EUROPEAN JOURNAL OF CANCER 46 (2010) 1399–1412

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journal homepage: www.ejconline.com

# The development of evidence-based guidelines on mouth care for children, teenagers and young adults treated for cancer

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ARTICLE INFO

*Article history:*
Received 9 July 2009
Received in revised form 4 January 2010
Accepted 15 January 2010
Available online 11 March 2010

*Keywords:*
Guideline
Mucositis
Candidiasis
Oral hygiene
Herpes simplex virus
Xerostomia
Radiotherapy
Chemotherapy
Cancer treatment protocols

ABSTRACT

The aim was to produce evidence-based guidelines on mouth care for children, teenagers and young adults receiving chemotherapy and/or radiotherapy.

Systematic reviews were undertaken and research was graded according to the methods of the Scottish Intercollegiate Guidelines Network. Where no relevant research was identified, an opinion-gathering process was undertaken.

'Best practice' recommendations were developed with regard to appropriate dental care and basic oral hygiene. An evaluation of oral assessment tools identified seven which had been assessed for reliability and/or validity. Only Eilers' Oral Assessment Guide was felt to be relevant for daily clinical practice.

A variety of interventions have been used for the management of oral mucositis, candidiasis, xerostomia and herpes simplex virus; few are supported by research evidence.

Careful oral management of children treated for cancer can improve the quality of life during treatment. The guidelines have the potential to improve patient care by promoting interventions of proven benefit and discouraging use of ineffective or potentially harmful practices which may result in adverse patient outcomes.



## 1. Introduction

Oral complications occurring during and following cancer treatment are common and can cause pain, difficulty in swallowing and phonation and poor nutrition. They can clearly impact severely on a patient's quality of life.[1] One of the most common side-effects of cancer treatment is mucositis. The prevalence of chemotherapy-induced oral mucositis has been shown to range from 30% to 75% of patients, depending upon the treatment type.[2,3] In about 50% of patients with mucositis, lesions can be severe causing significant pain, interfering with nutrition and often requiring modification of the chemotherapy regimen. In addition, mucositis may predispose a child to fungal infection (most commonly candidiasis), viral infection and bacterial infection, which may lead onto life-threatening systemic infection. An additional oral complication following cancer treatment is salivary gland dysfunction, which can be caused by both chemotherapy and radiotherapy. Salivary gland damage can also impact on a patient's quality of life, causing oral discomfort, taste disturbances, difficulty in chewing and swallowing and speech problems. In addition, patients suffering from salivary gland damage are at greater risk of oral infections, including oral candidiasis. Long-term consequences of salivary gland damage include dental caries.

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0959-8049/$ - see front matter 
doi:10.1016/j.ejca.2010.01.023

The careful oral management of children treated for cancer can improve the quality of life during treatment. However, there is 'confusion and conflict' surrounding what constitutes appropriate mouth care.[4] In recent years much emphasis has been placed on the development of clinical guidelines, as a means of improving the quality of health care.[5] Guidelines have been viewed as a way of helping to promote evidence-based practice; encouraging clinical practice based on relevant, scientifically rigorous, research evidence.

One of the potential benefits of guidelines is that they can reduce inappropriate variation in clinical practice. There is ample evidence that there are substantial variations in the provision of care in most clinical specialties, which may lead to inequalities in health care.[6] Indeed, a survey of mouth care provided to children, teenagers and young adults treated for cancer identified diversity in care across the United Kingdom.[7] A wide variety of interventions were shown to be used for both prevention and treatment of oral complications, only some of which have been shown to be effective.[8–12] In order to reduce this variation in practice the Children's Cancer and Leukaemia Group (CCLG) (formerly the United Kingdom Children's Cancer Study Group (UKCCSG)) and the Royal College of Nursing Paediatric Oncology Nurses Forum's (PONF) Mouth Care Group was established. The principle aim of the CCLG-PONF Mouth Care Group was to produce comprehensive evidence-based guidelines on mouth care for children, teenagers and young adults who have undergone or who are receiving chemotherapy and/or radiotherapy for a malignancy (including head and neck cancers), or stem cell transplant (both bone marrow and peripheral blood stem cell transplants).

