A review of quality assessment of the methodology used in guidelines and systematic reviews on oral mucositis

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ABSTRACT

Aims and objectives. The objective of this study was to identify and to assess the quality of evidence-based guidelines and systematic reviews we used in the case of oral mucositis, to apply general quality criteria for the prevention and treatment of oral mucositis in patients receiving chemotherapy, radiotherapy or both.

Design. Systematic review.

Methods. Literature searches were carried out in several electronic databases and websites.

Publications were included if they concerned oral mucositis involving adults treated for cancer and had been published after 1 January 2000. As far as systematic reviews were concerned, the article had to report a search strategy, if the search was minimally conducted in the database PubMed or Medline and the articles included in the review were subjected to some kind of methodological assessment.

The Appraisal of Guidelines for Research and Education (AGREE) instrument was used to assess the quality of the guidelines and the Overview Quality
Assessment Questionnaire (OQAQ) was used for the quality of systematic reviews.

Results. Thirty-one articles met the inclusion criteria of which 11 were guidelines and 20 were systematic reviews. Nine of the 11 guidelines did not explicitly describe how they identified, selected and summarised the available evidence. Reviews suffered from lack of clarity, for instance, in performing a thorough literature search. The quality varied among the different guidelines and reviews.

Conclusion. Most guidelines and systematic reviews had serious methodological flaws.

Relevance to clinical practice. There is a need to improve the methodological quality of guidelines and systematic reviews for the prevention and treatment of oral mucositis if they are to be used in clinical practice.

INTRODUCTION

Clinical guidelines are an important tool to provide effective and efficient care. They are 'systematically developed statements to assist practitioner decisions about appropriate healthcare for specific clinical circumstances' (Field & Lohr 1990). To ensure high quality, the guidelines should be based on the best available scientific evidence (Verkerk et al. 2006).

Existing guidelines and protocols seem mostly based on tradition, subjective observation and incomplete evidence. This results in uncertainty among nurses about which advice or treatment is the best for their patients. The development of an evidence-based guideline is essential for those taking care of patients. The development of such guidelines may promote uniformity of care both within a centre, as well as between centres and potentially increase the quality of care provided to patients. Clinicians use a variety of guidelines and protocols. These documents vary in the degree of detail and the evidence upon which these guidelines and protocols are based is unknown. Systematic reviews can aid in guideline development because they involve searching for, selecting, critically appraising and summarising the results of primary research. The more rigorous the review methods used and the higher the quality of the primary research that is synthesised, the more evidence-based the practice guideline is likely to be (Cook et al. 1997).

In recent years, the number of available clinical practice guidelines has rapidly increased. This recent increase in the production of clinical practice guidelines has been accompanied by growing concern about the variations in guideline recommendations and quality. In fact, several studies suggested that many existing guidelines are of poor quality (Burgers & van Everdingen 2004, Raine et al. 2004). To see whether these concerns about the quality of existing guidelines and systematic reviews are justified, we undertook a study to examine the quality of guidelines and systematic reviews using guidelines and systematic reviews developed for the prevention and treatment of oral mucositis.

Oral mucositis is a burdensome and potentially dangerous side-effect of many anti-cancer therapies that include chemotherapeutic agents or ionising radiation (Rubenstein et al. 2004). Oral mucositis plays a significant role in the physical and psychosocial aspects of patients undergoing cancer therapy and presents a larger problem than is currently recognised from a public health perspective.

Incidence as well as severity may vary from patient to patient and the likelihood of developing mucositis is dependent upon the cancer treatment. As the primary advocates for patients, nurses are central to recognising, preventing and managing oral mucositis to ameliorate its debilitating effects on patients. Nurses have three primary responsibilities in managing oral mucositis:

1 effective assessment and monitoring of the oral cavity as well as symptoms;
2 disease management focussing on ensuring that appropriate intervention is available to patients
3 patient education (Stone et al. 2005).
A potential mechanism for improving outcomes in patients with oral mucositis would be to ensure that those patients are receiving evidence-based care.

Aims

The primary objective of the current study is to identify and assess the quality of available guidelines and systematic reviews for the prevention and treatment of oral mucositis. Rather than focussing on their content, we critically reviewed the methods employed and documented in writing the reviews and guidelines.

