Metabolism Clinical and Experimental 100 (2019) 153956

Contents lists available at ScienceDirect

Metabolism Clinical and Experimental

journal homepage: www.metabolismjournal.com

Review

Evidence mapping of recommendations on diagnosis and therapeutic strategies for diabetes foot: an international review of 22 guidelines

Yue Sun [a,b,c,1], Ya Gao [b,c,1], Ji Chen [a,b,c], Hao Sun [d], Yi-tong Cai [a,b,c], Long Ge [b,c,e], Ya-nan Li [f], Junhua Zhang [g,*], Jin-hui Tian [a,b,c,**]

[a] Evidence-Based Nursing Center, School of Nursing, Lanzhou University, Lanzhou City, Gansu Province, China
[b] Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou City, Gansu Province, China
[c] WHO Collaborating Center for Guideline Implementation and Knowledge Translation, China
[d] School of Information Engineering, Zhengzhou University, Henan Province, China
[e] School of Public Health, Lanzhou University, Lanzhou City, Gansu Province, China
[f] Binzhou Maternal and Child Health Care Hospital, Binzhou City, Shandong Province, China
[g] Evidence-Based Medicine Center, Tianjin University of Traditional Chinese Medicine, Tianjin, China

ARTICLE INFO

Article history:
Received 1 June 2019
Accepted 1 August 2019

Keywords:
Evidence mapping
Diabetes foot
Clinical practice guideline
International review

ABSTRACT

To systematically review clinical practice guidelines (CPGs) on diabetes foot and assess the consistency of recommendations, quality of CPGs and to present an evidence-map for explicating research trends and gaps. We performed a literature search on PubMed, Embase, and Web of Science, guideline databases and websites of diabetes society to include the diabetic CPGs. The basic information, recommendations for the diabetic foot, methodological quality and reporting quality of diabetic CPGs were exacted by the Excel. Four researchers evaluated the methodological and reporting quality of diabetic foot CPGs by AGREE II instrument and RIGHT checklist. R3.5.1 software was used to create all bubble plots. A total of 22 diabetic CPGs were included, eight CPGs were from different professional diabetes societies. Recommendations on diabetic foot complications involve Diabetic foot ulcer (DFU), Charcot neuropathy (CN) and Osteomyelitis (OM). Eight DFU diagnostic systems presented in 22 CPGs. According to the recommendations of diabetic CPGs, the treatment of DFU can be summarized in four major items; six recommendations on CN diagnosis and six recommendations on treatment of CN were consistent among studies. However, there were inconsistencies in three OM diagnosis recommendations and four OM treatment recommendations. Some recommendations in CPGs were not very specific and clear, and hence they were not reliable for OM diagnosis and treatment. Once these inconsistencies are resolved, validated, accurate and effective diagnosis and treatment of diabetes foot will lead to reduced costs and adverse complications. The results of this review add to our knowledge and promote the development of trustworthy CPGs on diabetes.

Contents

Abbreviations: AACE, American Association of Clinical Endocrinologists; ADA, American Diabetes Association; ADFN, Australian Diabetes Foot Network; APMA, American Podiatric Medical Association and the Society for Vascular Medicine; CDA, Canadian Diabetes Association; DFU, Diabetic foot ulcer; CMA, Chinese Medical Association; CN, Charcot neuropathy; CPGs, Clinical practice guideline; ICSI, Institute for Clinical Systems Improvement; IDF, International Diabetes Federation; IWGDF, International Working Group on Foot Infections; IDSA, Infectious Diseases Society of America; JDS, Japan Diabetes Society; KDA, Korean Diabetes Association; MHS, Ministry Of Health Singapore; MH&FWGI, Ministry of Health & Family Welfare Government of India; NHMRC, Australian Government National Health and Medical Research Council; NICE, National Institute for Health and Care Excellence; OM, Osteomyelitis; PDA, Poland Diabetes Association; RNAO, Registered Nurses' Association of Ontario; RSSDI, Research Society for the Study of Diabetes in India; SIGN, Scottish Intercollegiate Guidelines Network; UHMS, Undersea & Hyperbaric Medical Society; WHS, Wound Healing Society.

* Correspondence to: J. Zhang, Evidence-Based Medicine Center, Tianjin University of Traditional Chinese Medicine, No. 312 Anshanxi Street, Nankai District, Tianjin 300193, China.
** Correspondence to: J. Tian, Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, No. 199, Dong gang West Road, Chengguan District, Lanzhou City, Gansu Province, China.
E-mail addresses: zjhtcm@foxmail.com (J. Zhang), tjh996@163.com (J. Tian).
[1] YS and YG contributed equally to this work.

https://doi.org/10.1016/j.metabol.2019.153956
0026-0495/

1. Introduction

The number of people living with diabetic mellitus has been increasing exponentially worldwide [1]. The International Diabetes Federation (IDF) estimated the overall prevalence of diabetes mellitus to be 366 million people in 2011, and predicted a rise to 552 million by 2030 [2]. Diabetic foot is one of the common complications of diabetes, which presents a major challenge to diabetologists, internists as well as surgeons [3], and affects nearly 6% of people with diabetes and is characterized by infection, ulceration, or destruction of tissues of the foot [4,5]. The foot is the most vulnerable part of diabetic patients, it is exposed to frequent trauma and requires sensitive sensory protection, which is often lacking in diabetic patients. The foot, being farthest away from the central nervous system and hemodynamically disadvantageously placed, becomes the common site of complicated lesions [6]. Due to loss of protective sensation (LOPS) and impaired vascular supply, diabetes mellitus can lead to serious foot complications including Diabetic foot ulcer (DFU), Charcot neuropathy (CN) and Osteomyelitis (OM), which remain prevalent and challenging to be treated. It is estimated that 10% of people with diabetes will have a diabetic foot ulcer at some point in their lives. After the first amputation, people with diabetes are twice as likely to have a subsequent amputation as people without diabetes [7]. Mortality rates after diabetic foot ulceration and amputation are high, with up to 70% of people dying within 5 years of after amputation and around 50% dying within 5 years of developing a diabetic foot ulcer. In conclusion, the diabetic foot should be recognized enough that it can lead to very serious consequences, including ulceration, infection, amputation and once these conditions are confirmed, concentrated and correct diabetes foot diagnosis and treatment will likely avoid the costly and adverse complications [5,6].

Clinical practice guidelines (CPGs) of diabetes mellitus can help the doctor to improve the clinical practice [8]. However, different organization's CPGs may give conflicting recommendations [9]. Conflicting recommendations from respected organizations can result in confusion and raise concern about the quality of the CPGs and the underlying evidence [10]. Therefore, we conducted a systematic investigation and critical evaluation of the authoritative CPGs, including the evaluation and collation of the quality and recommendations for the diabetic foot [11,12].

Evidence mapping is an emerging rapid review method that involves systematic search and characterization of existing research on topics of interest, aiming to identify the gap between knowledge and future research needs [13]. In this study, evidence mapping methods were used to present the CPGs about diagnosis, therapeutic strategies and recommendation conflicts for diabetic foot complications.

2. Methods

2.1. Search strategy and selection criteria

CPGs were searched in PubMed, Embase, and Web of Science using medical subject headings and keywords. At the same time, the guideline databases were searched, including National Guidelines Clearinghouse (NGC), National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN) and Guidelines International Network (GIN). The official websites for diabetes society were searched to identify additional CPGs which could have been missed.

CPGs meet the following criteria: ① the 1990 IOM definition of a guideline [14], ② documents developed by a nationally recognized committee, or a medical society that provided recommendations for the diabetes or diabetic foot, ③ the most recent version of publications, ④ containing recommendations on management for the diabetic foot, ⑤ limited to English-language.

2.2. Data extraction

First, two investigators (Y.S. and Y.G.) independently screened the acquired records. Secondly, two reviewers (Y.G. and J.C.) independently extracted the CPGs which met the inclusion criteria. Disagreements were resolved by discussion or by a third reviewer (L.G) if no consensus was reached. A standard form was constructed and CPGs data was extracted, including title, publication time, whether it was a novel publication or update, locations of the development, funding, methods of forming recommendations and the recommendations for the diabetic foot.

