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REVIEW

Venous Leg Ulcer Clinical Practice Guidelines: What is AGREEd?

Matthew K.H. Tan [a], Rong Luo [a], Sarah Onida [a], Stefano Maccatrozzo [b], Alun H. Davies [a,*]

[a] Department of Surgery and Cancer, Imperial College London, Charing Cross Hospital, London, UK
[b] Istituto Clinico Beato Matteo, Vigevano, Italy

WHAT THIS PAPER ADDS

Using a structured assessment tool, this review objectively assesses the quality of current venous leg ulcer clinical practice guidelines (CPGs) to assist healthcare professionals in choosing a high quality CPG to advise their practice. The authors have also identified shortfalls that can be addressed with the aim of improving future editions of CPGs. This review has identified a number of CPGs that are methodologically sound and recommended for clinical use. It also identifies specific areas for refinement in the other included CPGs, and this information may be used to guide CPG developers in future versions.

Objective: The aim was to evaluate the quality of current venous leg ulcer (VLU) clinical practice guidelines (CPGs) to assist healthcare professionals in choosing an accessible high quality CPG to advise their practice, and to identify areas for improvement in future versions of current CPGs.

Methods: A systematic review of PubMed, Embase, online CPG databases, and reference lists of included CPGs was carried out. Full text CPGs published no earlier than 1998 reporting evidence based recommendations on VLU diagnosis and management in English were included. CPGs that were only available if purchased were excluded. Two reviewers identified eligible CPGs, extracted data, and assessed the quality independently using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. Significant scoring discrepancies were discussed with a third reviewer.

Results: Fourteen eligible CPGs were identified (1999–2016). The majority of CPGs originated from Europe or North America. Overall, there was good inter-reviewer reliability of scores with an intraclass correlation coefficient of 0.986 (95% confidence interval 0.979–0.991). No single CPG achieved the highest score in all six domains. Significant methodological heterogeneity was observed across VLU CPGs; however, consistently, poor performance was noted in domain 5, concerning CPG applicability.

Conclusion: Four CPGs were considered of adequate quality for clinical use. Consolidation of efforts to drive high quality, comprehensive VLU CPGs is necessary to reduce the number of and heterogeneity seen in currently published guidelines. Elements of methodological quality are lacking and a structured approach with use of checklists and CPG creation tools, such as AGREE II or others, may bolster rigour in future VLU CPGs.

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INTRODUCTION

Venous leg ulcers (VLUs) represent a significant clinical, social, and economic healthcare burden. Affecting up to 1% of the population and with the prevalence increasing to >4% in the elderly,[1] they represent a chronic source of pain, discomfort and social embarrassment, and result in negative quality of life effects that are as severe as those of individuals with congestive cardiac failure.[2] This represents only part of the societal cost, with the costs of diagnosing, managing, and treating the condition representing up to 2% of the annual healthcare budget of Western societies, equating to €600–€900 million per annum.[3]

Despite the clear clinical and socioeconomic burden, treatment of VLU has progressed relatively little over the years. A number of conservative and interventional options exist, ranging from compression therapy to medical interventions in the form of topical and systemic agents to surgical intervention.[4] The evidence underlying these interventions is summarised in clinical practice guidelines (CPGs), developed by different guideline committee groups

* Corresponding author. Department of Surgery and Cancer, Imperial College London, Charing Cross Hospital, London W6 8RF, UK.
E-mail address: a.h.davies@imperial.ac.uk (Alun H. Davies).
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for different healthcare professionals involved in VLU care, including nurses, physicians, surgeons, phlebologists, and dermatologists.

Importantly, there exists marked heterogeneity between CPGs, particularly with respect to methodology, evidence grading, recommendation level, topics included, and professionals involved in their creation, as previously summarised by Maccatrozzo *et al*.[5] This can make interpretation of recommendations difficult for those with limited experience of VLU care, and is further complicated by the CPGs tailoring specific recommendations to particular groups of healthcare professionals.

To reduce this heterogeneity, critical appraisal tools may be used to identify shortfalls in current guidelines, assisting guideline development groups in improving future versions. The Appraisal of Guidelines for Research and Evaluation II (AGREE II) is one such instrument that can be used to assess the developmental process and reporting quality of guidelines.[6] This instrument has been validated extensively and is widely used in the assessment of guidelines in other clinical areas.[7–9] It must be noted that this instrument only reports on the methodological rigour of guideline formulation and clarity of presentation, and not on the accuracy of the recommendations included in the CPGs.

Over the last 20 years, multiple VLU evidence based CPGs have been published, with an even larger number of consensus based recommendations developed by various institutions and professional societies; given the number of guidelines available, healthcare professionals are faced with the difficult task of choosing a suitable VLU guideline for their patients. Utilising the AGREE II instrument, this review aims to (i) determine the quality of current VLU CPGs, to assist healthcare professionals in choosing an accessible, high quality guideline to advise their practice; and (ii) identify areas for improvement in future versions of current guidelines.