MATERIALS AND METHODS

Definitions

A systematic review uses a predefined, explicit methodology. The methods used include steps to minimise bias in all parts of the process: identifying relevant studies, selecting them for inclusion, and collecting and combining their data. Studies should be sought regardless of their results (The Cochrane Collaboration 2007). Guidelines are systematically developed statements to assist clinician and patient decisions about appropriate healthcare-specific clinical circumstances (Field & Lohr 1990).

Search strategy

To identify the guidelines focussed on prevention and treatment of oral mucositis, the websites of the main international institutions involved with the prevention and treatment of cancer were explored as recommended by various authors (Graham et al. 2000a, 2002, Craig 2002, Cox et al. 2004, Mistiaen 2004, van Everdingen et al. 2006). Guidelines on the prevention and treatment of oral mucositis published from 2000–May 2006 were identified and downloaded. In addition, four computerised databases: PubMed, CINAHL (Cumulative Index of Nursing and Allied Health Literature), PiCarta (OCLC PICA system consisting of the Dutch Central Catalogue and Online Content) and INVERT (Index of the Dutch nursing journal literature) were searched. All relevant English and Dutch websites were searched with the keywords: guidelines, stomatitis, mucositis, oral care and mouth care.

Relevant systematic reviews were identified by searching 8 electronic databases of articles published from 1 January 2000–31 May 2006. These were: PubMed, Embase, CINAHL, PiCarta, INVERT, DARE, Cochrane Database of Systematic Reviews and Psychinfo. This publication time frame guaranteed data from systematic reviews conducted in the recent past. Where one review clearly updated a previous review, only the most recent publication was used. To identify additional relevant studies, the Science Citation Index was used to search for studies that cited located relevant papers.

Search strategies for electronic databases were developed sequentially, starting with PubMed, as this was expected to yield the highest number of relevant papers. The review used a search strategy with Medical Subject Headings and text words (Table 1). Similar search strategies were created for the other databases. There were no language restrictions applied.

[TABLE 1]

Selection criteria

Two reviewers (CP and PM) independently conducted screening of relevant studies for inclusion. Disagreements were resolved by discussion with a third member of the team (TvA). The first level of screening using titles, publication years and abstracts, was to include papers only if they concerned oral mucositis involving adults treated for cancer and had been published after 1 January 2000 and were probably a guideline or a systematic review.

The second level of screening was based on full text, with the same criteria as described above. As far as systematic reviews are concerned, publications were only included, according to our definition of a systematic review, if: in the article reported (1) the search strategy was described (2) a search was minimally conducted in the database PubMed or Medline and (3) the articles included in the review were subjected to some kind of methodological assessment.

Instruments to assess quality

Quality of guidelines was assessed with the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument as it is an internationally recognised, rigorously developed and is a validated instrument that compares well with other instruments designed for this purpose (Graham et al. 2000b). Three reviewers (CP, PM and TvA) rated each guideline. The AGREE instrument instructs the reviewer to make a judgement as to the quality of the guideline, taking each of the appraisal criteria into consideration. The 23-item AGREE instrument is divided into the following six domains (see 'Appendix 1'): scope and purpose (three items); stakeholder involvement (four items); rigour of development (seven items); clarity and presentation (four items); applicability (three items); and editorial independence (two items) (The AGREE Collaboration 2003). Each item is rated on a four point scale ranging from 4 'Strongly Agree'–1 'Strongly Disagree', with two midpoints: 3 'Agree' and 2 'Disagree'. The scale measures the extent to which a criterion (item) has been fulfilled. The score for each domain is obtained by summing up all the scores of the individual items in a domain and then standardising as follows:

\[
\text{Obtained score} = \frac{\text{Maximum possible score} - \text{minimum possible score}}{\text{Maximum possible score} - \text{minimum possible score}}
\]

The maximum score for each domain would be the number of questions multiplied by the number of reviewers multiplied times 4 (i.e. the score for strongly agree). The minimum possible score for a domain would be the number of questions multiplied times the number of reviewers multiplied times 1 (i.e. the score for strongly disagree). The final component of the AGREE instrument involves a recommendation regarding the use of the guidelines in practice as follows:

