *Cochrane Database Syst Rev* 2013;8:CD006810.

- [4] Tirado R-A, del C, López JAF, et al. Guía de práctica clínica en el pie diabético. *Arch Med* 2014;10:1–7.
- [5] Sanverdi S, Eser F, Bilge Ergen , et al. Current challenges in imaging of the diabetic foot. *Diabet Foot Ankle* 2012;3:
- [6] Lepántalo M, Apelqvist J, Setacci C, et al. Chapter V: diabetic foot. *Eur J Vasc Endovasc Surg* 2011;42:S60–74.
- [7] National Research Council Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press; 2011.
- [8] Yazdanpanah L, Nasiri M, Adarvishi S. Literature review on the management of diabetic foot ulcer. *World J Diabetes* 2015;6:
- [9] Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. *Bmj* 2001;323:334–6.
- [10] Reducing Foot Complications for People with Diabetes. <https://rnao.ca/bpg/guidelines/reducing-foot-complications-people-diabetes>. Accessed October 15, 2018.
- [11] Kennon B. et al. Management of diabetes. A national clinical guideline. Edinburgh: Scottish Intercollegiate Guidelines Network (2010). Available at: <http://www.sign.ac.uk/guidelines/fulltext/116/index.html>. Accessed October 15, 2018.
- [12] Diabetic foot problems: prevention and management. London: National Institute for Health and Care Excellence (UK); 2015 Aug.
- [13] Formosa C, Gatt A, Chockalingam N. A critical evaluation of existing diabetic foot screening guidelines. *Rev Diabet Stud* 2016;13:158–86.
- [14] Dixit S, Maiya A. Diabetic peripheral neuropathy and its evaluation in a clinical scenario: a review. *J Postgrad Med* 2014;60:33–40.
- [15] Daza Asurmendi P, Etxeberria Agirre A, Ezkurra Agirre P, et al. Guía de Práctica clínica sobre diabetes tipo 2. *Guia Salud* 2008.
- [16] Reducing Foot Complications for People with Diabetes | Guidance and guidelines | RNAO. Disponible en: <http://rnao.ca/bpg/guidelines/reducing-foot-complications-people-diabetes>. Accessed October 15, 2018.
- [17] Feng Yuzhe , Felix Schlösser, Bauer E Sumpio . The Semmes Weinstein monofilament examination is a significant predictor of the risk of foot ulceration and amputation in patients with diabetes mellitus. *J Vasc Surg* 2011;53:220.
- [18] Katon Jodie G, Gayle E. Reiber, Karin M. Nelson. Peripheral Neuropathy Defined by Monofilament Insensitivity and Diabetes Status NHANES 1999-2004. *Diabetes Care*. 2013;36:6 1604–1606.
- [19] Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podi. 2016.
- [20] Wang F, Zhang J, Yu J, et al. Diagnostic Accuracy of Monofilament Tests for Detecting Diabetic Peripheral Neuropathy: A Systematic Review and Meta-Analysis. *J Diabetes Res* 2017;8787261.
- [21] Feng Y, Schlösser FJ, Sumpio BE. The Semmes Weinstein monofilament examination is a significant predictor of the risk of foot ulceration and amputation in patients with diabetes mellitus. *J Vasc Surg* 2011;53: 220–6.e5.
- [22] Feng Y, Schlösser FJ, Sumpio BE. The Semmes Weinstein monofilament examination as a screening tool for diabetic peripheral neuropathy. *J Vasc Surg* 2009;50:675–82.e1.
- [23] Chantelau EA. Nociception at the diabetic foot, an uncharted territory. *World J Diabetes* 2015;6:391–402.
- [24] Nather A, Lin WK, Aziz Z, et al. Assessment of sensory neuropathy in patients with diabetic foot problems. *Diabet Foot Ankle* 2011;2:
- [25] Oyer D, Saxon D, Shah A. Quantitative assessment of diabetic peripheral neuropathy with use of the clanging tuning fork test. *Endocr Pract* 2007;13:5–10.
- [26] 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.