## 2. Materials and methods

The guidelines were developed following the methods outlined by the Scottish Intercollegiate Network (SIGN).[13] However, for certain questions addressed in the guidelines, the SIGN methods were not deemed applicable, so adapted, or alternative, methods were used.

### 2.1. Guideline development panel

A multidisciplinary guideline development group, consisting of nationally and internationally recognised experts in the fields of paediatric oncology, oral care and evidence-based practice, was established.

### 2.2. Identification of questions

A consensus approach was used to establish the scope and basic structure of the guidelines. Three key areas were identified:

- Dental care and basic oral hygiene.
- Methods of oral assessment.
- Drugs and therapies used for the management of oral complications.

In order to address each of these areas, the Mouth Care Group was divided into subgroups, and a lead reviewer was assigned to each group. Each subgroup was responsible for producing a list of relevant questions to be addressed within its particular area. Scoping searches were undertaken for each area.

### 2.3. Scoping searches

The purpose of the scoping searches was to gain an overview of the volume of the literature; identify further questions that may need to be addressed; and establish the research methodologies used within each area. They were used to provide a basis upon which to make organisational and methodological decisions with regard to the guideline development process. All scoping searches were run on MEDLINE (OVID BIOMED).

### 2.4. Finalisation of questions

Each subgroup liaised by e-mail/telephone to finalise a list of questions to be addressed in the guidelines. The questions were circulated to the whole group for comments. Inclusion criteria were developed from the final list of questions to be addressed.

### 2.5. Searches

The searches were refined to reflect the final list of questions identified by each subgroup. English language articles were only included due to resource implications for reliable translation. Details of the search strategies used are available in the Methodological Report (http://www.cclg.org.uk).

### 2.6. Assessment of relevance

Within each subgroup, screening of titles and abstracts identified through the electronic searches was undertaken independently and in duplicate. When agreement could not be reached by the members of the subgroup with regard to the relevance of the study (based on the review of the abstract alone), the full article was sought for further clarification.

### 2.7. Assessment of validity

The full paper copies of each article identified as being relevant (or potentially relevant) for inclusion in the guideline were assessed by two of the lead authors and coded according to study design. The appropriate SIGN checklist was attached to each article and distributed to the relevant subgroup. As for the assessment of relevance, each article was assessed for validity independently and in duplicate. Disagreements in the validity assessment were resolved through a consensus process between the reviewers.

### 2.8. Data extraction

Data extraction was undertaken at the same time as the validity assessment. Details to be extracted from the articles included characteristics of the study population, characteristics of the study setting, specifics of any interventions, exposures or prognostic factors evaluated and the outcomes assessed.

### 2.9. Development of evidence tables

The results of the validity assessment and data extraction process were used to produce evidence tables. Within the evidence tables, each study was coded as illustrated in Table 1.

Once created, the evidence tables were distributed to members of the Mouth Care Group for comments. Provisional evidence statements were made after consideration of the volume of evidence, the applicability of the identified evidence, its generalisability, consistency and clinical impact. A meeting was held to discuss the evidence statements, amend them if necessary and use them to produce recommendations.

### 2.10. Grading of recommendations

The recommendations produced by the Mouth Care Group were graded according the SIGN guidelines[13] (Table 2). A draft of the graded recommendations was then circulated to all the Group members for further comments.

### 2.11. Peer review

Once the guidelines were drafted, a list of named referees from the guideline's major stakeholders was drawn up and the guidelines were distributed for review. Comments were also requested from families whose children were undergoing cancer treatment. The feedback form was structured so as to gather information on specific issues, and allow for the respondent to provide additional comments as necessary.