1. 1 'Strongly recommended,' if the guideline rated high on the majority of items and most domain scores were 60%, indicating that the guideline had a high overall quality and could be considered for use in practice without alterations;
2. 2 'Recommended' with provisos or alterations, if the guideline rated high or low on a similar number of items and most domain scores were 30–60%, indicating that the guideline had a moderate overall quality;
3. 3 'Would not recommend', if the guideline rated low on the majority of items and most domain scores were 30%, indicating that the guideline had a low overall quality and serious shortcomings, and thus should not be recommended for use in practice; and finally,
4. 4 'Unsure', if the guideline did not give sufficient information to enable assessment of its quality (AGREE Collaboration 2003).
Quality of systematic reviews was assessed with The Overview Quality Assessment Questionnaire (OQAQ) (Oxman & Guyatt 1991). This scale was selected because of its strong face validity and the availability of a published assessment of its construct validity (see 'Appendix 2'). The validity of the scale has been thoroughly tested and clearly validated using several different measures (Oxman et al. 1991, Oxman 1994). This instrument includes nine items pertaining to individual aspects in the reporting of a systematic review (e.g. were the search methods used to find evidence on the primary question stated?). Each item is assessed using a three-point scale (i.e. no, partially/can't tell or yes). A final question elicits an overall scientific quality of the systematic review based on the previous items on a scale of 1–7, with 7 indicating superior quality and a score of ≥5 indicating that the study has only minimal or minor flaws (Jadad & McQuay 1996). 'The Review Appraisal Form' was applied to each review independently by two researchers and then judged by consensus.

RESULTS

Availability and quality of guidelines and reviews

After removal of duplicates, a total of 493 citations were identified from the electronic searches (Fig. 1). Two reviewers screened the titles and abstracts for further review. It was decided that 165 (34%) of the citations were potentially relevant based on the predetermined inclusion criteria. After reading the full text, the reviewers came to a consensus that 34 of these met the criteria for selection.

Eleven of the 34 publications were guidelines. Six of the 11 guidelines were downloads from the Internet, of which three were English and three were Dutch. The five remaining guidelines were publications in peer-reviewed journals. Each guideline was scored for each of the six domains of the AGREE instrument, as shown in Table 2.

A first finding is that none of the guidelines were of good overall quality. None of the guidelines had scores >60% in all domains and none had a score between 30–60%, in all domains, indicating low overall quality for all guidelines according to the AGREE instrument. Almost all the guidelines were considered poor in the domains 'applicability' and 'editorial independence'. Applicability evaluates the likely organisational, behavioural and cost implications of applying the guideline, whereas editorial independence addressed potential conflicts of interest in guideline developers (e.g. because of sponsoring by companies selling products within the guideline scope). Nine of the 11 guidelines did not explicitly describe how they identified, selected and summarised the available evidence. Most of the guidelines did not provide an explicit link between the recommendations and the supporting evidence.

Systematic reviews

Only 23 of the 154 reviews were original systematic reviews. One review was an overview of two other included systematic reviews; and in two of the reviews, oral mucositis was not the primary topic, and hence they were excluded. A total of 20 systematic reviews remained
in this study. Agreement was reached on the scoring of all component scores and the overall quality scores with the need for an additional independent reviewer in two cases, because two of the 20 reviews were written by co-authors involved in this review.

Reviews suffered from lack of clarity, for instance, in performing a thorough literature search, avoiding bias in the inclusion of studies and properly referring to the quality of the included studies. Table 3 shows the systematic reviews and contains the quality score of the 20 identified reviews. Interventions for preventing oral mucositis were described in seven reviews, and only one review was found describing interventions for the treatment of oral mucositis. All reviews made formal assessment of methodological quality of included randomised studies and most had included trials that were not double blinded for the patient and the assessor. None of the reviews excluded trials from analysis because of low quality through a small sample size. Most of the reviews were clear in what types of participants included in the reviews ranged from 7–71 with a median of 25 studies per review. Four of the 20 reviews conducted a meta-analysis.

**TABLE 3**

**DISCUSSION**

For this study, guidelines and systematic reviews in the area of oral mucositis were used to assess their transparency and quality; however, the approach we used could be applied to any clinical topic.