2.3. Assessment of guideline quality

Four independent reviewers (Y.S., Y.G., J.C. and L.G.) who were trained to perform CPG appraisals using the Appraisal of Guidelines Research and Evaluation (second version) (AGREE II) and Reporting Items for Practice Guidelines in Healthcare (RIGHT) conducted an independent review of the quality of each eligible CPG. Whenever a disagreement arose, we resolved discordant evaluations by discussion to reach consensus and issued the final verdict. Finally, Intraclass correlation coefficients (ICCs) were calculated to assess inter-rater reliability.

The AGREE II instrument comprises 23 items (each with specific reporting criteria) in six domains, including scope and purpose; stakeholder involvement; rigor of development; clarity of presentation; applicability; and editorial independence [15]. The assessor must respond to 23 questions using a scale of 1 for "strongly disagree" to 7 for "strongly agree" based on examples and instructions described in the AGREE II [15]. The overall assessment included whether the CPG can be recommended for use in clinical practice [16]. The consensus was reached according to the performance of partial item assessment and the global judgment by reviewers. Each CPG was classified as: "strongly recommended" for overall scores >60%, "recommended with modifications" for scores between 30% and 60%, and "not recommended" for scores <30% [17]. The overall assessment was divided into three categories: recommended (R), recommended with modifications (RM), and not recommended (NR) [17].

In addition, the reporting quality of CPGs was appraised by the RIGHT checklist, which consists of 22 items: basic information (items 1 to 4), background (items 5 to 9), evidence (items 10 to 12), recommendations (items 13 to 15), review and quality assurance (items 16 and 17), funding, declaration and management of interests (items 18 and 19), as well as information (items 20 to 22) [18]. Four reviewers (Y.S., Y.G., J.C. and L.G.) independently assessed the adherence of CPGs with the RIGHT checklist, each item is evaluated as "Yes", "No" and "Partial" according to its own reporting content.

2.4. Data synthesis and analysis

2.4.1. Statistical analysis

For each CPG, the AGREE II score for each domain was calculated as a percentage of the maximum possible score and standardized range, and the descriptive values included mean and standard deviation (SD). Reporting quality data were presented as the number of RIGHT checklist items reported in each CPG, as well as the number of CPGs that reported individual RIGHT checklist items.

Intraclass correlation coefficients (ICCs) were calculated to assess inter-rater reliability [19] and the measure of agreement between reviewers. The degree of agreement between 0.01 and 0.20 was deemed minor, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, and 0.81–1.00 very good [20]. SPSS 12.0 software was used for statistical analysis.

2.4.2. Mapping the quality

After computing the scores of CPGs quality by the AGREE II and the number of reported items by the RIGHT checklist. The methodological overall assessment scores and the number of reported items of the included CPGs were ranked by Microsoft Excel 2013 (Microsoft Corp, Redmond, WA, www.microsoft.com).

2.4.3. Summarizing and grading diabetic foot recommendations

Descriptive analyses were conducted to summarize recommendations of the CPGs, including diagnosis and therapeutic strategies of foot complications including DFU, CN and OM. To visualize gaps in recommendations of diabetes or diabetic foot CPGs, all analyses were conducted and bubble plots were generated using R 3.5.1 software to visualize gaps in diabetes CPG recommendations. The number of the bubble was proportional to the number of CPGs and the color depth of the bubble represented the quality of CPGs.

2.5. Strength of recommendation and level of evidence

Information on the strength of the recommendation and the level of evidence was extracted to determine the main gap between evidence and treatment.

3. Results

Fig. 1 shows the detailed results of the CPGs, 22 CPGs [21–42] proved eligible, 10 CPGs [21–23,25,30,31,38–41] were devoted to diabetic foot practices; while the rest focused on practices for diabetes mellitus, and included recommendations for the diabetic foot. Of the 22 eligible CPGs, eight CPGs [27,32–34,36,37,40,42] were from different professional diabetes societies, two CPGs [25,26] were developed by the professional CPG development organizations, two CPGs [39,41] were from government Health and Medical Research and other CPGs [21–24,28–31,35,38] were from medical centers or health systems (Appendix A).

3.1. Analysis and grading of methodological quality and reporting quality of CPGs

The ICC for the assessment between the four reviewers in the study was 0.89 (95% CI: 0.87–0.92). The highest mean score was 75.82 ± 12.97 for scope and purpose, and the main low mean scores was 42.62 ± 19.37 for applicability and 52.84 ± 22.26 for rigor of development. 12 CPGs (54.55%) didn't clearly describe the strengths and limitations of the body of evidence and 17 CPGs (77.27%) poorly provided advice and tools on how the recommendations can be put into practice. The overall assessment of each CPG was showed in Appendix B. Generally, Seven CPGs [22,23,25,26,29,33,36] scored higher on all domains and were classified as recommended for clinical practice, 13 CPGs [21,24,27,28,30–32,34,35,37,38,40,41] were recommended with modifications; and two CPGs [39,42] were not recommended.

The RIGHT checklist contains 22 requirements organized into 7 sections with a total of 35 items. The CPGs with the largest number of reported items using RIGHT checklist was NICE and SIGN (34), followed by CDA (32) and RNAO (31). It was found that among the seven domains of RIGHT checklist, field one (basic information) had the highest reporting rate (86.31%) and field five (review and quality assurance) obtained the lowest reporting rate (40.91%). 13 CPGs (59.09%) just indicated whether the draft guideline underwent independent review, but did not clearly explain the process of review, which lead to the lowest score (Appendix C).

According to the ranking results of two evaluation tools by using Microsoft Excel 2013, the CPGs were divided into three levels and we used three different colored spheres to represent different levels. There were seven high-level CPGs [22,23,25,26,29,33,36] represented by seven green spheres, which were from NICE, SIGN, RNAO, IWGDF, ICSI, CDA and PDA. 13 yellow spheres shown 13 medium-level CPGs [21,24,27,28,30–32,34,35,37,38,40,41], including ADFN, AACE, JDS, IDSA, APMA, WHS, RSSDI, KDA, MHS, ADA, UHMS, IDF and NHMRC. The remaining two low-level CPGs [39,42] shown by red spheres were developed by CMA and MH&FWGI (Fig. 2).

3.2. Level of evidence and strength of recommendation

Of the 22 included CPGs, 16 CPGs [22–31,33–37,41] used 11 grading systems to rate the level of evidence and the strength of recommendation, among which, five CPGs [23,25,28–30] adopted GRADE system, two CPGs [22,26] used SIGN system, and other systems include NHMRC, ADA, KDA, WHS, AACE, JDS, PDA, CDA and MHS. The level of evidence was based on the type of study and the most system defined the strength of recommendation depending on the quality of evidence (Table 1).

3.3. Summarizing and grading recommendations for diabetes foot

The evidence map was created to summarize and describe recommendations of the CPGs for diabetic foot using R 3.5.1 software. A bubble plot can graphically present multiple categorical data on study