MATERIALS AND METHODS

Search strategy

A systematic search was performed in accordance with the PRISMA guidelines.[10] PubMed and Embase were searched from 1998 (major changes in the management of VLU occurred from a 1997 systematic review proving compression therapy effectiveness)[11] until 31 December 2017 using the following search strategy: ((((“clinical practice guideline*”) OR “practice guideline*”) OR guideline*) OR recommendation*) AND ((((management) OR diagnosis) OR assessment) OR treatment) AND ((((((“chronic venous disease”) OR “venous ulcer*”) OR “venous leg ulcer*”) OR “leg ulcer*”) OR “chronic venous insufficiency”) OR “chronic wound*”).

To further ensure that all relevant guidelines were included in this review, CPG databases listed on the AGREE Research Trust website were also searched,[12] using the term “venous leg ulcer”. Reference lists of included guidelines were then hand searched to identify relevant guidelines for inclusion.

Two reviewers (M.T., R.L.) performed the guidelines search and reviewed the full guidelines independently to ensure that inclusion criteria were met. Any conflict between reviewers was referred to a third reviewer (S.O.) to reach agreement.

Inclusion and exclusion criteria

Full text guidelines published no earlier than 1998 reporting evidence based recommendations on VLU diagnosis and management in English were included. Guidelines based on expert consensus, guideline summaries, or guidelines that were only available if purchased were excluded.

AGREE II assessment

Two reviewers (M.T., R.L.) independently assessed the included guidelines, rating them from 1 (lowest quality) to 7 (highest quality) on each statement in the six domains described in the AGREE II instrument (Table 1). Scores were then summed for each of the six domains and scaled to determine the quality score for each guideline. To determine the quality score for each guideline, the raw total was then scaled as a percentage of the maximum possible score for that domain by using the following equation: [Obtained score − Minimum possible score/Maximum possible score − Minimum possible score] ×100. All assessment and scaling of scores were performed according to the guidance provided in the user manual available from the AGREE Research Trust website.[12]

Inter-reviewer reliability was calculated using a two way mixed model to determine intraclass correlation coefficients (ICCs). An overall guideline assessment scaled score of ≥80% was considered of adequate quality to recommend use in daily clinical practice.

All statistical analysis was performed using SPSS Statistics v. 24 (IBM, Armonk, NY, USA).

RESULTS

Selected guidelines

The literature search identified 1566 articles, from which 13 guidelines were identified.[4,13–25] Two were excluded as they were updates of earlier guidelines and used the same methodology.[24,25] Two were found on CPG databases,[26,27] and one was found by searching the reference lists of included guidelines.[28] Therefore, a total of 14 guidelines were included (Fig. 1).

The earliest and latest guidelines were published in 1999 and 2016, respectively. Guideline development groups included a variety of healthcare professionals, with surgeons, nurses, general practitioners, and dermatologists included among their ranks. The majority of guidelines originated from Europe ($n = 8$ [57.1%])[13,16,17,19,21–23,26] or North America ($n = 4$ [28.6%]).[4,14,18,28] Only one guideline was created by an international development group.[20] Other guideline characteristics are summarised in Table S1 (Supplementary Material).

Table 1. Domains and statements included in the AGREE II instrument

Domain	Statements
1 — Scope and Purpose	1. The overall objective(s) of the guideline is (are) specifically described. 2. The health question(s) covered by the guideline is (are) specifically described. 3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.
2 — Stakeholder Involvement	4. The guideline development group includes individuals from all relevant professional groups. 5. The views and preferences of the target population (patients, public, etc.) have been sought. 6. The target users of the guideline are clearly defined.
3 — Rigour of Development	7. Systematic methods were used to search for evidence. 8. The criteria for selecting the evidence are clearly described. 9. The strengths and limitations of the body of evidence are clearly described. 10. The methods for formulating the recommendations are clearly described. 11. The health benefits, side effects, and risks have been considered in formulating the recommendations. 12. There is an explicit link between the recommendations and the supporting evidence. 13. The guideline has been externally reviewed by experts prior to its publication. 14. A procedure for updating the guideline is provided.
4 — Clarity of Presentation	15. The recommendations are specific and unambiguous. 16. The different options for management of the condition or health issue are clearly presented. 17. Key recommendations are easily identifiable.
5 — Applicability	18. The guideline describes facilitators and barriers to its application. 19. The guideline provides advice and/or tools on how the recommendations can be put into practice. 20. The potential resource implications of applying the recommendations have been considered. 21. The guideline presents monitoring and/or auditing criteria.
6 — Editorial Independence	22. The views of the funding body have not influenced the content of the guideline. 23. Competing interests of guideline development group members have been recorded and addressed.
Overall Assessment	1. Rate the overall quality of this guideline. 2. I would recommend this guideline for use. (Yes, Yes with modifications, No)

AGREE = Appraisal of Guidelines for Research and Evaluation.

Quality scores

There were no obvious disagreements on scores between the first two reviewers and no referral of any scores to the third reviewer. On statistical analysis, there was good inter-reviewer reliability of scores, with an overall ICC of 0.986 (95% confidence interval [CI] 0.979—0.990). Individual domain ICCs were all >0.80. These are summarised in Table 2.