This review shows that the quality of most of the guidelines and systematic reviews for the prevention and treatment of oral mucositis was low. Although some guidelines seem to have been more rigorously developed than others, many methodological flaws were identified. The AGREE instrument for quality assessment was used in screening the guidelines. This questionnaire has been endorsed by the WHO and the European Commission. The AGREE instrument is a generic and validated questionnaire to assess both the quality of reporting and the methodological quality of some aspects of recommendations. It provides an assessment of the predicted validity of a guideline, i.e. the likelihood that it will achieve its intended use. It does not investigate, however, the accuracy of the recommendations within a guideline, nor its impact on patients' outcomes (AGREE Collaboration 2007). This instrument was developed in 2003 before five of the 11 guidelines included in this study were developed. This suggests that provided the committees that are developing or updating guidelines use the AGREE recommendations, the quality of future guidelines will likely improve. In cases where no information was available on a certain topic, the AGREE instrument recommends the rating 'strongly disagree'. This method of operation is a conservative approach, because in such a case the quality of a guideline is possibly not rated as high as it actually is. It may be that many of the processes evaluated by the AGREE instrument were performed but not reported. In these cases, transparency of methods is the issue whereas quality may be acceptable. Although none of the guidelines scored well on all the domains, the guidelines of the National Cancer Institute (National Cancer Institute 2005) scored relatively low compared with the other ones. Important experts in the field developed this guideline; nevertheless, an explicit description and justification of the process of developing the guideline was not given within the guideline.

Considering these results, one could argue that, perhaps, the AGREE instrument is too strict. On the contrary, however, one could question if guideline developers are aware of the AGREE instrument and its criteria for transparency of guideline development. Given the time, the AGREE criteria are likely to become more known and adopted as the need to distinguish between poor and good quality guidelines will increase. Explicit and detailed information about the objectives and context of the guideline development, including the methods used and the people and organisations involved in the
development process are very important. Clinical practice guideline users will have more confidence in guidelines with these elements (Grol et al. 1998, Burgers et al. 2003). Indeed, one could argue that large-scale implementation of guidelines is not justified when guideline developers do not report their methods. Therefore, in our opinion, the AGREE instrument is a helpful tool in the process of guideline development and the assessment of guideline quality.

A limitation of this study is that, although we used several methods to identify guidelines that were published, there is the possibility that we may have missed some. However, if guidelines were not published in major journals or readily available through the Internet, then most potential users would probably miss them as well. Another limitation of the study is that in assessing the quality of guidelines, only the guidelines themselves and relevant documents referred to in the guidelines were used and we did not systematically search for supplementary materials that may have been published elsewhere. However, if users lack clear references and easy access to such background documents, this would be problematic in itself.

The majority of the reviews were non-systematic literature reviews, often referred to as narrative reviews. Such literature reviews are almost always selective, in that they do not involve a systematic, rigorous and exhaustive search of all the relevant literature, using electronic and print media (Davies 2000) and therefore give only a subjective judgement of the included studies (Blettner et al. 1999).

The 20 systematic reviews of prevention and treatment of oral mucositis published since 2000 represent what should be the highest level of evidence available. One of the major weaknesses of these reviews was that the search strategies reported were not always clear or adequate. The aim of a systematic review is to provide a comprehensive summary of current research evidence. To achieve this aim, a systematic review should employ a transparent and exhaustive search. This may be due to the fact that such reports may not always reflect how the review was actually conducted but only what has been published.

The difficulty in interpreting results strengthens the argument that a systematic review should be a transparent process, with the reader of the review being able to identify what has been carried out.

CONCLUSION

Although many guidelines on oral mucositis are classified as evidence-based, a profound review of their quality applying the AGREE instrument revealed that none of the guidelines could be recommended. The majority of the guidelines are of middling quality. In addition, systematic reviews have methodological limitations despite their clinical relevance.

Specific changes must be made at multiple levels by publishers, authors and readers of systematic reviews. First, journals should focus on accepting high-quality systematic reviews and on ensuring that the Methods sections outline the methods in a clearer manner (Jadad & McQuay 1996).

Authors need to pay particular attention to the methods used in systematic reviews, preferably before beginning on this research activity. Finally, readers need to become more familiar with critically appraising systematic reviews and developing a healthy scepticism before incorporating the results into practice.