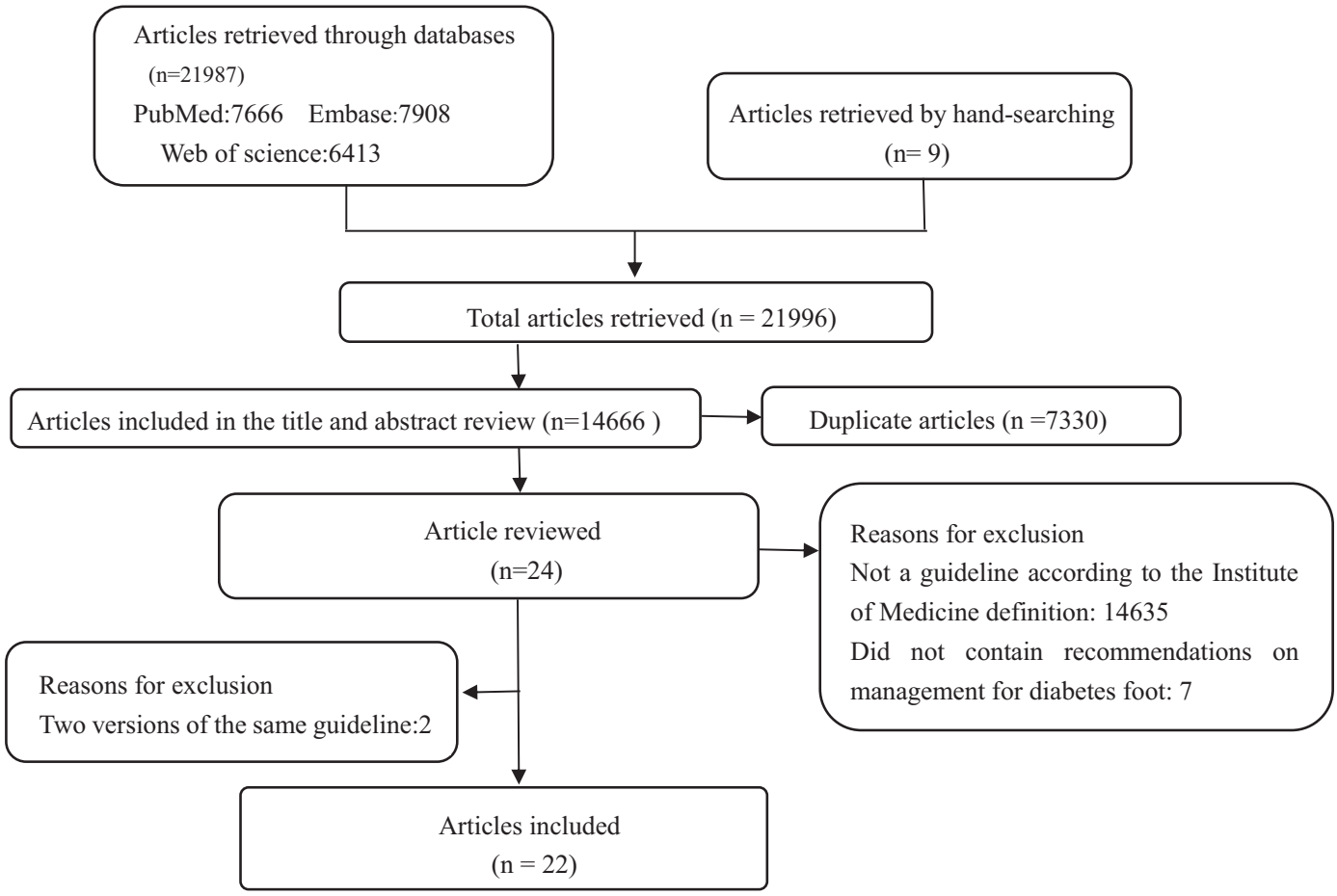

Fig. 1. Summary of evidence search and selection.

characteristics in a single, two-dimension chart by displaying the evidence-map data according to specific, special locations defined by the X-axis and Y-axis, as well as according to the color, shape or size of bubbles [43]. In the bubble chart, the Y-axis represented the strength of the recommendations, which were divided into strong, weak and not mentioned. The X-axis represented different recommendations of the

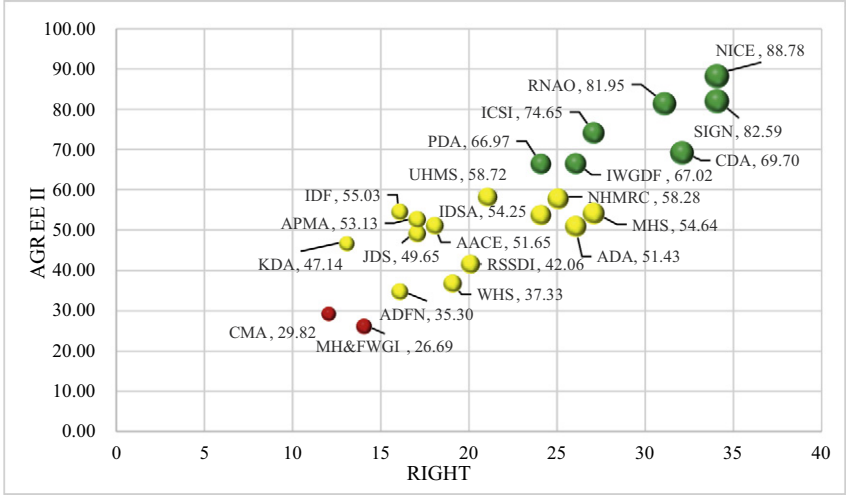

Fig. 2. Grading and analysis of reporting and methodological quality of CPGs ($n = 22$). ADFN = Australian Diabetes Foot Network; RNAO = Registered Nurses' Association of Ontario; IWGDF=International Working Group on Foot Infections; AACE = American Association of Clinical Endocrinologists; NICE = National Institute for Health and Care Excellence; SIGN= Scottish Intercollegiate Guidelines Network; JDS = Japan Diabetes Society; IDSA = Infectious Diseases Society of America; ICSI=Institute for Clinical Systems Improvement; APMA = American Podiatric Medical Association and the Society for Vascular Medicine; WHS=Wound Healing Society; RSSDI = Research Society for the Study of Diabetes in India; CDA = Canadian Diabetes Association; KDA = Korean Diabetes Association; MHS = Ministry Of Health Singapore; PDA = Poland Diabetes Association; ADA = American Diabetes Association; UHMS=Undersea & Hyperbaric Medical Society; MH&FWGI = Ministry of Health & Family Welfare Government of India; IDF=International Diabetes Federation; NHMRC = Australian Government National Health and Medical Research Council; CMA = Chinese Medical Association Legends: Different colors represent different quality of CPGs. Green for high quality CPGs, yellow for middle-level CPGs, and red for low-level CPGs. The size of the sphere represents the number of items reported.

Table 1
Grading systems used in the included CPGs.

Grading system	Codes of evidence and recommendation		Number of guidelines	Guidelines organization
	Level of evidence	Strength of recommendation		
GRADE	A, B, C, D[a]	1, 2[b]	5	IWGDF [23], NICE [25], IDSA [28], ICSI [29], APMA [30]
SIGN	1, 2, 3, 4[a]	A, B, C, D[c]	2	RNAO [22], SIGN [26]
AACE	1, 2, 3, 4[a]	A, B, C, D[d]	1	AACE [24]
JDS	1, 2, 3, 4[a]	A, B[e]	1	JDS [27]
WHS	I, II, III[a]		1	WHS [31]
CDA	1, 2, 3, 4[a]	A, B, C, D[c]	1	CDA [33]
KDA	A, B, C, D, E[a]		1	KDA [34]
MHS	1, 2, 3, 4[a]	A, B, C, D[c]	1	MHS [35]
PDA	A, B, C, D, E[a]		1	PDA [36]
ADA	A, B, C, D, E[a]	A, B, C[c]	1	ADA [37]
NHMRC	I, II, III, IV[a]	A, B, C, D[c]	1	NHMRC [41]

GRADE: Grading of Recommendations Assessment, Development and Evaluation.
SIGN: Scottish Intercollegiate Guidelines Network.
AACE: American Association of Clinical Endocrinologists.
JDS: Japan Diabetes Society.
WHS: Wound Healing Society.
CDA: Canadian Diabetes Association.
KDA: Korean Diabetes Association.
MHS: Ministry of Health Singapore.
PDA: Poland Diabetes Association.
ADA: American Diabetes Association.
NHMRC: Australian Government National Health and Medical Research Council.
[a] The level of evidence is based on the type of study.
[b] The strength of a recommendation reflects the extent to which we can be confident that the composite desirable effects of a management strategy outweigh the composite undesirable effects.
[c] Grade of recommendation depending on the quality of evidence.
[d] Grade of recommendation based on best evidence levels (BELs), subjective factors, and consensus map to recommendation grades.
[e] Grade of recommendation based on the total body of evidence as well as the risk-benefit balance, value, patient preferences, cost, and resources.

CPGs. Bubble color corresponded to the quality of CPGs and the depth of the bubble color represented the three levels of the CPGs.

