

The quality of guidelines in non-pharmacological prevention and management of chemotherapy-induced neuropathy: A review

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Abstract

Chemotherapy-induced peripheral neuropathy is a common adverse effect occurring in patients undergoing neurotoxic chemotherapy. However, there is no FDA-approved treatment option for it. Given the importance of clinical practice guidelines in this area, this study aimed to determine the methodological quality of extant CIPN guidelines. The study was done as part of the adaptation process of CIPN related CPGs at Isfahan University of Medical Sciences, Iran. A systematic search of published CPGs about chemotherapy-induced CIPN in which the AGREE II instrument was applied for appraising CPGs of CIPN was performed. In general, amongst all of the AGREE II Instrument's domains in the evaluated CPGs, the clarity of presentation and stakeholder involvement domains took favorable scores; and other domains obtained unfavorable and relatively favorable scores. The quality of cancer therapy-induced neuropathy CPGs needs to be improved and designing high-quality CPGs must be considered.

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Introduction

Worldwide, the numbers of cancer survivors have increased significantly. Most of them experience treatment-related persistence toxicities. For example, chemotherapy-induced peripheral neuropathy (CIPN)¹ is a common adverse effect and occurs in 90% of patients undergoing neurotoxic chemotherapy. Given the increase in the survival rate of cancer patients due to new more effective and advanced treatments, symptom management including CIPN has become more troublesome.²

CIPN is a toxic neuropathy that is caused by direct damage to the nervous system by a chemotherapy agent.³ It is an unpleasant sensory pain and sensation experience that can have a serious impact on quality of life, general health, psychological well-being and social and economic welfare of the individual.⁴ This is a serious and dose-restricting side effect, and there is no approved FDA treatment option for it.⁵

Clinical practice guidelines (CPGs) are systematically developed statements for decision making on clinical practice used around the world to improve the quality of healthcare.^{6,7} They can cover all aspects of care, prevention, and self-care.⁸ Also, these CPGs explain the implementation stages of clinical care and prevent non-standard clinical practices⁹ and are valuable instruments for cancer patients care.¹⁰ But the variety of the applied ways for designing CPGs among different clinical care settings and their quality are worrying.^{6,7} Given that CPGs are an important component of clinical practice, the quality of CPGs will affect health care quality.¹¹ On the other hand, existent CPGs could be appraised and adapted for local conditions through an active, systematic and collaborative process.¹² Therefore, in the adaptation process of CPGs, it is necessary to know which CPGs have desirable qualities, because the main purpose of the guideline adaptation is the using of extant CPGs' benefits for designing high quality adapted guidelines.¹³

We found by literature review that Font-Gonzalez *et al.* showed only about one-third of the well-known CPGs were found to be of good quality.¹⁴ Other studies found the quality of CPGs needed to be improved.¹⁵⁻¹⁸ The quality of CPGs was defined as: *Ensuring that the potential biases for the development of the guideline are properly addressed and that the recommendations are valid and are practically feasible.*^{19,20} For this reason, the CPGs must have specific qualitative indexes. These indicators are defined and validated by the AGREE Collaboration.²¹ This instrument has been validated and approved by the World Health Organization and is considered by many organizations to be a standard tool in the assessment of the Guidelines.²² The objective of the AGREE II Instrument is to prepare a framework for appraising the quality of the guidelines; provide a methodological plan for the development

of the guidelines; and to know what recommendations and how to report them on the CPGs.^{19,20} It is helpful for health care providers who want to appraise the quality of CPGs before using their recommendations.⁶ Deng *et al.* assessed the quality of peripheral neuropathy guidelines with different causes and interventions, and included 16 CPGs in their study.²³ However, our study is a step of the guideline adaptation about CIPN for our own nursing practice. We focused on CPGs, which had non-pharmacological interventions for CIPN. This study aimed to determine the methodological quality of extant CIPN guidelines.

Method of research

The study was done as part of the adaptation process of CIPN related CPGs in Isfahan University of Medical Sciences, Iran. A systematic search of published CPGs about chemotherapy-induced CIPN in which the AGREE II Instrument was applied for appraising CPGs of CIPN was performed. The AGREE II Instrument contains 6 domains and subcategories as 23 items.⁶

Selection criteria

Inclusion criteria: i) The CPG has been presented as a *guideline*; ii) adults aged ≥ 18 years old are the target population; iii) neuropathy has been induced by cancer therapy; iv) the guideline is in the English language; v) the CPG had recommendations about CIPN; vi) related institutions, communities, societies, associations, cancer care groups which developed the CPG were mentioned.