#### 2.11.1. Dental care and basic oral hygiene

Due to the paucity of evidence addressing issues covering dental care and basic oral hygiene for those undergoing treatment for cancer, we sought the views from members of relevant health professionals using a formal consensus approach. A Delphi technique approach was undertaken. A list of statements regarding basic oral hygiene and dental care was drawn up by members of the Mouth Care Group. These statements were not based upon the research evidence but reflected the expert opinions of the group members involved, or were prompted by results obtained through a survey of CCLG centres with regard to current oral care practice.[7] The list was distributed electronically to members of the CCLG and PONF, and paediatric dentists and dental hygienists. Respondents were asked to grade each statement from 1 to 5 (strongly disagree to strongly agree), for example:

The oncology team must include a paediatric dentist

| *Disagree Strongly* | | | | *Agree Strongly* |
|---|---|---|---|---|
| *1* | *2* | *3* | *4* | *5* |
| | | | | |

Space was provided for additional comments. The first round produced a high level of consensus and it was felt unnecessary to ask the participants to re-score the statements. Instead, the responses were used to draw up provisional

**Table 1 – SIGN grading system for levels of evidence.[13]**

| | |
|---|---|
| 1++ | High quality meta-analyses/systematic reviews of RCTs or RCTs with a very low risk of bias |
| 1+ | Well conducted meta-analyses/systematic review of RCTs, or RCTs with low risk of bias |
| 1– | Meta-analyses/systematic reviews of RCTs, or RCTs with high risk of bias |
| 2++ | High quality systematic reviews of case-control or cohort studies; high quality case-control or cohort studies with a very low risk of confounding, bias or chance and high probability that the relationship is causal |
| 2+ | Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal |
| 2– | Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal |
| 3 | Non-analytic studies, e.g. case series and cross-sectional surveys |
| 4 | Expert opinion/non-systematic review article |

**Table 2 – SIGN grading of recommendations.[13]**

| Grade | |
|---|---|
| A | At least one meta analysis, systematic review or RCT rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results |
| B | A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+ |
| C | A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++ |
| D | Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+ |

For certain recommendations it was felt appropriate to grade them as 'Best Practice'; these were assigned the symbol '√'.

recommendations that would be subjected to peer-review, in the context of the full guideline document. The recommendations were coded as 'Best Practice'.

#### 2.11.2. *Oral assessment*

Following the literature search, full paper copies of 77 studies identified as being potentially relevant for oral assessment

**Table 3 – Example of evidence statement and preliminary recommendations.**

| Evidence statement | Level | Preliminary recommendations | Grade |
|---|---|---|---|
| There is weak and unreliable evidence from two trials that allopurinol mouthwash may prevent severe mucositis in adults with solid tumours treated with 5-fluorouracil (5-FU). There are no trials of allopurinol mouthwash for the prevention of radiotherapy-induced mucositis in adults or children.[9,26] | 1++ | *There is insufficient evidence to support the routine use of allopurinol mouthwash in children receiving chemotherapy. Future use should be within the constraints of an RCT.*<br>*There is no evidence to support the use of allopurinol mouthwash for the prevention of radiotherapy-induced mucositis in children.* | B |

| RECOMMENDATIONS FOR ORAL CARE AT TIME OF CANCER DIAGNOSIS | |
|---|---|
| For paediatric dental units working with a cancer centre there should be a mechanism of notification for new patients. | √ |
| All children should undergo a dental assessment at the time of cancer diagnosis, if possible, before cancer treatment commences. | √ |
| The people most suitable to undertake the initial dental assessment are a paediatric dentist or a dental hygienist. | √ |
| If any invasive dental treatment is required, this should be undertaken by either a consultant or specialist paediatric dentist as appropriate. | √ |
| All children diagnosed with cancer should be registered with a General Dental Practitioner or community dental service. Registration should be maintained during and following the cancer treatment. | √ |
| All children diagnosed with cancer should have access to an NHS General Dental Practitioner. | √ |
| The routine dental care provider in the general or community dental service should be notified of the cancer diagnosis and arrangements for care during cancer treatment as directed by the hospital dental team. | √ |
| If there is not a paediatric dental unit liaising with a cancer centre there should be clear communication between the cancer centre and routine dental provider. | √ |
| Appropriate training in oral assessment should be available within the cancer centre, ideally in collaboration with a member of the dental team. | √ |