Raw domain scores and scaled quality scores for domains 1—6 are illustrated in Fig. S1 (Supplementary Material) and summarised in Table 3. There was significant heterogeneity of scores between guidelines, especially in domains 1, 2, 3, 5 and overall quality. This is illustrated in Fig. 2, with large interquartile ranges seen in these domains. Less heterogeneity was seen in domains 4 and 6.

Additionally, while high quality guidelines consistently achieved high scores in most or all domains, and vice versa for low quality guidelines, there was no clear relationship between inter-domain performance of individual guidelines. All included guidelines also showcased shortfalls in specific domains.

Performance of guidelines in the different domains is discussed in further detail below.

Guideline performance in individual domains

Domain 1 focuses on the intended goals of the guideline, the health questions that are considered in its development, and the target patient population. There was a wide range of scores in this domain, with good inter-reviewer reliability (see Table 2).

CPGs scoring highly clearly listed specific health questions of interest and whether the developed recommendations would be applicable to their specific community or healthcare setting. This second point was considered particularly well in ANZ 2011,[27] which considered whether the CPG would apply to minority groups living in Australia or New Zealand. Failure to address the statements in this domain or discuss these areas in specific terms resulted in lower scores.

Domain 2 considers whether the guideline was developed by relevant stakeholders and if the developers considered the perspectives of the intended users. Scores for this domain ranged from 5.6% to 97.2% and there was good inter-reviewer agreement of scores.

Relevant stakeholders included members of the multidisciplinary team, such as nursing, surgical and medical team members. CPGs that scored highly made efforts to

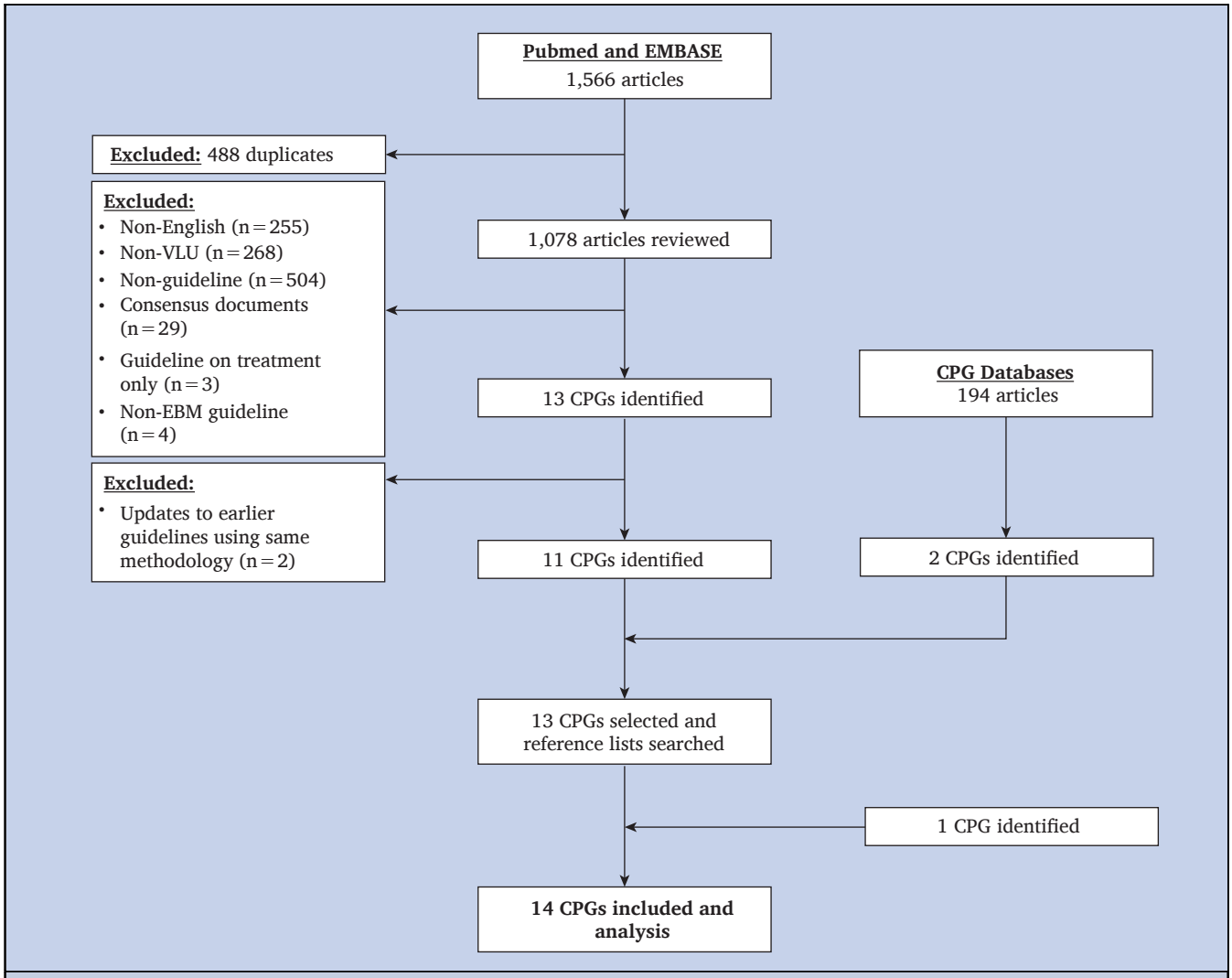

Figure 1. PRISMA diagram showing the clinical practice guideline (CPG) selection process. VLU = venous leg ulcer; EBM = evidence based medicine.