Exclusion criteria: systematic reviews, clinical pathways, protocols, editorial, instructional booklets, patients' guides, books, and narrative reviews were excluded.

Search strategy

We conducted a systematic search for finding the guidelines of the databases and sites as follows: NCCN (National Comprehensive Cancer Network), NGC (National Guideline Clearinghouse), NICE (National Institute for Clinical Excellence), SIGN (Scottish Intercollegiate Guidelines Network), CCO (Cancer Care Ontario), G-IN (<http://www.g-i-n.net/>), ONS (Oncology Nursing Society), NHSC (<http://www.health.gov.au>), Science Direct, Cochrane Library, Scopus, ProQuest, PubMed, Google Scholar, Google, Yahoo, CINAHL (Cumulative Index to Nursing and Allied Health Literature) and the following mentioned sites:

<http://www.health.govt.nz/> <http://www.cancerview.ca/> <http://www.esmo.org/> <http://www.guideline.gov/> <http://www.health.govt.nz/> <http://www.rch.org.au/> <http://www.worldgastroenterology.org/> <http://www.cancercare.mb.ca/> <http://bestpractice.bmj.com> to find eligible guidelines published from observation time until January 2018. The search strategy was done by applying these keywords in the English language: neuropathy OR peripheral neuropathy AND cancer OR chemotherapy OR cancer therapy AND recommendations OR guideline and/or combinations of these keywords were searched. After finding relevant documents, our research team screened their titles, abstracts and full text based on the eligibility criteria.

Quality appraisal of CPGs

After selecting CPGs (Table 1), five appraisers evaluated independently the screened CPGs by AGREE II Instrument (updated version in 2013).⁶ The AGREE II Instrument comprises six domains and 23 items. Six domains are *scope and purpose* (3 items), *stakeholder involvement* (3 items), *rigor of development* (8 items), *clarity of presentation* (3 items), *applicability* (4 items), and *editorial independence* (2 items). Appraisers scored each item from 1 (strongly disagree or lacking information) to 7 (strongly agree or the quality of reporting is exceptional). The scores between 2 to 6 indicates the reporting of the item have not completely criteria.^{6,15,24-26} The overall assessment section of CPGs (3-recommended, 2-recommended with modifications, 1-not recommended) was scored independently by each reviewer. The final score of each domain was the summation of appraisers' scores, and the maximum possible score and the difference between the maximum and minimum possible scores for each domain were determined.²⁷ The significant differences between the appraisers' scores were resolved by revision, then by discussion and consensus, but the minor differences were ignored. Each of the six domains was scored as a percentage separately, and calculated by following formula: $\text{Obtained score} - \text{Minimum possible score} / \text{Maximum possible score} - \text{Minimum possible score}$.^{23,28} E.g. in domain 1 (scope and purpose), Maximum possible score = 7 (strongly agree) \times 3 (items) \times 5 (appraisers) = 105; and Minimum possible score = 1 (strongly disagree) \times 3 (items) \times 5 (appraisers) = 15; were calculated (Table 2).^{6,15}

Given we conducted this study as a part of the adaptation

Table 1. Summary and characteristics of clinical practice guidelines on cancer therapy-induced neuropathy.

Guideline title	Date released	Country or region	Institute	Update	Type of guideline	Focus of guideline	Funding	Size of complete guideline
Neuropathic pain - pharmacological management	2010	UK	NICE clinical guideline 173	(1)2013 (2)2014 (3)2017	Evidence-based guideline	To improve quality of life for people with conditions such as neuralgia, shingles, and diabetic neuropathy by reducing pain and promoting increased participation in all aspects of daily living	Not disclose	138 pp
Peripheral neuropathy	2012	Europe	European Oncology Nursing Society	-	Adapted guideline	Improving symptom management in cancer care through evidence-based practice	European Oncology Nursing Society	18 pp
Neuropathic pain guideline	2010	UK	GMMMG	(1)2013 (2)2014 (3)2015	Adapted guideline	To promote the rational use of analgesics, and associated adjuvant treatment, so that neuropathic pain is optimally managed in a patient	Not disclose	17 pp

process for our own practice, for the clear recognition of the potential useful CPGs about CIPN, we determined the ranking of the methodological quality of CPGs as follows: the quality of CPGs was appraised according to the percentage score of each domain. If a guideline has more than five domains scored 60%, it is strongly recommended; If a guideline has more than four domains scored 30% and at least one domain scored >60%, it is weakly recommended; and if a guideline has more than three domains scored <30%, it is not recommended.²⁹ Also, we determined satisfactory quality for any domain of CPGs, median scores under 30% (unfavorable), median scores between 30-60% (relatively favorable), and above 60% (favorable).