**Fig. 1 – Final Guideline Recommendations (for grading of recommendations see Table 2).**

| RECOMMENDATIONS FOR ORAL HYGIENE AT DIAGNOSIS AND DURING CANCER TREATMENT | |
|---|---|
| Oral hygiene advice should be given to children and parents prior to commencing cancer treatment and this should be provided both verbally and in writing. | √ |
| Oral hygiene advice should be given by a designated member of the dental team or, in the absence of a dentally trained individual, a member of the medical or nursing team who has received appropriate training. | √ |
| Advice should be to brush at least twice a day, with a fluoride toothpaste (containing 1,000 ppm fluoride +/- 10%).[a] The toothbrush should be for the sole use of the child and changed on a 3 monthly basis, or when bristles splay if earlier. If the child has a sore mouth a soft brush with a small head should be used. | √ |
| For children up to the age of 6 years, parents/carers should be instructed on how to brush their child's teeth. | √ |
| For babies without teeth, parents/carers should be instructed on how to clean the mouth with oral sponges. The sponge should be moistened with water. | √ |
| For children where it is not possible to brush teeth, parents/carers should be instructed on how to clean the mouth with oral sponges, as a temporary measure. The sponge should be moistened with water or an antimicrobial agent such as diluted chlorhexidine. | √ |

[a] Data regarding fluoride concentration comes from: Scottish Intercollegiate Guidelines Network (SIGN). Guidelines on prevention and management of dental decay in the pre-school child. Edinburgh: SIGN

**Fig 1.** *(continued)*

content were reviewed by two authors and coded according to the study design. The initial plan was to assess the identified studies using the relevant SIGN checklists. However, due to the nature of the research identified, this was felt inappropriate. Instead, each study was screened and all assessment tools described within each study were recorded.

Any studies providing some form of validity or reliability testing were subsequently assessed using an adaptation of the SIGN 'Diagnostic studies' checklist.[13] Disagreements in the validity assessment process were taken to a third party.

### 2.11.3. *Drugs and therapies*

Given that the drugs and therapies section of the guideline deals with the effectiveness of interventions, it was felt appropriate to focus on evidence from systematic reviews or RCTs only. The included systematic reviews and RCTs could assess the effectiveness of any intervention to either prevent or treat a disease of the tongue or oro-naso-pharynx, arising as a result of cancer treatment. Children, teenagers and young adults were the focus of the guidelines. However, due to the paucity of trials in this area recruiting children with cancer, trials including adults with cancer were also included.

The following decisions were made with regard to the recommendation of interventions:

1. The guidelines would not support routine use of an intervention for use in children for which there is evidence of clinically important harm from trials of either adults or children.
2. Where there was weak/insufficient/no evidence from trials in adults or children the guidelines would recommend the use of an intervention only within the constraints of an RCT.

| | |
|---|---|
| Additional aids, such as flossing and fluoride supplements should be prescribed only according to risk assessment by a member of the dental team. | √ |
| The need to restrict sugary food and drink to meal times only should be emphasised.[b] | C |
| RECOMMENDATIONS FOR DENTAL/ORAL CARE DURING CANCER TREATMENT | |
| A dental assessment should be undertaken every three to four months by a member of the dental team. | √ |
| The dental team should be consulted of any dental, or difficult to manage oral problems arising during cancer treatment and the cancer team should be informed of the type and extent of dental treatment required. | √ |
| If there is not a dedicated dental team there needs to be clear communication between the cancer team and a routine dental provider. | √ |
| RECOMMENDATIONS FOR DENTAL/ORAL CARE AFTER CANCER TREATMENT | |
| Parents and children should be informed, at an appropriate time, of the possible long-term dental/orofacial effects of childhood cancer and treatment. Children should continue to be monitored during the period of growth and development. | √ |

[b] Following peer review it was felt necessary to include an additional statement with regard to diet. The SIGN publication Number 47 has previously appraised the research evidence with regard to dietary advice for children at high caries risk and the recommendations to reduce the frequency of sugar intake has been incorporated into this document.

**Fig 1.** *(continued)*

3. Where there was strong evidence in adults or children, the guidelines would recommend the use of an intervention in children unless there is a contra-indication to therapy in this age group.

The following operational definitions were used when determining the evidence in support of a given intervention:

- *No evidence:* no trials, or trials showing no statistically significant difference (several interventions have been assessed predominantly in trials recruiting adults only. When trials have shown no statistically significant difference between interventions for adults, this has been classified as 'no evidence' with regard to effectiveness for children).
- *Weak evidence:* limited number of trials and/or trials at risk of bias
- *Strong evidence:* several high quality RCTs showing the same direction of effect.