gain opinions from patients through consumer representatives[27] or public consultations.[26]

Domain 3 appraises the rigour of the literature search methodology, procedure followed in the formulation of recommendations and if there was a process to update the guideline. This domain had a highest ICC at 0.973 (95% CI 0.918—0.991; Table 2).

Good evidence based CPGs reported a comprehensive systematic literature review, clear eligibility and exclusion criteria, validated methods for critical appraisal and unbiased peer review. SIGN 2010 performed exceptionally in this aspect, with a separate independent editorial team reviewing the review comments and assessing whether these opinions had been adequately addressed by the CPG development group.[26]

Domain 4 considers the organisation of the guideline, discussing language and format in the appraisal questions. On average, guidelines performed best in this domain with less variability (Table 2). ICC values demonstrated an acceptable level of agreement between reviewers for a more subjective domain.

CPGs performing well had standardised formatting with clear signposting or boxes indicating different sections. These CPGs were also more likely to provide summaries of evidence and key recommendations, allowing users to

Table 2. Individual domain intraclass correlation of reviewer ratings across all guidelines

Domain	ICC	95% CI	
		Lower bound	Upper bound
1	0.953	0.861	0.985
2	0.946	0.841	0.982
3	0.973	0.918	0.991
4	0.876	0.660	0.959
5	0.971	0.913	0.991
6	0.953	0.862	0.985
Overall quality	0.817	0.552	0.937

ICC = intraclass correlation; CI = confidence interval.

Table 3. Individual reviewer, raw total, and scaled quality scores for individual domains of guidelines

Guideline	Domain (min. score, max. score)						
	1 (min. 3, max. 21)	2 (min. 3, max. 21)	3 (min. 8, max. 56)	4 (min. 3, max. 21)	5 (min. 4, max. 28)	6 (min. 2, max. 14)	Overall (min. 1, max. 7)
The Management of Patients with Venous Leg Ulcers (RCN, 1999)[22]							
Reviewer 1	19	21	46	20	16	6	7
Reviewer 2	19	20	48	16	14	6	6
Raw total	38	41	94	36	30	12	13
Scaled (%)	88.9	97.2	81.3	83.3	45.8	33.3	91.7
Guidelines for the Diagnosis and Therapy of the Vein and Lymphatic Disorders (ICP, 2005)[13]							
Reviewer 1	4	7	15	12	7	7	2
Reviewer 2	3	9	15	13	8	7	3
Raw total	7	16	30	25	15	14	5
Scaled (%)	2.8	27.8	14.6	52.8	14.6	41.7	25.0
Managing Venous Leg Ulcers (Excluding Dressings) (HAS, 2006)[16]							
Reviewer 1	15	15	28	18	6	6	5
Reviewer 2	17	17	24	20	7	5	4
Raw total	32	32	52	38	13	11	9
Scaled (%)	72.2	72.2	37.5	88.9	10.4	29.2	58.3
Guidelines for the Treatment of Venous Ulcers (WHS, 2006)[20]							
Reviewer 1	7	6	22	17	4	5	3
Reviewer 2	4	9	23	15	4	5	4
Raw total	11	15	45	32	8	10	7
Scaled (%)	13.9	25.0	30.2	72.2	0.0	25.0	41.7
Assessment and Management of Venous Leg Ulcers (RNAO, 2007)[28]							
Reviewer 1	12	17	44	18	25	8	6
Reviewer 2	13	18	45	17	22	8	7
Raw total	25	35	89	35	47	16	13
Scaled (%)	52.8	80.6	76.0	80.6	81.3	50.0	91.7
Guidelines for Diagnosis and Therapy of Venous Ulcers (DGP, 2008)[17]							
Reviewer 1	4	5	28	8	14	5	3
Reviewer 2	4	3	24	9	17	4	4
Raw total	8	8	52	17	31	9	7
Scaled (%)	5.6	5.6	37.5	30.6	47.9	20.8	41.7
Management of Chronic Venous Leg Ulcers (SIGN, 2010)[26]							
Reviewer 1	19	19	51	20	24	11	7
Reviewer 2	18	18	50	20	26	10	7
Raw total	37	37	101	40	50	21	14
Scaled (%)	86.1	86.1	88.54	94.4	87.5	70.8	100.0
Australian and New Zealand Clinical Practice Guidelines for Prevention and Management of Venous Leg Ulcers (ANZ, 2011)[27]							
Reviewer 1	20	18	46	18	10	9	7
Reviewer 2	19	20	48	19	11	8	6
Raw total	39	38	94	37	21	17	13
Scaled (%)	91.7	88.9	81.3	86.1	27.1	54.2	91.7
Evidence based Recommendations for the Use of NPWT in Chronic Wounds (TVS, 2011)[21]							
Reviewer 1	16	8	43	15	6	14	6
Reviewer 2	20	9	45	14	4	14	5
Raw total	36	17	88	29	10	28	11
Scaled (%)	83.3	30.6	75.0	63.9	4.2	100.0	75.0
The Care of Patients with Varicose Veins and Associated Chronic Venous Diseases: Clinical Practice Guidelines of the Society for Vascular Surgery and the American Venous Forum (SVS/AVF, 2011)[18]							
Reviewer 1	14	5	16	15	4	6	3
Reviewer 2	16	3	17	13	5	7	3
Raw total	30	8	33	28	9	13	6
Scaled (%)	66.7	5.6	17.7	61.1	2.1	37.5	33.3
The Association for the Advancement of Wound Care Venous and Pressure Ulcer Guidelines (AAWC, 2014)[14]							
Reviewer 1	6	8	30	16	14	6	4
Reviewer 2	7	10	28	14	14	5	5
Raw total	13	18	58	30	28	11	9
Scaled (%)	19.4	33.3	43.8	66.7	41.7	29.2	58.3
Management of Venous Leg Ulcers: Clinical Practice Guidelines of the Society for Vascular Surgery and the American Venous Forum (SVS/AVF, 2014)[4]							
Reviewer 1	16	11	26	20	6	5	5
Reviewer 2	16	10	29	18	8	7	6