- [27] Bus SA. Innovations in plantar pressure and foot temperature measurements in diabetes. *Diabetes Metab Res Rev* 2016;32(Suppl 1):221–6.
- [28] Yetzer EA. Incorporating foot care education into diabetic foot screening. *Rehabil Nurs* 2004 May-Jun 2004;29:80–4.
- [29] Jones NJ, Harding K. 2015 International Working Group on the Diabetic Foot Guidance on the prevention and management of foot problems in diabetes. *Int Wound J* 2015;12:373–4.
- [30] Barry P, Adler A, Berendt A. et al. Diabetic foot problems: Inpatient management of diabetic foot problems. London: National Institute for Health and Clinical Excellence. 2011. Disponible en: <https://www.nice.org.uk/guidance/cg119>.
- [31] Antón Miguel MA, Corcóstegui Santiago B, Cortazar Galarza A. et al. Guía de Práctica Clínica sobre Diabetes mellitus tipo 1. Plan de Calidad para el Sistema Nacional de Salud del Ministerio de Sanidad y Política Social. Agencia de Evaluación de Tecnologías Sanitarias del País Vasco-Osteba; 2012.
- [32] Abu-Qamar MZ. Diabetic foot screening: why is it neglected? *Int Wound J* 2006;3:203–13.
- [33] Kaynak G, Birsal O, Güven MF, et al. An overview of the Charcot foot pathophysiology. *Diabet Foot Ankle* 2013;4.
- [34] Varma AK. Charcot neuroarthropathy of the foot and ankle: a review. *J Foot Ankle Surg* 2013;52:740–9.
- [35] Madan SS, Pai DR. Charcot neuroarthropathy of the foot and ankle. *Orthop Surg mayo de* 2013;5:86–93.
- [36] Petrova NL, Edmonds ME. Conservative and pharmacologic treatments for the diabetic charcot foot. *Clin Podiatr Med Surg* 2017;34:15–24.
- [37] Astbury J, Bailey C, Barnes S. et al. Type 1 diabetes in adults National clinical guideline for diagnosis and management in primary and secondary care. London: National Institute for Health and Clinical Excellence. 2004. Disponible en: <https://www.nice.org.uk/guidance/cg15>.
- [38] Ministry Health and Family Welfare of India. Standard treatment guidelines: The diabetic foot: prevention and management in India, 2016. Ministry Health and Family Welfare, India. 2016. [www.nhm.gov.in/nrhm-instate/520-standard-treatment-guidelines.html](http://www.nhm.gov.in/nrhm-instate/520-standard-treatment-guidelines.html).
- [39] Bus SA, Waaijman R, Arts M, et al. Effect of Custom-Made Footwear on Foot Ulcer Recurrence in Diabetes. *Diabetes Care* 2013;36:4109–16.
- [40] van Netten JJ, Lazzarini PA, Armstrong DG, et al. Diabetic Foot Australia guideline on footwear for people with diabetes. *J Foot Ankle Res* 2018;11:2.
- [41] Teague LM, et al. Assessment and Management of Foot Ulcers for People with Diabetes, Second Edition. [Internet]. Toronto, ON: Registered Nurses' Association of Ontario; 2013. Disponible en: <http://rnao.ca/bpg/guidelines/assessment-and-management-foot-ulcer>.
- [42] Diabetes Canada Clinical Practice Guidelines Expert Committee. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes* 2018;42(Suppl 1):S1–325.
- [43] Elraiyah T, Domecq JP, Prutsky G, et al. A systematic review and meta-analysis of débridement methods for chronic diabetic foot ulcers. *J Vasc Surg* 2016;63:375–45Se2.
- [44] Edwards J, Stapley S. Debridement of diabetic foot ulcers. *Cochrane Database Syst Rev* 2010;1:CD003556.
- [45] Wu L, Norman G, Dumville JC, et al. Dressings for treating foot ulcers in people with diabetes: an overview of systematic reviews. *Cochrane Database Syst Rev* 2015;7:CD010471.
- [46] Kasiya MM, Mang'anda GD, Heyes S, et al. The challenge of diabetic foot care: review of the literature and experience at Queen Elizabeth Central Hospital in Blantyre. *Malawi Malawi Med J* 2017;29:218–23.