These categories were determined following the appraisal of the literature and were used to finalise the evidence statements and draw up preliminary recommendations.

| | |
|---|---|
| Children should be referred back to their routine dental provider who should be advised of the preventive regime recommended by the consultant/specialist paediatric dental team and advised of future care arrangements and systems for referral as necessary. | √ |
| RECOMMENDATIONS FOR ORAL ASSESSMENT DURING CANCER TREATMENT | |
| There is a variety of oral assessment tools from which to choose. Using those which have been shown to be valid and reliable would be most valuable. | √ |
| The Eilers' Oral Assessment Guide (OAG) offers a valid, reliable and clinically useful tool for assessing oral status. | D |
| Those responsible for assessment of the oral cavity should be appropriately trained in the use of the selected assessment tool. Ideally, some form of reliability (inter and/or intra-rater) testing of the tool in the clinical setting should be conducted. | √ |
| Nursing staff are best placed for the regular assessment of the child's oral status. | D |
| The frequency with which a child's mouth is assessed should be determined on an individual basis. Frequency should increase at the onset of oral complications. | D |
| Oral assessment should be used to check good basic oral hygiene is being maintained. | √ |
| For a child with oral complications (e.g. as indicated by an OAG score of greater than 8) an appropriate pain assessment tool should be used to ensure adequate pain control and therapeutic interventions are available. | √ |

**Fig 1.** *(continued)*

## 3. Results

### 3.1. *Dental care and basic oral hygiene*

A total of 73 responses were obtained from the Delphi. Due to the electronic method of distribution, the specific number of health professionals receiving the questionnaire is unknown. The forms were completed by 26 nursing staff (35.6%), 24 medical staff (31.6%), 12 dentists (15.8%) and two dental hygienists (2.6%). Nine respondents (11.8%) did not provide details of their profession.

The median value achieved for 29/32 (90.6%) of the statements was four or five, indicating that the majority of the respondents agreed with the statements to some extent. The full responses of those participating in the opinion-gathering process are presented in the Methodological Report (http://www.cclg.org.uk).

### 3.2. *Oral assessment*

Twenty-seven individual oral assessment tools were identified, with seven studies providing some assessment of validity and/or reliability testing of specific oral assessment tools.

| | |
|---|---|
| The timing of assessment should be consistent in relation to the child's oral hygiene routine. | D |
| RECOMMENDATIONS FOR THE PREVENTION OF ORAL MUCOSITIS | |
| Parents and patients should be informed of the importance of keeping the mouth clean and encouraged to practice good, basic oral hygiene. | √ |
| The following have all been shown to be potentially beneficial for the prevention of mucositis in adult populations. Their use in children for the prevention of radiotherapy and/or chemotherapy induced mucositis can only be considered within the constraints of an RCT;<br>Amifostine<br>Allopurinol mouthwash (for 5-FU therapy)<br>Ice-chips<br>GM-CSF/GCSF<br>Benzydamine<br>Antibiotic pastilles/pastes (containing PTA)<br>Povidone-iodine<br>Pilocarpine (not currently available in a form suitable for children)<br>Hydrolytic enzymes | B |
| RCTs of allopurinol mouthwash are not recommended for children receiving cancer treatment other than 5-FU. | D |
| Prostaglandin E is not recommended for the prevention of chemotherapy or radiotherapy induced mucositis as there is evidence that it may promote mucositis. | B |

**Fig 1.** *(continued)*

### 3.3. *Drugs and therapies*

A total of 973 articles were identified through the electronic searches. Following screening of the titles and abstracts for the drugs and therapies section, 111 full articles were retrieved for review. The evidence tables produced as a result of this process are presented in the full Methodological Report. Table 3 provides an example of how evidence statements were used to make preliminary recommendations. Fig. 1 presents the final guideline recommendations.

### 3.4. *Publication of guidelines*

Three versions of the guidelines were produced for distribution and implementation:

- The Methodological Report, detailing all the methods used throughout the guideline development process, to be used as a reference document.
- The Guideline Report, an abbreviated document focusing on the recommendations, to be available in the clinical area.
- At-a-glance document, which allows for some local adaptation and is clear and succinct enough to be accessible to both health care workers and parents and young adults.