All the systematic reviews came to the same conclusion that it is important that more well-designed, randomised, controlled trials are conducted to investigate new treatments for prevention and management of oral mucositis. In line with this, we conclude that there is also considerable room for improvement in formulating guidelines as well as systematic reviews for the prevention and treatment of oral mucositis.
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CONTRIBUTIONS

Study design: CP, PM; data collection: CP, PM; analysis: CP, PM, EP, TvA and manuscript preparation: CP, NB, PD, TvA.

REFERENCES


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APPENDIX 1

AGREE Instrument
Response categories for each question are as follows:
1 Strongly disagree
2 Disagree
3 Agree
4 Strongly agree

Scope and purpose
1 The overall objectives of the guideline are specifically described.
2 The clinical questions covered by the guideline are specifically described.
3 The patients to whom the guideline is meant to apply are specifically described.

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Stakeholder involvement
1 The guideline development group includes individuals from all the relevant professional groups.
2 The patients' views and preferences have been sought.
3 The target users of the guideline are clearly defined.
4 The guideline has been piloted among end-users.

Rigour of development
1 Systematic methods were used to search for evidence.
2 The criteria for selecting the evidence are clearly described.
3 The methods used for formulating the recommendations are clearly described.
4 The health benefits, side-effects, and risks have been considered in formulating the recommendations.
5 There is an explicit link between the recommendations and the supporting evidence.
6 The guideline was externally reviewed by experts prior to its publication.
7 A procedure for updating the guideline is provided.

Clarity and presentation
1 The recommendations are specific and unambiguous.
2 The different options for management of the condition are clearly presented.
3 Key recommendations are easily identifiable.
4 The guideline is supported with tools for application.

Applicability
1 The potential organisational barriers in applying the recommendations have been discussed.
2 The potential cost implications of applying the recommendations have been considered.
3 The guideline presents key review criteria for monitoring and/or audit purposes.

Editorial independence
1 The guideline is editorially independent from the funding body.
2 Conflicts of interest of the guideline development members have been recorded.

APPENDIX 2

Review appraisal form

Review appraisal form
The Oxman and Guyatt's index of the scientific quality of research overviews
Reference:
Reviewed by:
1 Were the search methods used to find the evidence (original research) on the primary questions(s) stated?
   Yes/Partially (Can't tell)/No
2 Was the search for evidence reasonably comprehensive?
   Yes/Partially (Can't tell)/No
3 Were the criteria used for deciding which studies to include in the overview reported?
   Yes/Partially (Can't tell)/No
4 Was bias in the selection of studies avoided?
Yes/Partially (Can't tell)/No
5 Were the criteria used for assessing the validity of the included studies reported?
Yes/Partially (Can't tell)/No
6 Was the validity of all studies referred to in the text assessed using appropriate criteria (either in selecting studies for inclusion or in analysing the studies that are cited?)
Yes/Partially (Can't tell)/No
7 Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported?
Yes/Partially (Can't tell)/No
8 Were the findings of the relevant studies combined appropriately relative to the primary question the overview addresses?
Yes/Partially (Can't tell)/No
9 Were the conclusions made by the author(s) supported by the data and/or analysis reported in the overview?
Yes/Partially (Can't tell)/No
10 How would you rate the scientific quality of the overview?

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TABLES AND FIGURES

Table 1 Search strategy PubMed


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Figure 1 Flow diagram.

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<th>Table 2 Quality assessment guidelines (averaged AGREE scores by domain)</th>
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Table 3: Quality assessment of systematic reviews (averaged QoRA score by question)

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<td>B</td>
<td>B</td>
<td>C</td>
<td>C</td>
<td>C</td>
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<tr>
<td>Sharma et al. 2005</td>
<td>B</td>
<td>B</td>
<td>C</td>
<td>C</td>
<td>C</td>
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<td>C</td>
<td>C</td>
<td>3</td>
</tr>
</tbody>
</table>

*The score was obtained by analysing the results to each of the nine questions, using a standardised set of instructions provided by the developers of the index (Judd & McQuay 1996). A = Yes, B = Partially (Can’t tell), C = No.