Continued

Table 3-*continued*

Guideline	Domain (min. score, max. score)						
	1 (min. 3, max. 21)	2 (min. 3, max. 21)	3 (min. 8, max. 56)	4 (min. 3, max. 21)	5 (min. 4, max. 28)	6 (min. 2, max. 14)	Overall (min. 1, max. 7)
Raw total	32	21	55	38	14	12	11
Scaled (%)	72.2	41.7	40.6	88.9	12.5	33.3	75.0
Management of Chronic Venous Disease (ESVS, 2015)[23]							
Reviewer 1	13	6	34	21	4	13	5
Reviewer 2	15	9	37	20	4	12	6
Raw total	28	15	71	41	8	25	11
Scaled (%)	61.1	25.0	57.3	97.2	0.0	87.5	75.0
Evidence based (S3) Guidelines for Diagnostics and Treatment of Venous Leg Ulcers (EDF, 2016)[19]							
Reviewer 1	14	9	30	15	4	6	4
Reviewer 2	16	7	36	16	4	6	5
Raw total	30	16	66	31	8	12	9
Scaled (%)	66.7	27.8	52.1	69.4	0.0	33.3	58.3
Average scaled scores							
Mean ± SD (%)	56.0 ± 32.0	46.2 ± 31.9	52.4 ± 24.6	74.0 ± 18.3	26.8 ± 29.9	46.1 ± 24.1	65.5 ± 24.0

Cells with scaled scores ≤25%, 26–50%, 51–75%, and ≥76% are highlighted with red, orange, yellow, and green, respectively. Bolded scaled scores reflect the lowest and highest scores in each domain. RCN = Royal College of Nursing; ICP = Italian College of Phlebology; HAS = Haute Autorité de Santé; WHS = Wound Healing Society; RNAO = Registered Nurses' Association of Ontario; DGP = Deutsche Gesellschaft für Phlebologie; SIGN = Scottish Intercollegiate Guidelines Network; ANZ = Australia and New Zealand; TVS = Tissue Viability Society; SVS/AVF = Society for Vascular Surgery; AVF = American Venous Forum; AAWC = Association for the Advancement of Wound Care; ESVS = European Society for Vascular Surgery; EDF = European Dermatology Forum.

quickly identify recommendations relevant to their clinical scenario. Poorly formatted CPGs made recommendations difficult to differentiate from the body of text.

Domain 5 asks if guideline developers take into account translation of recommendations into clinical practice. Questions pertained to barriers and facilitators to implementation, uptake improvement strategies, and resource needs for implementation. The majority of guidelines did poorly in this domain, with both reviewers consistently awarding low scores to most guidelines (Table 2), with a mean score of 26.9 ± 29.9% (Table 3). Scaled quality scores ranged from 0.0% to 87.5%, with 12 guidelines scoring <50% and eight scoring <30%.

CPGs who addressed this domain developed strategies to identify barriers to actual clinical practice, including pilot implementation[22] and auditing outcomes.[26] However, most CPGs failed to address this.