3.3.1. Diagnosis and therapeutic strategies of DFU

3.3.1.1. CPG recommendations on DFU diagnosis. If the DFU is identified, a thorough assessment of the ulcer should be completed. This is achieved by the following recommendations: Wagner classification system; The size (area, depth), sepsis, arteriopathy, denervation system (SAD) systems; Site, ischemia, neuropathy, bacterial infection and depth (SINBAD) score; International Working Group of Diabetic Foot (IWGDF); Perfusion (ischemia), Extent(area), Depth, Infection, Sensation (neuropathy) (PEDIS) system; University of Texas classification system (TEXAS); wound, ischemia, and foot infection (WIFI); Depth, extent of bacterial colonization, phase of healing and associated etiology (DEPA) scoring system. Eight diagnostic systems were presented in 22 CPGs. Six CPGs [22,24,28,36,38,39] supported the use of the PEDIS system as a DFU classification system and three diagnostic systems were only proposed once, including SAD, SINBAD and DEPA classification system (Table 2).

3.3.1.2. CPG recommendations on DFU treatment. According to Fig. 3, 13 CPGs [22–27,30–34,41,42] contained four major recommendations for DFU treatment as follows. We summarized the treatment therapeutic strategies of recommendations in Appendix D.

Recommendation on DFU treatment (1) Provided wound care with consideration of choice of wound dressings (strong recommendation [25,27,30], weak recommendation [23], and not mentioned the strength of recommendation [22,26,31–33,41,42]);

(2) Multi-disciplinary foot care team/service (strong recommendation [25,27], and not mentioned the strength of recommendation [24,26,33,34,41,42]);

(3) Debridement of wounds should be performed as it improves ulcer healing (strong recommendation [25,30], and not mentioned the strength of recommendation [22,31–33,41,42]);

(4) Redistribute pressure was applied to foot ulcer(s) by the use of offloading devices (strong recommendation [23,25,27,30], and not mentioned the strength of recommendation [22,26,32,33,42]).

3.3.2. Diagnosis and therapeutic approaches of CN

3.3.2.1. CPG recommendations on CN diagnosis. Fig. 4 shows the six recommendations of CN diagnosis, which included six CPGs [24,25,30,33,39,40]. Recommendation summarized in Appendix E.

Recommendations on CN diagnosis (1) Technetium bone scans are generally nonspecific when assisting OM and acute CN (not mentioned the strength of recommendation [24]);

(2) If acute CN is suspected, arrange a weight-bearing X-ray of the affected foot and ankle (strong recommendation [25]);

(3) Plain radiographs have low sensitivity and specificity in differentiating OM from CN changes (not mentioned the strength of recommendation [33]);

(4) If acute CN is suspected, and the X-ray is normal but clinical suspicion still remains, an MRI is considered (strong recommendation [25], not mentioned the strength of recommendation [39,40]);

(5) The risk of MRI to patients is minimal in the differentiation between OM and CN changes (weak recommendation [30], and not mentioned the strength of recommendation [33]);

Table 2
Diabetic foot ulcer classification systems.

Classification system	Year	CPG recommended system	Characteristics	
Wagner [31,33,41]	1981	WHS, CDA, NHMRC	Based on depth or penetration of ulcer and presence gangrene	Gangrene in five grades
SAD [41]	1999	NHMRC	Scored on ulcer size (area, depth), infection, arteriopathy and denervation	Matrix (0, 1, 2, 3) × (A, B, C, D, E)
SINBAD [25]	Unclear	NICE	Scoring based on site, ischemia, neuropathy, bacterial infection, area, depth	A score (ranging from 0 to 6) resulting into a four-risk grade classification
IDSA/IWGDF [23,24,28,38,39]	2012	IWGDF, AACE, IDSA, UHMS, MH&FWGI	Divides ulcer infection into four grades: classification of foot ulcers uninfected, mild moderate and severe infection	Gangrene in four grades
PEDIS [22,24,28,36,38,39]	2003	RNAO, AACE, IDSA, PDA, UHMS, MH&FWGI	Designed specifically to provide a framework for defining ulcer populations in research. Graded according to perfusion, extent, depth, Infection and sensation.	Matrix (1, 2, 3, 4) × (A, B, C, D)
TEXAS [22,24,25,28,31,33]	1998	RNAO, NICE, IDSA, WHS, AACE, CDA	Evaluation of diabetic foot ulcers and gangrene from two aspects of lesion severity and etiology	Matrix (0, 1, 2, 3) × (A, B, C, D)
WIFI [30,38]	2014	APMA, UHMS	Assess tissue loss, ischemia, and foot infection	64-Choice matrix (0, 1, 2, 3) × (0, 1, 2, 3) × (0, 1, 2, 3)
DEPA [41]	2002	NHMRC	Includes the depth of the ulcer (D), the extent of bacterial colonization (E), the phase of ulcer healing (P) and the associated underlying etiology (A)	12-Choice matrix (1, 2, 3) × (D, E, P, A)

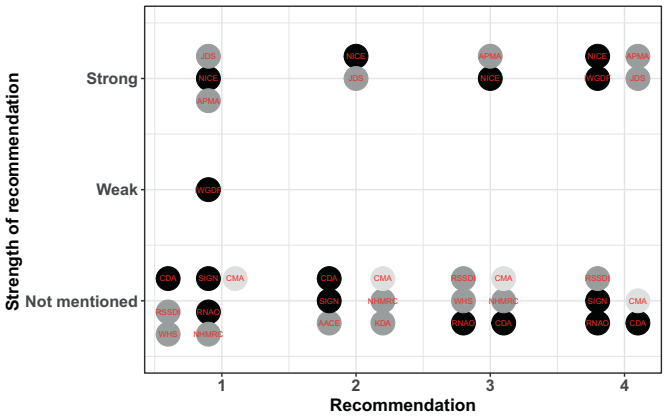

Fig. 3. Evidence map of DFU therapeutic strategies recommendation of CPGs.

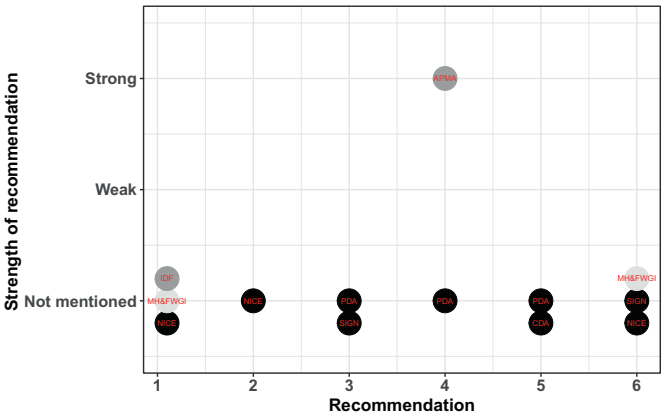

Fig. 5. Evidence map of CN therapeutic strategies recommendation of CPGs.

(6) When examining the foot, there is usually a temperature difference between the affected feet (not mentioned the strength of recommendation [40]).

3.3.2.2. CPG recommendations on CN treatment. Seven CPGs [25,26,30,33,36,39,40] focused on six recommendations of CN treatment in Fig. 5. The summary of recommendations was shown in Appendix E:

Recommendation on CN treatment (1) If suspecting acute CN, the treatment with a non-removable offloading device is offered (not mentioned the strength of recommendation [25,39,40]);

(2) If a non-removable device is not advisable because of the clinical, or the person's circumstances, the treatment with a removable offloading device is considered (not mentioned the strength of recommendation [25]);

(3) Suspected CN of the foot is an emergency and should be referred immediately to the multidisciplinary foot team (not mentioned the strength of recommendation [26,36]);

(4) In high-risk patients with healed CN, wearing specific therapeutic footwear with pressure-relieving insoles to aid in the prevention of new or recurrent DFUs was recommended (strong recommendation [30], and not mentioned the strength of recommendation [36]);

(5) Further studies are necessary to fully evaluate bisphosphonate in the routine treatment of CN (not mentioned the strength of recommendation [33,36]);

(6) Do not offer bisphosphonates to treat acute CN, unless as part of a clinical trial (not mentioned the strength of recommendation [25,26,39]).