Results

Study selection

A total of 87 relevant documents were found, which were screened by the research team. Three CPGs were included and were determined for adaptation (Figure 1). Then five appraisers evaluated these three CPGs using the AGREE II Instrument. One of the three CPGs was evidence-based and another two CPGs were the adapted CPGs.

Guideline 1 was strongly recommended and guidelines 2 and 3 were weakly recommended. The evaluated CPGs obtained the

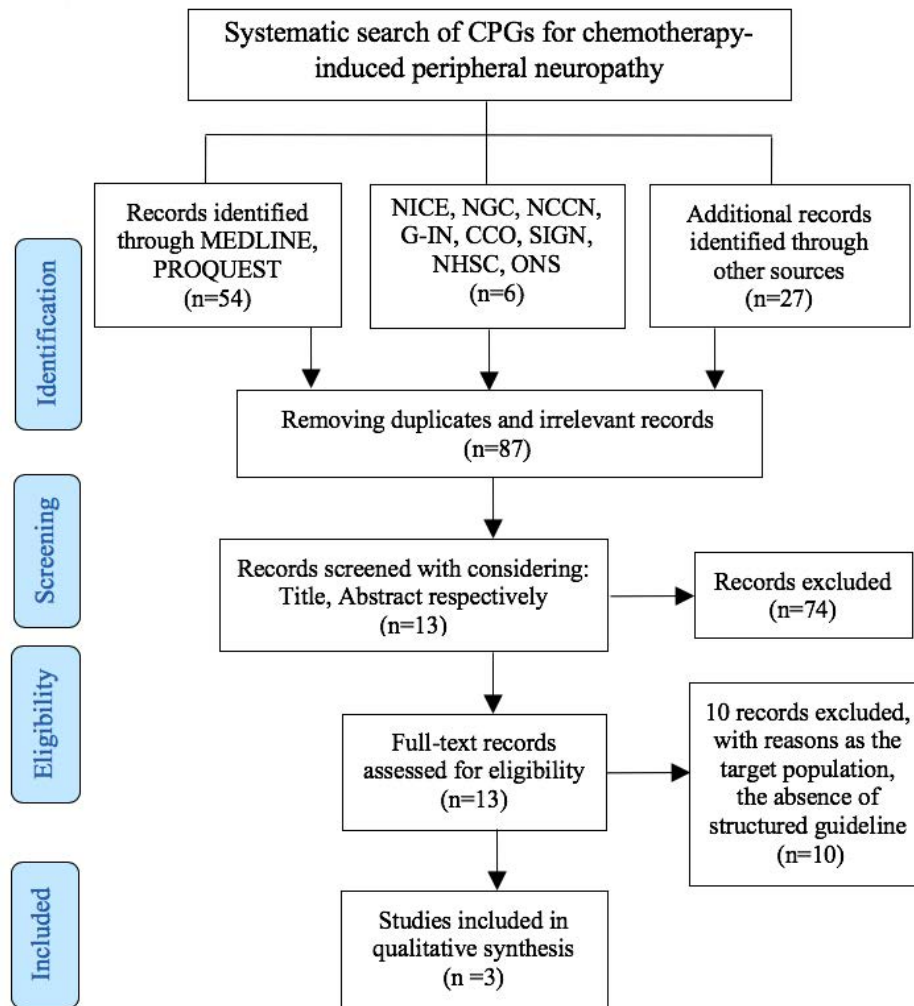


Figure 1. Flowchart of selecting included clinical practice guidelines.

Table 2. Individual AGREE II domain results for each cancer therapy-induced neuropathy guideline.

Guideline title	Scope and purpose	Stakeholder involvement	Rigour of development	Clarity of presentation	Applicability	Editorial independence	Overall assessment	Recommendation
Neuropathic pain - pharmacological management	88.9%	73.3%	60%	86.6%	60%	51.7%	85	Strongly recommended
Peripheral neuropathy	55.5%	63.3%	41.7%	94.4%	49.2%	45%	58	Weakly recommended
Neuropathic pain guideline	51.1%	26.6%	33.3%	85.5%	37.5%	11.6%	50	Weakly recommended
Median domain score	55.5%	63.3%	41.7%	86.6%	49.2%	45%	58	-

highest score in the clarity of presentation domain and the lowest score in the rigor of development domain. None of them discussed the application of the implementation resources of the guideline. Guideline 1 obtained a higher score than other guidelines. The overall results of the AGREE II Instrument's domains descending respectively as follows: *clarity of presentation* (median score, 86.6%), *stakeholder involvement* (median score, 63.3%), *scope and purpose* (median score, 55.5%), *applicability* (median score, 49.2%), *editorial independence* (median score, 45%), *rigor of development* (median score, 41.7%), and *overall assessment* (58%).