- [47] Selva Olid A, Solà I, Barajas-Nava LA, et al. Systemic antibiotics for treating diabetic foot infections. *Cochrane Database Syst Rev* 2015;9: CD009061.
- [48] Crouzet J, Lavigne JP, Richard JL, et al. Diabetic foot infection: a critical review of recent randomized clinical trials on antibiotic therapy. *Int J Infect Dis* 2011;15:e601–10.
- [49] Cruciani M, Lipsky BA, Mengoli C, et al. Granulocyte-colony stimulating factors as adjunctive therapy for diabetic foot infections. *Cochrane Database Syst Rev* 2009;3:CD006810.
- [50] Liu S, He C, Cai Y, et al. Evaluation of negative-pressure wound therapy for patients with diabetic foot ulcers: systematic review and meta-analysis. *Ther Clin Risk Manag* 2017;13:533–44.
- [51] Argoff CE, Backonja M-M, Belgrade MJ, et al. Consensus guidelines: treatment planning and options. *Diabetic Peripheral Neuropathic Pain Mayo Clin Proc* 2006;81:512–25.
- [52] Bellows B, King J, Schauerhamer M. A review of the clinical utility of duloxetine in the treatment of diabetic peripheral neuropathic pain. *Ther Clin Risk Manag* 2015;11:1163.
- [53] Iyer S, Tanenberg RJ. Pharmacologic management of diabetic peripheral neuropathic pain. *Expert Opin Pharmacother* 2013;14:1765–75.
- [54] Hartmann B, Fottner C, Herrmann K, et al. Interdisciplinary treatment of diabetic foot wounds in the elderly: low risk of amputations and mortality and good chance of being mobile with good quality of life. *Diabetes Vasc Dis Res* 2017;14:55–8.
- [55] Wright PR, Lawrence SM, Campbell DA, et al. Creation of a multidisciplinary, evidence based, clinical guideline for the assessment, investigation and management of acute diabetes related foot complications. *Diabet Med* 2005;22:127–36.

- [56] Apelqvist J, Ragnarson-Tennvall G, Persson U, et al. Diabetic foot ulcers in a multidisciplinary setting. An economic analysis of primary healing and healing with amputation. *J Intern Med* May 1994;235:463–71.
- [57] Wang C, Mai L, Yang C, et al. Reducing major lower extremity amputations after the introduction of a multidisciplinary team in patient with diabetes foot ulcer. *BMC Endocr Disord* 2016;16:38.
- [58] Buggy A, Moore Z. The impact of the multidisciplinary team in the management of individuals with diabetic foot ulcers: a systematic review. *J Wound Care* 2017;26:324–39.
- [59] Munro N, Felton A, McIntosh C. Is multidisciplinary learning effective among those caring for people with diabetes? *Diabet Med* 2002;19:799–803.
- [60] Markakis K, Bowling FL, Boulton AJM. The diabetic foot in 2015: an overview. *Diabetes Metab Res Rev* 2016;32(Suppl 1):169–78.
- [61] Iquize RCC, Theodoro FCET, Carvalho KA, et al. Educational practices in diabetic patient and perspective of health professional: a systematic review. *Brazilian J Nephrol* 2017;39:196–204.
- [62] Dorresteijn JA, Kriegsman DM, Assendelft WJ, et al. Patient education for preventing diabetic foot ulceration. In: *The Cochrane Library*. 2014; John Wiley & Sons, Ltd,
- [63] Cunningham AT, Crittendon DR, White N, et al. The effect of diabetes self-management education on HbA1c and quality of life in African-Americans: a systematic review and meta-analysis. *BMC Health Serv Res* 2018;18:367.
- [64] Beck J, Greenwood DA, Blanton L, et al. 2017 National Standards for Diabetes Self-Management Education and Support; 2017 Standards Revision Task Force.
- [65] Gatlin TK, Serafica R, Johnson M. Systematic review of peer education intervention programmes among individuals with type 2 diabetes. *J Clin Nurs* 2017;26:4212–22.