3.3.3. Diagnosis and therapeutic strategies of OM

3.3.3.1. CPG recommendations on OM diagnosis. Fig. 6 shows the 11 recommendations of OM diagnosis, which included 13 CPGs [21–25,28–31,36,39–41]. Recommendations were summarized in Appendix F.

Recommendation on OM diagnosis (1) "Probe to bone" test is highly suggestive of OM and inserting a sterile instrument into the ulcer to determine whether bone can be probed at the base (strong recommendation [23,25,28], and not mentioned the strength of recommendation [21,22,24]);

(2) Taking X-ray to the patient's foot to determine the severity of the diabetic foot problem (strong recommendation [25], weak recommendation [30],and not mentioned the strength of recommendation [36]);

(3) If OM is suspected in a person with diabetes but is not confirmed by initial X-ray, consider an MRI to confirm the diagnosis (strong recommendation [25,28,30], and not mentioned the strength of recommendation [21,39]);

(4) Markedly elevated serum inflammatory markers, especially erythrocyte sedimentation rate (ESR) are suggestive of OM in suspected cases (weak recommendation [23], and not mentioned the strength of recommendation [36]);

(5) A definite diagnosis of bone infection usually requires positive results on both histological and microbiological examinations of an aseptically obtained bone sample (strong recommendation [23,28,30], and not mentioned the strength of recommendation [40]);

(6) MRI has emerged as the investigative modality of choice to distinguish OM (strong recommendation [23], and not mentioned the strength of recommendation [41]);

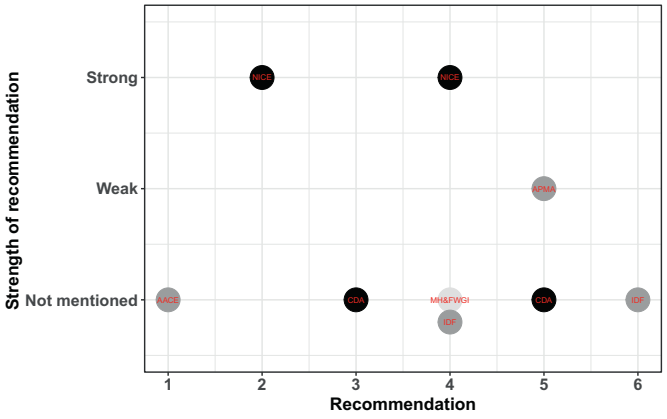

Fig. 4. Evidence map of CN diagnosis recommendation of CPGs.

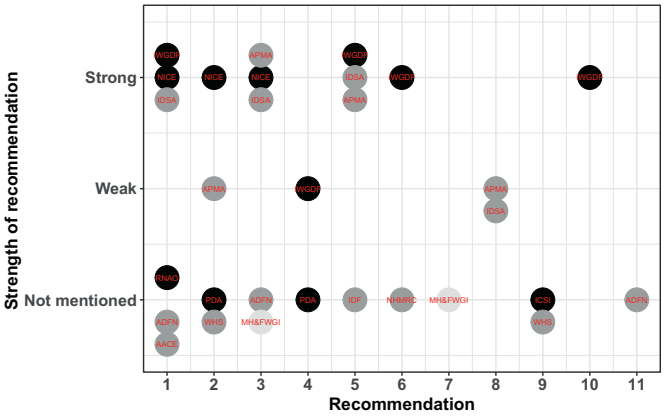

Fig. 6. Evidence map of OM diagnosis recommendation of CPGs.

(7) Tests for serum inflammatory markers are costly and not widely available (not mentioned the strength of recommendation [39]);

(8) When MRI is contraindicated or unavailable, leukocyte or anti granulocyte scan, preferably combined with a bone scan was the best alternative (weak recommendation [28,30]);

(9) Suspected OM, bone biopsy to determine the type of pathogen (not mentioned the strength of recommendation [29,31]);

(10) Avoid using results of soft tissue or sinus tract specimens for selecting antibiotic therapy for OM (strong recommendation [23]).

(11) Bone scans and white cell scans generally lack specificity for diagnosing OM (not mentioned the strength of recommendation [21]).

3.3.3.2. CPG recommendations on OM treatment. There were 11 recommendations for OM treatment included in 11 GPGs [21–23,25,28,31,33,39–42]. The summary of the recommendations was as follows in Fig. 7 and Appendix G.

Recommendation on OM diagnosis (1): Medical management of focal OM with antibiotics or antibiotics combined with limited surgical resection is the main treatment (not mentioned the strength of recommendation [21,41]);

(2) For diabetic foot OM, 6 weeks of antibiotic therapy is required for patients who do not undergo resection of infected bone (not mentioned the strength of recommendation [31]);

(3) Patients who have not undergone bone resection require at least 4–6 weeks of antibiotic treatment (not mentioned the strength of recommendation [33]);

(4) OM is treated by removal of the infected bone, followed by 2–4 weeks of antibiotics (not mentioned the strength of recommendation [42]);

(5) When the affected bone is resected, and residual bone is in the wound, the client will require 4 to 8 weeks of antibiotic therapy based on wound culture results (not mentioned the strength of recommendation [22]);

(6) When the affected bone is resected and residual bone is in the wound, the client will require 6 weeks of antibiotic therapy based on wound culture results (strong recommendation [23,25]);

(7) No more than a week of antibiotic therapy is needed if all infected bone is resected (not mentioned the strength of recommendation [40]);

(8) 2 weeks of antibiotic therapy is needed if all infected bone is resected (not mentioned the strength of recommendation [42]);

(9) When a radical resection leaves no remaining infected tissue, prescribing antibiotic therapy for only a short duration (2–5 days) was suggested (weak recommendation [28], not mentioned the strength of recommendation [39]);

(10) When there is persistent infected or necrotic bone, at least 4 weeks antibiotic treatment was suggested (weak recommendation [28], not mentioned the strength of recommendation [39]);

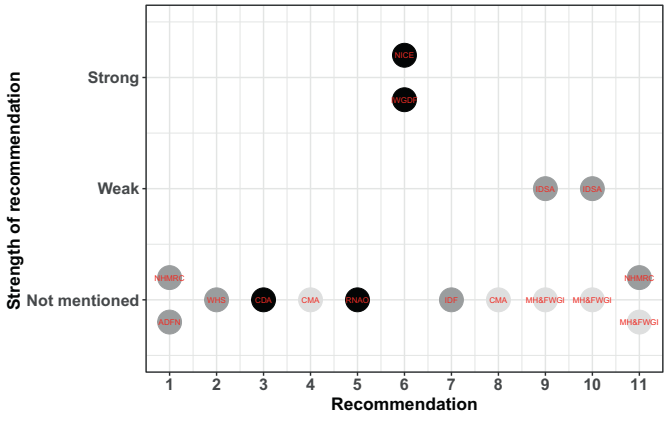

Fig. 7. Evidence map of OM therapeutic strategies recommendation of CPGs.

(11) No available evidence supports the use of any adjunctive therapies, such as hyperbaric oxygen, granulocyte-colony stimulating factor or larvae (not mentioned the strength of recommendation [39,41]);

4. Discussion

A total of 22 CPGs were identified in the current international review of CPGs on diagnosis and treating diabetic foot complications. Based on the results of the CPGs quality evaluation, it was found that the quality of the included CPGs varied. The quality of CPGs [22,23,25,26,29,33,36] developed by RNAO, IWGDF, NICE, SIGN, ICSI, CDA and PDA were relatively high. The diabetic CPGs were analyzed and evaluated to summarize their recommendations using standardized grades as a basis. But we found the level of evidence distribution and the strength of the recommendations varied widely between the different categories of criteria. Different grading systems using various coding systems were used to classify the evidence quality and strength of recommendations in diabetic CPGs, which may confuse and hinder communication between CPGs developer. Therefore, a standardized grading system, such as GRADE should be used to provide clear information on the level of evidence and the strength of recommendation.

Clinical diagnosis and treatments of CPGs were reviewed to establish the challenges that may be encountered when managing diabetes complications, including DFU, CN and OM. However, there were some conflicts in some important organization's CPGs.