## 4. Discussion

Clinical guidelines are considered to have an important role to play in reducing inappropriate variation in clinical practice,

| | |
|---|---|
| i.v. folinic acid is not recommended for the routine prevention of chemotherapy or radiotherapy induced mucositis as there is evidence that it may promote mucositis. | B |
| However, i.v./oral folinic acid may be used for the prevention of toxicity following methotrexate. | √ |
| There is no evidence to support or refute the use of folinic acid mouthwash for the prevention of mucositis. | |
| There is no evidence to support the use of the following agents for the prevention of chemotherapy or radiotherapy induced mucositis in children;<br>Lozenges containing bacitracin, clotrimazole, and gentamicin (BCoG)<br>Propathelene<br>Chlorhexidine<br>Fluconazole<br>Amphotericin B<br>Sucralfate<br>Prednisone<br>Glutamine<br>Pentoxifyline<br>Na-sucrose gel<br>Traumeel<br>Chamomile<br><br>Their use in children for the prevention of radiotherapy and/or chemotherapy induced mucositis can only be considered within the constraints of an RCT. | B |

**Fig 1.** *(continued)*

some of which may be ineffective or potentially harmful. In order to be of most use, guidelines need to be comprehensive, valid and relevant. A comprehensive and systematic approach was undertaken in the development of the CCLG-PONF Mouth Care Guidelines and internationally recognised methods of guideline development were followed where possible.[14]

Previous guidelines or guidance documents (and associated materials) are available that provide recommendations on some aspect of mouth care for adults and/or children receiving treatment for cancer.[15–21] However, the methods used to produce these documents, and the recommendations presented, vary. It is acknowledged that the target populations of these documents also differ, so some variation in recommendations is to be expected. However, discrepancies in the recommendations also appear to be due to misinterpretation, or the inappropriate use, of research evidence. For example, the National Institute for Health and Clinical Excellence (NICE) guidance[15,16] recommends ice-chips as the most effective intervention for preventing oral mucositis, based on evidence from a Cochrane review. Whilst the systematic review[9] demonstrates the effectiveness of ice-chips (from two RCTs), the recommendation that it is the most effective intervention cannot be drawn (and is not described as such) from the review. The trials included in the review compare ice-chips with a no treatment control; there are no head-to-head trials of ice-chips with other interventions, therefore it is inappropriate to make statements of relative effectiveness.

Similarly, the PRODIGY guidance recommends that acupuncture may be an effective alternative to pilocarpine for the treatment of xerostomia in '*resistant cases*'.[20] The evidence comes from a single pre-test/post-test study, with no direct

| RECOMMENDATIONS FOR THE TREATMENT OF ORAL MUCOSITIS | |
|---|---|
| Appropriate pain control is recommended and the continuation of good oral hygiene, as tolerated. | √ |
| Pain associated with mucositis can be severe. Opiates are required for the control of such pain. | √ |
| RCTs of patient controlled analgesia versus continuous infusion for controlling oral pain in children are required. | B |
| The following have been shown to be potentially beneficial for the treatment of mucositis in adult populations. Their use in children receiving radiotherapy and/or chemotherapy can only be considered within the constraints of an RCT;<br>Vitamin E<br>Immunoglobulin<br>Allopurinol mouthwash (for 5-FU therapy) | B |
| RCTs of allopurinol mouthwash are not recommended for children receiving cancer treatment other than 5-FU. | D |
| There is no evidence to support the use of the following for the treatment of chemotherapy or radiotherapy induced mucositis in children;<br>Benzydamine<br>Chlorhexidine<br>Sucralfate<br>Tetrachlorodecaoxide<br>'Magic' (lidocaine solution, diphenhydramine hydrochloride and aluminium hydroxide suspension).<br><br>Their use in children for the treatment of radiotherapy and/or chemotherapy induced mucositis can only be considered within the constraints of an RCT. | B |

**Fig 1.** *(continued)*

comparison of acupuncture and pilocarpine being made. In addition, the PRODIGY guidance recommends the use of nystatin as first line-therapy for the treatment or prevention of oral candidiasis,[8,10] a therapy not supported by research evidence.