Domain 6 concerns bias introduced by competing interests, both at an individual (declaration of interests of development group members) and institutional level (in-

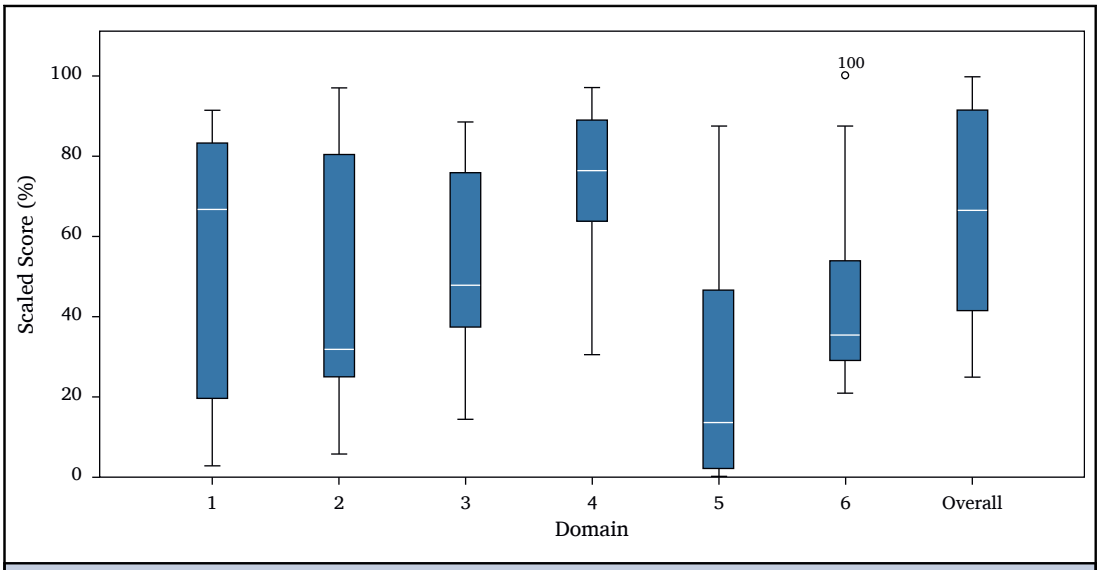

Figure 2. Boxplot showcasing distribution of scaled scores in each domain.

fluence of funding bodies). The mean score in this domain was 46.1 ± 24.1%, with scaled quality scores ranging from 20.8% to 100.0%. ICC was 0.953 (95% CI 0.856–0.983). There was one outlier scoring 100%.[21,23]

CPGs that had obvious statements regarding guideline development and group members' competing interests and funding agencies scored highly. Two CPGs did not explicitly outline these competing interests but stated that a copy of all member declarations were on file and available on request.[23,26]

Overall guideline assessment contains two components, the overall quality rating of the guideline and whether the assessor would recommend its use in clinical practice.

Four guidelines were rated as ≥ 80% and of adequate quality for recommendation for clinical practice.[22,26,28] Only one guideline achieved 100%.[26] Notably, the ICC was lowest in this assessment, suggesting that reviewers may have weighted domains differently when considering the overall quality of the guideline.

DISCUSSION

In this analysis, no single guideline achieved the highest scores in all domains. The majority of CPGs showed merit, but also contained shortcomings that should be addressed. This should not be viewed as a criticism, but rather as constructive feedback to improve future versions of these CPGs. While scores from the nursing CPGs were generally better than average,[22,28] no other single characteristic of the CPG development groups appeared to have an influence on the scores. Conversely, a strong performance in domain 1 set the tone for scores in the other domains, a clear objective, specific health questions and patient population understandably helped frame further detailed methodology. However, it must be noted that there was no statistical inter-domain correlation within each CPG. This reminds authors that the rigour in each area of methodological quality is unrelated. Independent efforts have to be made to address all issues identified.

The highest overall score in this series was achieved by the SIGN guideline,[26] which was formulated using a standard methodology outlined in the SIGN 50 manual,[29] available from the SIGN website.[30] This manual recommends that guidelines follow the quality standards as outlined in the AGREE II instrument. Clearly, this adds an element of bias in the spirit of this review, but, conversely, this represents an opportunity for future guideline development. The six domains outlined in the AGREE II instrument may be used as a framework to improve the rigour of guideline development and reporting standards across all future iterations of current guidelines.

The European Society for Vascular Surgery guidelines,[23] to which the authors have previously contributed, demonstrated high scores for domains 4 and 6, relating to clarity of presentation and editorial independence, respectively, whereas lower scores were achieved for domains relating to stakeholder (and therefore multidisciplinary) involvement and guideline applicability. This is unsurprising considering that the guidance is developed by a vascular surgery society and therefore the committee comprises of vascular surgeons. Future updates may want to consider the AGREE principles, including participation of multidisciplinary team members and discussing the practicalities of applying the recommendations to different healthcare systems in Europe.

Methodological heterogeneity was clearly seen in this set of VLU CPGs. It is not possible to pinpoint exactly how this heterogeneity arises, especially for certain domains when guidelines failed to include any relevant information. As a whole, CPG development groups adopted varying methods from inception to implementation. For example, various evidence based methods were used to formulate recommendations—the majority of CPGs based recommendations on evidence from pre-existing high level evidence and previous CPGs,[4,13,16–21,23,26,27] one from an independently performed systematic review and/or meta-analysis in addition to available literature,[22] whereas two were "guideline of guidelines", only updating recommendations from previous guidelines using more recent literature.[14,28] The focus of CPGs also differed slightly, with nurse led CPG development groups focusing on primary care and on details regarding compression bandaging, whereas clinician led CPG development groups focused on secondary care and other medical or surgical interventions.