For the diagnosis of DFU, many CPGs recommended a series of classification systems. The purpose of the research classification was to enable the categorization of different populations of diabetic patients with a DFU, at a certain time point, according to strict criteria and using terms that are relevant and unambiguous [44]. Each of these classifications systems can be used in clinical practice, but they had not been compared in a large prospective trial. Furthermore, there were some recommendation conflicts, thus CPGs developed by WHS, CDA and NHMRC were proposed Wagner classification system as DFU diagnostic strategy [31,33,41]. However, NICE CPG [25] clearly disregarded the use of the Wagner classification system in assessing the severity of a DFU.

Standard care for DFU management includes offloading of high-pressure areas, wound care, multi-disciplinary foot care team/service, and wound debridement. These recommendations were highly advocated for in the CPGs. The offloading or taking pressure away from the wounded portion of the foot, is paramount for wound healing and redistribute pressure applied to DFUs by the use of offloading devices. Although many CPGs were explicitly proposed, off-loading was universally acceptable in reducing the pressure and strain rate on a DFU. A real-world study showed that only 2.2% of 221,192 visits involving DFU documented offloading, and confirmed that its practice remains underutilized in wound care [45]. An important tenet of DFU care includes regular debridement of the wound which removes the obvious necrotic tissue, excessive bacterial burden, and cellular burden of dead and senescent cells. Maintenance debridement is necessary to keep the appearance and readiness of the wound bed for healing. The health care provider can choose from a number of debridement methods including surgery [31]. Multidisciplinary team-based (MDT) care was reported to improve the treatment outcomes of DFUs [46,47]. A systematic review revealed some positive effects of the MDT on DFUs, namely; amputation rate, the severity of amputation and resource use [48]. With the establishment of multidisciplinary team care, the incidence of amputation is gradually reduced, indicating that multidisciplinary disease team care is effective in preventing DFU [49]. The principal function of a wound dressing is to help achieve an optimal healing environment. Many types of dressings were designed to suit a variety of different needs, such as protecting wounds, encouraging wound healing, and preventing or treating infections. However, there is no sufficient evidence for recommending one specific dressing type over another in CPGs.

CN is a painless and progressive degeneration, which is most notable in the ankle or midfoot joints. Autonomic neuropathy with increased

blood flow, peripheral neuropathy with repeated insensible trauma, leading to the development of CN, remains one of the most challenging late complications of diabetic foot [50,51]. In the acute active stage, the patient typically presents with unilateral-dependent erythema, edema, increased skin temperature, and joint effusion in an insensate foot [52,53]. It is always difficult to distinguish the onset of acute CN from other conditions, as skin infections or deep vein thrombosis can easily be misdiagnosed by clinicians who are less experienced in the diabetic foot. Although plain radiographs are valuable in working towards the diagnosis of CN, they have low sensitivity and specificity in differentiating OM from CN changes, and signs indicative of CN occur as the condition progresses [54,55]. According to the AACE CPG recommendation [24], technetium bone scans were generally nonspecific in assisting in the differentiation between OM and acute CN. However, other advanced NI techniques are able to provide increased specificity making them more valuable to the clinician. One such NI technique is the labelled white blood cell bone scans. This process involves taking a sample of the patient's blood, separating the white blood cells and processing them so they are tagged with a radiotracer, either indium-111 or Tc-99m. Leukocyte imaging with indium-111 or Tc-99m has varying reported sensitivities and specificities for detection of OM ranging from 50% to 100% and 29% to 100% respectively [56,57]. The use of fluorodeoxyglucose (FDG) PET is a NI technique that uses FDG. According to a study [58], the sensitivity and accuracy for diagnosing CN was 100% and 93.8%, whereas those for MRI was 76.9% and 75%, respectively. The diagnosis of acute CN in the early stages is crucial to avoid the detrimental consequences of fractures and foot deformities, as this may stop the progression of the deformity and reduce the occurrence of complications [59,60]. However, if the diagnosis is initially missed, there is always a high risk of amputation [61].

CPGs developed by NICE, MH&FWGI, and IDF suggested that acute CN treatment should be offered with a non-removable offloading device [25,39,40]. When a non-removable device is not advisable because of the clinical, or the person's circumstances, NICE CPG emphasized the treatment with a removable offloading device [25]. A systematic review [62] showed that offloading is a key treatment strategy for the management of DFUs and total contact casts were found to be the gold standard immobilization therapy for acute CN and most effective devices to achieve ulcer healing. It occurs by reducing mechanical stress and edema and redistributes plantar pressure while maintaining the weight of the sole. However, the offloading device is not without complications, CPGs have no specific analysis of costs, and the impact on the quality of life is unclear. CN of the foot is considered to be an emergency and should be immediately referred to the multidisciplinary foot team and prompt immediate referral to a dedicated multi-disciplinary foot care service. PDA CPG [36] support the involvement of a multidisciplinary team including a cardiologist, respiratory medicine specialist, psychologist or psychiatrist, anesthesiologist, and dietician in patient selection. In high-risk patients with healed CN, wearing specific therapeutic footwear with pressure-relieving insoles to aid was recommended by MH&FWGI [39] in prevention of new or recurrent DFUs, but the time for wearing and material of the shoes are not clearly defined; It's worth noting that bisphosphonate therapy was not clear, CDA and PDA CPGs [33,36] emphasized that further studies are necessary to fully evaluate bisphosphonate in the routine treatment of CN. SIGN, NICE and MH&FWGI CPGs [25,26,39] discourages the use of bisphosphonates to in treating acute CN, unless as part of a clinical trial.

OM is the most common diabetic foot infection, with >20% of moderate infections, >50% of serious infections, and a high rate of amputation [63]. The diagnosis of OM often begins with a clinically suspected infection. When OM is associated with soft tissue infection, ulcers near the bony bulge have clinical signs of pain, fever, redness, swelling, and cellulitis. However, a previous study found that the clinical signs associated with bone infection are not very relevant for diagnosis [64]. “Probe to bone” test was strongly recommended by six CPGs from ADFN, RNAO, IWGDF, AACE, NICE, IDSA [21–25,28]. Probe-to-bone (PTB) test, which consists of bone palpation through the ulcer with a sterile blunt probe and can be used as a means of the first screening. If the PTB test is negative and a positive PTB test is poorly specific, taking X-ray is recommended by NICE and PDA CPGs [25,36] to determine the severity of the diabetic foot. However, five CPGs emphasized on the consideration of an MRI to confirm the diagnosis, when OM is suspected not to have been confirmed by the initial X-ray. CPGs [23,41] from IWGDF and NHMRC suggested that MRI has emerged as the investigative modality of choice to distinguish OM. There was no cost analysis for X-ray and MRI; Recommendations from IWGDF and NHMRC CPGs [23,41] suggested, when MRI was contraindicated or unavailable, leukocyte or anti-granulocyte scan, preferably combined with a bone scan could be the best alternative. However, ADFN [21] CPG questioned bone scans and white cell scans, which generally lack specificity for diagnosing OM. When diagnostic suspicion is supplemented with the mentioned above clinical tests, it is advisable to have laboratory tests providing information related to OM [65]. Markedly elevated serum inflammatory markers, especially ESR were suggestive of OM in suspected cases in IWGDF and PDA CPGs recommendations [23,36]. Malabu et al. found that ESR was the hematological parameter which best discriminated between OM and cellulitis [66]. However, according to MH&FWGI CPGs [39], tests for serum inflammatory markers are costly and not widely available. It is crucial to isolate pathogens that cause infection, especially for patients who only use antibiotics. A definite diagnosis of bone infection usually requires positive results on both histological and microbiological examinations of an aseptically obtained bone sample, when the diagnosis is in doubtful, determining the causative pathogen's antibiotic susceptibility is crucial [23,28,30,40]. CPGs from IDSA and APMA [28,30] proposed bone biopsy to determine the type of pathogen and IWGDF CPG [23] supported percutaneous bone sampling as the best alternative. However, there is need to be aware that sampling procedures for bone culture may also affect results, as there may be false positives from positive potential contamination during sampling through ulcers, or false negatives from areas that have not been infected during prior treatment [63].