Every attempt has been made within the development of the CCLG-PONF Mouth Care Guidelines for children and teenagers to ensure that the recommendations are truly evidence-based and comprehensive. The guideline development process has been documented carefully to enhance transparency.

The development of evidence-based guidelines is a long process. A major issue in the development of guidelines over a long period of time is the emergence of new, relevant material. To overcome this, guidelines need to be 'living documents', undergoing regular updates. The timing of updates should be determined by the volume of the literature published in the chosen field. There are currently 30 ongoing trials, examining the effectiveness of interventions for the management of oral complications associated with cancer treatment, listed on Current Controlled Trials[22] and the National Research Register.[23] The reported funding varies from £1200 to over £95,000 per trial. Given the impact that oral mucositis, candidiasis and other oral complications can have on cancer patients' quality of life, it is imperative that the re-

| RECOMMENDATIONS FOR THE PREVENTION OF ORAL CANDIDIASIS | |
|---|---|
| Some groups of patients are more likely to get candidiasis than others. Evidence cannot necessarily be generalised. Preventative therapy is not recommended for most patients (for example, those receiving treatment for solid tumours). A decision needs to be made by the clinician on whether to provide treatment to try and prevent candidiasis according to the patient's risks. Further studies are recommended to identify risk factors. | D |
| When choosing an antifungal agent for the prevention of candidiasis, one that is absorbed from the GI tract is recommended (for example fluconazole, itraconazole or ketoconazole). | A |
| Drug doses should be prescribed according to the British National Formulary for Children. | √ |
| Oral amphotericin B is recommended for the prevention of candidiasis only within the constraints of an RCT. | B |
| There is no evidence to support the use of nystatin or chlorhexidine for the prevention of candidiasis in children treated for cancer. | A |
| **RECOMMENDATIONS FOR THE TREATMENT OF ORAL CANDIDIASIS** | |
| There is no research evidence to demonstrate the effect of either topical or systemic antifungal agents for the treatment of oral candidiasis. Based on evidence for prevention of oral candidiasis, absorbed or partially absorbed antifungal agents could be used for the treatment of visible oral candidiasis. | D |

**Fig 1.** *(continued)*

sults of such trials are utilised in practice. It could be argued that the substantial funding and resources used in the undertaking of clinical trials in this area are wasted if the findings are not being used appropriately to inform practice. One of the proposed advantages of guidelines is that they may help to close the gap between research evidence and clinical practice.[24] It is imperative that implementation of new and emerging research evidence is not delayed by waiting for the production of guidelines. However, it is also important to recognise that new evidence should be carefully evaluated, in light of existing research, before being used to influence practice. In order to try and address this issue, the Mouth Care Guidelines for children and teenagers aim to be regularly updated but, realistically, this will not be more frequent than every 2 years. As with the current version of the guideline, any recently completed or ongoing trials that are not available for inclusion at the time of publication will be recorded. These trials will be identified through Current Controlled Trials[22] and the National Research Register.[23] It is hoped that by presenting such data, users of the guideline will be alerted to the fact that evidence in this field is not static, and what is found to be effective today may be superseded by new and emerging evidence tomorrow.

An issue that arose during the production of the Mouth Care Guideline was how to make evidence-based recommendations when there was a lack of evidence. This was a particular issue for the section on dental care and basic oral hygiene where there was a lack of evidence for those undergoing treatment for cancer. A variety of methods for developing guidelines and recommendations have been used in the

| | |
|---|---|
| Further controlled trials assessing the effectiveness of current antifungal agents and new interventions for treating oral candidiasis are required. | D |
| **RECOMMENDATIONS FOR THE PREVENTION OF XEROSTOMIA** | |
| There is insufficient evidence to support the use of amifostine for the prevention of salivary gland damage, or pilocarpine (not currently available in a form suitable for children) or biperiden for the prevention of xerostomia, in children treated for cancer. Future use of any such pharmacological agents for the prevention of salivary gland damage and xerostomia should be within the constraints of an RCT only. | B |
| **RECOMMENDATIONS FOR THE TREATMENT OF XEROSTOMIA** | |
| Consideration should be given to the use of saliva stimulants, artificial saliva, chewing sugar free gum or frequent sips of water for the relief of dry mouth. | D |
| **RECOMMENDATIONS FOR THE PREVENTION OF HERPES SIMPLEX VIRUS** | |
| Aciclovir is only recommended as a preventative strategy for herpes simplex in patients undergoing high dose chemotherapy with stem cell transplant. | B |
| Aciclovir is not recommended for routine use due to rarity of problem and cost. | D |
| **RECOMMENDATIONS FOR THE TREATMENT OF HERPES SIMPLEX VIRUS** | |
| Aciclovir is effective for the treatment of herpes simplex virus in patients receiving chemotherapy and/or radiotherapy. | A |