In general, amongst all of the AGREE II Instrument's domains, in evaluated CPGs, clarity of presentation, stakeholder involvement domains were given favorable scores and other domains obtained unfavorable and relatively favorable scores.

Discussion

This study indicates the methodological quality of existing CPGs about CIPN from different countries and websites and suggested the quality assessment of existing CPGs of CIPN by AGREE II Instrument.

The scope and purpose domain is related to the overall aim, the target population, and the specific healthcare questions (items 1-3).⁶ The present study indicated that the scores of this domain for the 3 assessed guidelines was relatively favorable (median score, 55.5%). In the study of Sabharwal *et al.* the scope and purpose domain had the highest score (median score, 95%) in comparing to other domains of AGREE II Instrument.³⁰ But in our study, the obtained highest score was in the clarity of presentation (median score, 86.6%). Clarity of presentation is concerned with the language, structure, and framework of the guideline and emphasizes clarity, specificity, and unambiguous recommendations (items 15-17).^{6,31} The study of Birken *et al.* and Deng *et al.* showed that assessed guidelines obtained the highest score in this domain.^{16,23} Also, in the study of Sabharwal *et al.* another domain taking high scores was clarity of presentation (median score, 92%) as appraisers found guidelines providing clear recommendations were easily identifiable.³⁰

In stakeholders' involvement domain, it was assessed whether a professional group is presented, patients' preference and perspective have been searched, and intended users of guideline clearly has been defined (items 4-6).³² In the present study, the stakeholder involvement domain had a higher score than other domains except for clarity of presentation (median score, 63.3%). The study of Sabharwal *et al.* showed the stakeholder involvement domain (median score, 83%) obtained a favorable score and after 3 domains: scope and purpose, rigor of development and clarity of presentation, had a higher score than other domains.³⁰ Applicability domain focuses on potential barriers and facilitators for implementing guidelines, strategies for promoting, and implications of resources for using the guideline (items 18-21).⁶ In the present study, applicability (median score, 49.2%) took a relatively favorable score. In 3 studies of Sabharwal *et al.*, Xie *et al.* and Deng *et al.*, this domain obtained the lowest score amongst all domains of the AGREE II Instrument and in other studies, the applicability domain took a weak score among the 6 domains of AGREE II Instrument.^{17,23,26,30,32,33}

The rigor of development is the core of the methodology of guidelines and continued search processes of evidence, grading, briefing and formulating of recommendations (items 7-14).³² The present study showed the rigor of development domain (median score, 41.7%) was in relatively favorable condition and at the pres-

ent study, we found this domain scored the lowest. The findings of the study of Cranney *et al.* showed that consistency with the methodological quality of current osteoporosis CPGs was low, practically none of CPGs cover dissemination subjects, and only a few guidelines were judged as acceptable for use in their current format.³⁴ Moreover, other studies found that most of the CPGs had serious methodological defects.^{17,35}

The domain of editorial independence focuses on the investment of issues and conflict of interest for all of the involvement members (items 22-23).³² The median scores were not at a favorable level (median score, 45%). Two other studies showed that almost all of the assessed CPGs were evaluated as weak in the domain of editorial independence.^{17,26} Given that the conflict of interest is the most common source of bias in guideline development.³⁶

The overall quality assessment in the present study, scored (median score, 58%) which has had a relatively favorable level by appraisers and it necessitates undertaking modification and promoting the quality of CPGs. The Pottings study showed that it is necessary to improve the methodological quality of guidelines if they were applied in clinical practice.³⁵ The results of Briken, *et al.* indicated that the quality of survivorship of CPGs was weak.¹⁶ In addition, the overall recommendation domain is related to rating overall quality of guidelines and whether the guideline is recommended for use in clinical practice.⁶ In the present study, guideline number 1 scored the highest and was strongly recommended. Several studies have shown a variation to the recommendation of CPGs.^{16,17,30,32,33,35}

Conclusions

It was concluded in this study that the quality of cancer therapy-induced neuropathy CPGs must be improved and the designing high-quality CPGs should be noticed. Incorporating the process of applying resources and monitoring and standardization of the implementation of the CPGs needs to be improved. Therefore, conducting studies to recognise barriers and facilitators of guideline implementation are necessary.

Implications for practice

Enhancing the methodological quality of CPGs for the prevention and treatment of chemotherapy induced neuropathy is important.

Ethical considerations

The present study is a part of a Ph.D. thesis, with the confirmation of the Vice-Chancellor in Research Affairs at Isfahan university of medical sciences. (Code: 395651).

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