The CPGs published by ADFN and NHMRC [21,41] defined medical management of focal OM with antibiotics or antibiotics combined with limited surgical resection as the main treatment. There were multiple recommendations on the treatment of OM from different CPGs, but there was no agreement regarding the most appropriate option. Standardization of a single treatment option was far from easy and DFO may have several clinical presentations. Conservative surgery (defined as the removal of infected bone only, without amputation) combined with antibiotic treatment is an attractive option because it may reduce the changes in foot biomechanics and minimize the duration of antibiotic therapy [67]. CDA CPG [33] suggested that patients who have not undergone bone resection requiring at least 4–6 weeks of antibiotic treatment. But in the same situation, CMA [42] CPG defined 6 weeks of antibiotic therapy and there was almost no difference in non-surgical antibiotic treatment time. On the basis of WHS CPG [31], OM was best treated by removal of the infected bone, followed by 2–4 weeks of antibiotics. At the same time, 2 weeks of antibiotic therapy was recommended by MH&FWGI CPG [39]. It was noticed that these two CPGs did not clarify the specifics of the procedure and didn't specify how to treat any remaining infected tissue after antibiotic therapy. When a radical resection leaves no remaining infected tissue, the recommendations on the time of antibiotic therapy were different. IDF CPG [40] suggested that antibiotics should not be administered for more than a week if all the infected bone was resected; However, IDSA and MH&FWGI CPGs [28,39] supported prescribing antibiotic therapy for a short duration (2–5 days). Two CPGs recommended taking out infected bones and then using antibiotics for a period of time and while WHS CPG [31] suggested 2–4 weeks of antibiotics, however, CPG developed by MH&FWGI [39] defined 2 weeks of antibiotic therapy as the most appropriate. The recommended duration of antibiotic therapy depends on the presence of residual tissue infection and prior surgical debridement. According to the RNAO CPG [22], When the affected bone is

removed and the remaining bone was in the wound, 4 to 8 weeks of antibiotic treatment was performed. But IWGDF and NICE CPGs [23,25] strongly recommended 6 weeks. In addition to surgery and anti-infective treatment, there is no available evidence in NHMRC CPG which supports the use of any adjunctive therapies, such as hyperbaric oxygen, granulocyte-colony stimulating factor or larvae.

4.1. Limitations and strengths

This is the first study to analyze the CPGs recommendations on major complications of the diabetic foot. Meanwhile, on the basis of combining two guideline quality evaluation tools, we presented the CPGs recommendations, CPGs quality and strength of recommendation by evidence mapping. The results from this study enriched the development of CPGs recommendations for diabetes and promote the efficient application of CPGs to improve patient prognosis.

Many of the CPGs analyzed in this study did not show an explicit link between the recommendations and the supporting evidence (for example, systematic reviews). At the same time, different grading systems based on various coding systems were used to classify the evidence quality and strength of recommendations in diabetic CPGs. Therefore, it is hard for us to identify the components of the body of evidence relevant to each recommendation and make a further study.

5. Conclusions

To improve the treatment outcomes of DFU, CN and OM, we used the CPGs recommendations to recognize the disease and treat it accordingly. However, the recommendations in some CPGs were not very specific and clear, and they even showed inconsistencies. Application of evidence mapping can facilitate the process of knowledge transfer and reduce research waste [13,43]. The results of this study can be used to promote improvement in the development of trustworthy CPGs on diabetes.

Disclosures

We thank all authors whose data are included in this international review. This study did not receive funding support.

Author contributions

YS and JH-T did the study design. YG and JH-T performed literature search. YS, YG, JC and LG contributed to the data acquisition. YS and HS contributed to data interpretation and statistical analysis. LG and JH-Z supervised and provide mentorship. YS and YT-C wrote the first draft of the report. YS and YG edited the report and all authors contributed to revision of the report. All authors reviewed the manuscript, approved the final draft and agreed to submit it for publication.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.metabol.2019.153956.

Declaration of Competing Interest

No potential conflicts of interest relevant to this article were reported.

Acknowledgments

The authors appreciate Xiaoqing Wang and Nan Yang (Chinese GRADE Center) for their methodological support and assistance with the final editing of the article.

References

[1] Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3:e442.
[2] Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 2011;94:311–21.
[3] Williams DR. Hospital admissions of diabetic patients: information from hospital activity analysis. Diabet Med 1985;2:27–32.
[4] Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis (dagger). Ann Med 2017;49:106–16.
[5] Schaper NC, Apelqvist J, Bakker K. The international consensus and practical guidelines on the management and prevention of the diabetic foot. Curr Diab Rep 2003;3:475–9.
[6] Lavery LA, Ashry HR, van Houtum W, Pugh JA, Harkless LB, Basu S. Variation in the incidence and proportion of diabetes-related amputations in minorities. Diabetes Care 1996;19:48–52.
[7] Gomes JMG, Costa JA, Alfenas RCG. Metabolic endotoxemia and diabetes mellitus: a systematic review. Metabolism 2017;68:133–44.
[8] Chakhtoura MT, Nakhoul N, Akl EA, Mantzoros CS, El Hajj Fuleihan GA. Guidelines on vitamin D replacement in bariatric surgery: identification and systematic appraisal. Metabolism 2016;65(4):586–97.
[9] Ge L, Tian JH, Li YN, Pan JX, Li G, Wei D, et al. Association between prospective registration and overall reporting and methodological quality of systematic reviews: a meta-epidemiological study. J Clin Epidemiol 2018;93:45–55.
[10] Ferket BS, Colkesen EB, Visser JJ, Spronk S, Kraaijenhagen RA, Steyerberg EW, et al. Systematic review of guidelines on cardiovascular risk assessment: which recommendations should clinicians follow for a cardiovascular health check? Arch Intern Med 2010;170:27–40.
[11] Wang X, Zhou Q, Chen Y, Yao L, Wang Q, Wang M, et al. Protocol of reporting items for public versions of guidelines: the Reporting Tool for Practice Guidelines in Health Care-public versions of guidelines. BMJ Open 2019;9:e023147.
[12] Erickson J, Sadeghirad B, Lytvyn L, Slavin J, Johnston BC. The scientific basis of guideline recommendations on sugar intake: a systematic review. Ann Intern Med 2017;166:257–67.
[13] Miake-Lye IM, Hempel S, Shanman R, Shekelle PG. What is an evidence map? A systematic review of published evidence maps and their definitions, methods, and products. Syst Rev 2016;5:28.
[14] Graham R, Miller Wolman D, Greenfield S, et al. Clinical practice guidelines we can trust. Institute of Medicine (US) Committee on Standards for developing trustworthy clinical practice guidelines. Washington (DC): The National Academies Press (US); 2011.
[15] Sanclemente G, Acosta JL, Tamayo ME, Bonfill X, Alonso-Coello P. Clinical practice guidelines for treatment of acne vulgaris: a critical appraisal using the AGREE II instrument. Arch Dermatol Res 2014;306:269–77.
[16] Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ 2010;182:E839–42.
[17] Jiang M, Guan WJ, Fang ZF, Xie YQ, Xie JX, Chen H, et al. A critical review of the quality of cough clinical practice guidelines. Chest 2016;150:777–88.
[18] Chen Y, Yang K, Marusic A, Qaseem A, Meerpohl JJ, Flottorp S, et al. A reporting tool for practice guidelines in health care: the RIGHT statement. Ann Intern Med 2017;166:128–32.
[19] Bartko JJ. The intraclass correlation coefficient as a measure of reliability. Psychol Rep 1966;19:3–11.
[20] Alonso-Coello P, Irfan A, Sola I, Gich I, Delgado-Noguera M, Rigau D, et al. The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. Qual Saf Health Care 2010;19:e58.
[21] van Netten JJ, Lazzarini PA, Armstrong DG, Bus SA, Fitridge R, Harding K, et al. Diabetic Foot Australia guideline on footwear for people with diabetes. J Foot Ankle Res 2018;11:2.
[22] Registered Nurses' Association of Ontario (RNAO) Assessment and management of foot ulcers for people with diabetes second edition; 2013.
[23] Bus SA, Armstrong DG, van Deursen RW, Lewis JE, Caravaggi CF, Cavanagh PR. IWGDF guidance on footwear and offloading interventions to prevent and heal foot ulcers in patients with diabetes. Diabetes Metab Res Rev 2016;32(Suppl. 1):25–36.
[24] Handelsman Y, Bloomgarden ZT, Grunberger G, Umpierrez G, Zimmerman RS, Bailey TS, et al. American Association of Clinical Endocrinologists and American College of Endocrinology - clinical practice guidelines for developing a diabetes mellitus comprehensive care plan - 2015. Endocr Pract 2015;21(Suppl. 1):1–87.
[25] National Institute for Health and Care Excellence (NICE). Diabetic foot problems: prevention and management. London (UK); 2015.
[26] Scottish Intercollegiate Guidelines Networ (SIGN) Management of diabetes a national clinical guideline. Part of NHS quality improvement Scotland; 2010.
[27] Haneda M, Noda M, Origasa H, Noto H, Yabe D, Fujita Y, et al. Japanese clinical practice guideline for diabetes 2016. Diabetol Int 2018;9:1–45.
[28] Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54:e132–73.
[29] Institute for Clinical Systems Improvement (ICSI) Diagnosis and management of type 2 diabetes mellitus in adults; 2014.
[30] Hingorani A, LaMuraglia GM, Henke P, Meissner MH, Loretz L, Zinszer KM, et al. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg 2016;63:3S–21S.
[31] Lavery LA, Davis KE, Berriman SJ, Braun L, Nichols A, Kim PJ, et al. WHS guidelines update: diabetic foot ulcer treatment guidelines. Wound Repair Regen 2016;24:112–26.
[32] Bajaj S. RSSDI clinical practice recommendations for the management of type 2 diabetes mellitus 2017. Int J Diabetes Dev Ctries 2018;38:1–115.
[33] Punthakee Z, Goldenberg R, Katz P. Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. Can J Diabetes 2018;42(Suppl. 1):10–S5.