**Fig 1.** *(continued)*

past, including informal and formal consensus methods. Some research into different formal consensus methods has already been undertaken, however, questions still remain.[25] For example, when using a technique such as the Delphi method, what effect does the framing of the initial statements/questions have on individual judgements? Does the method of gathering participants' judgements (via e-mail, post or face-to-face) influence their response? How to present and interpret lack of agreement between participants? Further research into the choice of methodology used within guideline development, the associated costs and the impact on patient outcomes is required.

Another issue that arose during the development of the Mouth Care Guideline was the lack of evidence relevant to children. The majority of the trials examining the effectiveness of interventions for the prevention and/or treatment of mucositis, candidiasis recruited adults. All the trials examining the effectiveness of interventions for xerostomia recruited adults only. Whilst the results of the trials were felt to be fully applicable to adult oncology units within the UK, their applicability to paediatric oncology units needed to be considered, and the findings graded accordingly. The SIGN grading system[13] allows for extrapolation of evidence. For example, much of the evidence on drugs and therapies came from high

| | |
|---|---|
| Mild and non-progressing lesions on the lip should be treated with topical aciclovir. | D |
| Progressing and severe lesions on the lip should be treated with oral aciclovir. | D |
| Intra-oral lesions should be treated with oral aciclovir. | D |
| For severe cases, or where oral administration not tolerated, i.v. aciclovir should be used. | D |
| Drug doses should be prescribed according to Medicines for Children. | √ |
| Thymostimulin and vidarabine are not recommended for routine treatment of herpes simplex unless within the constraints of an RCT. | B |

**Fig 1.** *(continued)*

quality systematic reviews, rated 1++. Ordinarily, recommendations supported by such evidence would be graded 'A'. However, many of the recommendations on drugs and therapies within the Mouth Care Guideline, supported by high quality evidence, had to be graded 'B' to account for the lack of trials in the relevant paediatric population. In addition, consideration needed to be given to the licencing of certain drugs for use in children within the UK. For example, pilocarpine has been shown to be effective for the management of xerostomia in adults treated for cancer. However, it was not feasible to recommend its use for children as it is not currently available in a form suitable, and licenced, for children.

A major task for any guideline development group is ensuring that the end product is user-friendly. The results of the peer-review process, whilst generally positive about the methodology, highlighted the need for a practical document that could be used easily on the ward. It is hoped that the 'At a glance' document, which allows for some local adaptation, is clear and succinct enough to be useful to both health care workers and parents and young adults, and will promote implementation of the guidelines. The development of parent/patient information leaflets based upon the findings of the guideline is encouraged at a local level, again to aid with the implementation of the guideline. Implementation is a huge issue for any guideline. It is hoped that the involvement of the relevant professions within the CCLG survey,[7] Delphi method and peer-review process, and the dissemination of Newsletters will help to increase the uptake of the guidelines. However, the publication and widespread dissemination of guidelines may not be enough to ensure their use. Further consideration needs to be given to the monitoring and promotion of their uptake. A great deal of time and effort goes into the development of valid and comprehensive guidelines. It is important to recognise that this process is just one small step towards the delivery of high quality, evidence-based health care. In order to reduce inappropriate clinical practice and improve patient outcomes, clinical guidelines that are deemed to be comprehensive, valid and relevant must be implemented.

## Conflict of interest statement

None declared.

## Acknowledgement

The CCLG is funded by a grant from Cancer Research UK (CRUK). The CCLG-PONF Mouth Care Group also received funding from CLIC-Sargent.

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