Yet another point of concern arises when considering that the majority of guidelines performed poorly in domain 5, which concerns CPG applicability. This has been identified as a recurring issue with different CPGs, not only in venous disease but in other clinical areas.[7–9] This suggests that VLU CPGs fail to identify obstacles to their implementation or neglect to provide methods to improve their uptake. It is frustrating when good evidence based recommendations fail to be implemented owing to resource limitations, restricting their clinical impact. It is imperative that future CPG developers consider approaches to ease uptake of recommendations.

This analysis is not without limitations. Firstly, assessment was only performed by two reviewers. As the AGREE II suggests the tool be implemented with up to four reviewers, additional reviewers would represent more opinions in the methodological assessment. Secondly, this analysis does not include evaluation of the validity of the recommendations themselves. Further appraisal of the recommendations included in each CPG is required in future work, using a validated instrument such as the GRADE system.[31]

Despite the limitations stated above, given the number of CPGs assessed and the observed heterogeneity between them, there clearly needs to be a consolidation of efforts to drive high quality, comprehensive guideline development in VLU diagnosis and management. Without experts agreeing on a specific framework for future CPG development, it is clear that these heterogeneous methods will only continue. However, it is not the authors' intention to advocate use of the AGREE II instrument in guiding CPG reporting. Other

frameworks, such as the G-I-N Standards,[32] or Guidelines 2.0,[33] are widely available with very similar checklist statements to those in the AGREE II domains; the international community must come to a consensus before future versions of current CPGs are produced.

As such, using the AGREE II domains as a guide, the CPG development group should include expert members from all related medical professions and also involve patients, be it through direct input on proposed recommendations or indirectly through patient opinion surveys or literature search for evidence detailing patient views. The CPG development group should define target users, then seek to answer specific key questions related to VLU diagnosis and management through systematic review of available evidence. The draft recommendations should reach consensus internationally through established methods such as the modified Delphi technique, following which barriers to their application must be identified through approaches such as economic cost based analysis or pilot testing. Efforts must then be made to overcome these obstacles through resource management or CPG aids like pocket flowcharts or algorithms.

CONCLUSION

The complexity of VLU diagnosis and management is reflected in the variety of evidence based CPGs available for the healthcare professional's use. Slight shifts in focus between VLU CPGs reflect the expert domain of the CPG development group members, but the recommendations are consistent and soundly based in literature, where available. Where evidence is lacking, these expert members are key to ascertaining and eliminating potential bias before reaching the consensus recommendations seen in all the guidelines.

As such, methodological quality of a guideline is important. This analysis has shown that for VLU CPGs, elements of methodology are lacking in each CPG. The want of rigour provides opportunities to introduce bias, preventing sound recommendations or consensus statements from being created. A structured approach underlies an organised outcome, with clear rigour giving clinicians confidence in the validity of the document for use in their clinical practice.

While four CPGs in this analysis were considered of adequate quality for clinician use in daily practice, consolidation of efforts to drive high quality, comprehensive VLU CPG development is required. In this article, the authors used the AGREE II instrument to identify shortfalls in current VLU CPGs. This instrument, together with other checklists, may also be used to design future CPGs and should be part of the arsenal of every future CPG development.

CONFLICT OF INTEREST

None.

FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2018.08.043.