[34] Korean Diabetes Association (KDA). Guidelines for diabetes, 2015.
[35] Goh SY, Ang SB, Bee YM, Chen YT, Gardner DS, Ho ET, et al. Ministry of health clinical practice guidelines: diabetes mellitus. Singapore Med J 2014;55:334–47.
[36] Polish Diabetes Association (PDA) Guidelines on the management of diabetic patients. A position of diabetes Poland; 2018; 2018.
[37] American Diabetes Association (ADA). Standards of medical care in diabetes; 2017.
[38] Huang ET, Mansouri J, Murad MH, Joseph WS, Strauss MB, Tettelbach W, et al. A clinical practice guideline for the use of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers. Undersea Hyperb Med 2015;42:205–47.
[39] Ministry of Health & Family Welfare Government of India (MH&FWGI). The diabetic foot prevention and management in India; 2016.
[40] Aschner P. New IDF clinical practice recommendations for managing type 2 diabetes in primary care. Diabetes Res Clin Pract 2017;132:169–70.
[41] National Health and Medical Research Council (NHMRC). Prevention, identification and management of foot complications in diabetes. Australia, 2017.
[42] Chinese Medical Association (CMA). Guidelines for the prevention and treatment of type 2 diabetes in China. China; 2017.
[43] Wang DD, Shams-White M, Bright OJ, Parrott JS, Chung M. Creating a literature database of low-calorie sweeteners and health studies: evidence mapping. BMC Med Res Methodol 2016;16(1).
[44] Schaper NC. Diabetic foot ulcer classification system for research purposes: a progress report on criteria for including patients in research studies. Diabetes Metab Res Rev 2004;20(Suppl. 1):S90–5.
[45] Fife CE, Carter MJ, Walker D, Thomson B, Eckert KA. Diabetic foot ulcer off-loading: the gap between evidence and practice. Data from the US Wound Registry. Adv Skin Wound Care 2014;27:310–6.
[46] Armstrong DG, Bharara M, White M, Lepow B, Bhatnagar S, Fisher T, et al. The impact and outcomes of establishing an integrated interdisciplinary surgical team to care for the diabetic foot. Diabetes Metab Res Rev 2012;28:514–8.
[47] Kintiraki E, Goulis DG. Gestational diabetes mellitus: multi-disciplinary treatment approaches. Metabolism 2018;86:91–101.
[48] 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.
[49] Holstein P, Ellitsgaard N, Olsen BB, Ellitsgaard V. Decreasing incidence of major amputations in people with diabetes. Diabetologia 2000;43:844–7.
[50] Emara KM, Ahmed Diab R, Amr Hemida M. Tibio-calcaneal fusion by retrograde intramedullary nailing in charcot neuroarthropathy. Foot (Edinb) 2018;34:6–10.
[51] La Fontaine J, Lavery L, Jude E. Current concepts of charcot foot in diabetic patients. Foot (Edinb) 2016;26:7–14.
[52] Rogers LC, Bevilacqua NJ. The diagnosis of charcot foot. Clin Podiatr Med Surg 2008; 25:43–51.
[53] Baglioni P, Malik M, Okosieme OE. Acute charcot foot. BMJ 2012;344:e1397.
[54] Chantelau E, Poll LW. Evaluation of the diabetic charcot foot by MR imaging or plain radiography-an observational study. Exp Clin Endocrinol Diabetes 2006;114: 428–31.
[55] Ergen FB, Sanverdi SE, Oznur A. Charcot foot in diabetes and an update on imaging. Diabet Foot Ankle 2013;4.
[56] Wang GL, Zhao K, Liu ZF, Dong MJ, Yang SY. A meta-analysis of fluorodeoxyglucose-positron emission tomography versus scintigraphy in the evaluation of suspected osteomyelitis. Nucl Med Commun 2011;32:1134–42.
[57] Short DJ, Zgonis T. Medical imaging in differentiating the diabetic charcot foot from osteomyelitis. Clin Podiatr Med Surg 2017;34:9–14.
[58] Basu S, Chryssikos T, Houseni M, Scot Malay D, Shah J, Zhuang H, et al. Potential role of FDG PET in the setting of diabetic neuro-osteoarthropathy: can it differentiate uncomplicated charcot's neuroarthropathy from osteomyelitis and soft-tissue infection? Nucl Med Commun 2007;28:465–72.
[59] Berli M, Vlachopoulos L, Leupi S, Boni T, Baltin C. Treatment of charcot neuroarthropathy and osteomyelitis of the same foot: a retrospective cohort study. BMC Musculoskelet Disord 2017;18:460.
[60] Pan B, Ge L, Xun YQ, Chen YJ, Gao CY, Han X, et al. Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. Int J Behav Nutr Phys Act 2018;15:72.
[61] Illgner U, Podella M, Rummler M, Wuhr J, Busch HG, Wetz HH. Reconstructive surgery for charcot foot. Long-term 5-year outcome. Orthopade 2009;38:1180–6.
[62] de Oliveira AL, Moore Z. Treatment of the diabetic foot by offloading: a systematic review. J Wound Care 2015;24:560–70.
[63] Lipsky BA. Bone of contention: diagnosing diabetic foot osteomyelitis. Clin Infect Dis 2008;47:528–30.
[64] Peled C, Kraus M, Kaplan D. Diagnosis and treatment of necrotising otitis externa and diabetic foot osteomyelitis - similarities and differences. J Laryngol Otol 2018;132: 775–9.
[65] Alvaro-Afonso FJ, Lazaro-Martinez JL, Aragon-Sanchez J, Garcia-Morales E, Garcia-Alvarez Y, Molines-Barroso RJ. Inter-observer reproducibility of diagnosis of diabetic foot osteomyelitis based on a combination of probe-to-bone test and simple radiography. Diabetes Res Clin Pract 2014;105:e3–5.
[66] Malabu UH, Al-Rubeaan KA, Al-Derewish M. Diabetic foot osteomyelitis: usefulness of erythrocyte sedimentation rate in its diagnosis. West Afr J Med 2007;26:113–6.
[67] Aragon-Sanchez J. Treatment of diabetic foot osteomyelitis: a surgical critique. Int J Low Extrem Wounds 2010;9:37–59.