REFERENCES

1 Lal BK. Venous ulcers of the lower extremity: definition, epidemiology, and economic and social burdens. *Semin Vasc Surg* 2015;**28**:3–5.
2 Carradice D. Superficial venous insufficiency from the infernal to the endothermal. *Ann R Coll Surg Engl* 2014;**96**:5–10.
3 Rabe E, Pannier F. Societal costs of chronic venous disease in CEAP C4, C5, C6 disease. *Phlebology* 2010;**25**:64–7.
4 O'Donnell Jr TF, Passman MA, Marston WA, Ennis WJ, Dalsing M, Kistner RL, et al. Management of venous leg ulcers: clinical practice guidelines of the society for vascular surgery (R) and the American venous Forum. *J Vasc Surg* 2014;**60**:3S–59S.
5 Maccatrozzo S, Onida S, Davies AH. Guidelines on venous ulceration: a mess. *Phlebology* 2017;**32**:369–70.
6 Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. Development of the AGREE II, part 2: assessment of validity of items and tools to support application. *Can Med Assoc J* 2010;**182**:E472–8.
7 Sabharwal S, Patel NK, Gauher S, Holloway I, Athansiou T. High methodologic quality but poor applicability: assessment of the AAOS guidelines using the AGREE II instrument. *Clin Orthop Relat Res* 2014;**472**:1982–8.
8 Sabharwal S, Patel V, Nijjer SS, Kirresh A, Darzi A, Chambers JC, et al. Guidelines in cardiac clinical practice: evaluation of their methodological quality using the AGREE II instrument. *J R Soc Med* 2013;**106**:315–22.
9 Werner Rn, Marinović B, Rosumeck S, Strohal R, Haering Ns, Weberschock T, et al. The quality of European dermatological guidelines: critical appraisal of the quality of EDF guidelines using the AGREE II instrument. *J Eur Acad Dermatol Venereol* 2016;**30**:395–403.
10 Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009;**62**:e1–34.
11 Fletcher A, Cullum N, Sheldon TA. A systematic review of compression treatment for venous leg ulcers. *Br Med J* 1997;**315**:576–80.
12 *Where Can I Find a Practice Guidelines? AGREE Enterprise Website.* 2018. updated 2018. Available at: https://www.agreetrust.org [Accessed 25 July 2018].
13 Agus GB, Allegra C, Antignani PL, Arpaia G, Bianchini G, Bonadeo P, et al. Guidelines for the diagnosis and therapy of the vein and lymphatic disorders. *Int Angiol* 2005;**24**:107–68.
14 Bolton LL, Girolami S, Corbett L, van Rijswijk L. The Association for the Advancement of Wound Care (AAWC) venous and pressure ulcer guidelines. *Ostomy Wound Manage* 2014;**60**:24–66.
15 Burrows C, Miller R, Townsend D, Bellefontaine R, Mackean G, Orsted HL, et al. Best practice recommendations for the prevention and treatment of venous leg ulcers: update 2006. *Adv Skin Wound Care* 2007;**20**:611–21.
16 Autorité de Santé Haute. [Management of leg ulcers of predominantly venous origin (dressing excluded)]. *J Mal Vasc* 2007;**32**:100–11.
17 Gallenkemper G. Guidelines for diagnosis and therapy of venous ulcers (version 8 2008). *Phlebologie* 2008;**37**:308–29.
18 Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Gloviczki ML, et al. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg* 2011;**53**:2S–48S.
19 Neumann HA, Cornu-Thenard A, Junger M, Mosti G, Munte K, Partsch H, et al. Evidence-based (S3) guidelines for diagnostics

and treatment of venous leg ulcers. *J Eur Acad Dermatol Venereol* 2016;**30**:1843–75.
20 Robson MC, Cooper DM, Aslam R, Gould LJ, Harding KG, Margolis DJ, et al. Guidelines for the treatment of venous ulcers. *Wound Repair Regen* 2006;**14**:649–62.
21 Vig S, Dowsett C, Berg L, Caravaggi C, Rome P, Birke-Sorensen H, et al. Evidence-based recommendations for the use of negative pressure wound therapy in chronic wounds: steps towards an international consensus. *J Tissue Viability* 2011;**20**(suppl. 1):S1–18.
22 Williams C. The management of patients with venous leg ulcers: new guidelines. *Br J Nurs* 1999;**8**:489.
23 Wittens C, Davies AH, Baekgaard N, Broholm R, Cavezzi A, Chastanet S, et al. Editor's choice – management of chronic venous disease: clinical practice guidelines of the European society for vascular surgery (ESVS). *Eur J Vasc Endovasc Surg* 2015;**49**:678–737.
24 Collins LG, Seraj S. Diagnosis and treatment of venous ulcers. *Am Fam Physician* 2010;**81**:989–96.
25 Couch KS, Corbett L, Gould L, Girolami S, Bolton L. The International Consolidated Venous Ulcer Guideline Update 2015: process improvement, evidence analysis, and future goals. *Ostomy Wound Manage* 2017;**63**:42–6.
26 SIGN Network. *SIGN guideline 120: management of chronic venous leg ulcers*. Available at: https://www.sign.ac.uk/sign-120-management-of-chronic-venous-leg-ulcers.html. [Accessed 25 July 2018].
27 Angel D, Barker J, Blanchfield D, Carville K, Haesler E, Hillier S, et al. *Australian and New Zealand clinical practice guideline for prevention and management of venous leg ulcers*. Available at: http://www.woundsaustralia.com.au/publications/2011_awma_vlug.pdf. [Accessed 25 July 2018].
28 Virani T, Santos J, McConnell H. *Assessment and management of venous leg ulcers. Nursing best practice guideline: shaping the future of nursing*. Available at: https://rnao.ca/sites/rnao-ca/files/Assessment_and_Management_of_Venous_Leg_Ulcers.pdf. [Accessed 25 July 2018].
29 Scottish Intercollegiate Guidelines Network. *SIGN 50: a guideline developer's handbook. Edinburgh (Scotland): NHS Quality Improvement Scotland (NHS QIS)*. Available at: https://www.sign.ac.uk/assets/sign50_2011.pdf. [Accessed 25 July 2018].
30 Scottish Intercollegiate Guidelines Network. *Scottish Intercollegiate Guidelines Network (SIGN)*. Available at: http://sign.ac.uk/. [Accessed 25 July 2018].
31 Kavanagh BP. The GRADE system for rating clinical guidelines. *PLOS Med* 2009;**6**. e1000094.
32 Qaseem A. Guidelines international network: toward international standards for clinical practice guidelines. *Ann Intern Med* 2012;**156**:525.
33 Schünemann HJ, Wiercioch W, Etxeandia I, Falavigna M, Santesso N, Mustafa R, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. *Can Med Assoc J* 2014;**186**:E123–42.