**Reviewer’s report**

**Title:** Assessment and prevention of behavioural and social risk factors associated with oral cancer: protocol for a systematic review of clinical guidelines and systematic reviews to inform Primary Care dental professionals

**Version:** 0  **Date:** 01 Oct 2015

**Reviewer:** Reint Meursinge Reynders

**Reviewer's report:**

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Submitted to: Systematic Reviews

Full Title: Oral cancer risk assessment and prevention for dental professionals: protocol for an overview of clinical guidelines and systematic reviews

Reviewer: Reint Meursinge Reynders

Date: September 30 2015

**SUMMARY OF COMMENTS**

I have tried not to be too decisive in what authors should do and have proposed some alternative options in undertaking a systematic review on the health condition 'oral cancer'. I have highlighted some areas where improvements can be made. Some of my comments could be out of place, but this is partly a result of the context of the current format of this protocol. I suggest to carefully assess my comments and consult the PRISMA-P 2015 statement and pertinent chapters of the Cochrane Handbook for systematic reviews of interventions. Since this research study is still in the protocol phase, the authors are in time to improve on this manuscript through major revisions of most sections of the article.

Six key comments are summarized under here:

1) **Prioritize treatment uncertainties**

This paper addresses oral cancer, which is a serious health condition. Great scrutiny is therefore necessary to design research protocols that prioritize treatment uncertainties. Besides literature searches, a variety of stakeholders (patients, carers, clinicians, and researchers) should be consulted to identify these uncertainties and to develop priority research questions in the field of oral cancer (Cowan 2013). For example the American Dental Association Council on Scientific
Affairs Expert Panel on Screening for Oral Squamous Cell Carcinomas have provided a list of recommendations for future research regarding screening for oral squamous cell carcinomas (Rethman 2010). Such recommendations should be consulted when developing research questions.

2) The rationale

The rationale for the objectives are not completely clear. On the one hand authors want to find out which interventions for preventing oral cancer are most effective (lines 32 and 33), but on the other hand they want to use the findings of this systematic review to explore the views of dental teams in Scotland on oral cancer prevention guidelines (Lines 196-199). Possibly the authors should aim at exploring the implementation/uptake of clinical guidelines of oral cancer.

3) Underreporting

Underreporting is a key problem. Many items of the PRISMA-P 2015 statement were not adopted.

4) Not a protocol for a systematic review

This paper is mostly a protocol for a narrative review (NOT a narrative systematic review) with some systematic elements.

5) Too broad-spectrum

The broad-spectrum character of this protocol could make it difficult to handle. One could split this protocol in 2 separate papers: One for methods for assessing risk factors of oral cancer and one for methods to prevent oral cancer.

6) Combining data sources

Combining data from systematic reviews and clinical guidelines is also complicated (issues of overlap). Assessing them separately or consulting only one of these sources or the other could be an option.

All comments are further explained under here and follow the order of each section of the manuscript.

TITLE

Comment on modifying the title

I would suggest to change the current title. However, all decisions on modifying the title depend on the objectives of the manuscript. Potential title: 'Risk factors and prevention of oral cancer: protocol of a systematic review of clinical guidelines and systematic reviews'.
ABSTRACT

Comment why the abstract was not critically appraised

I have not critically appraised the "Abstract", because various items in the following sections need to be resolved first.

BACKGROUND

Comment on knowledge gaps, why this study is important, and which stakeholders are involved

The condition 'oral cancer', its risk factors, and prevention are clearly explained in the 'Background section'.

However, I need additional information (concentrated in one section of the introduction) on the following issues:

1) What information is lacking?

2) Why it is important to obtain this information?

3) What are the stakeholders involved?

4) Who benefits? etc.

The authors base their rationale for their objectives on the following sentences:

1) (Lines 136 and 137) However it is often still hard to establish which components of interventions are most effective, particularly in dental practice settings [25].

2) (Lines 176-178) 'However, details of evidence based approaches for risk factor assessment and prevention need to be more clearly presented for dental professionals [33].'

This is an opinion paper by Lewis (2015). The authors do not further expand on the issues raised by this author.

3) (Lines 196-199) This systematic review is part of a wider study and will help design a mixed-method study (using an e-survey and semi-structured interviews) to explore the views of dental teams in Scotland on oral cancer prevention guidelines (e.g. evaluation of current knowledge, and barriers and facilitators to implementing guidelines).
I would like the authors of this protocol to address these issues and clearly explain what is lacking, because otherwise the research objectives do not make sense. The authors should also present additional evidence from the literature that this information is lacking and why it is important to obtain this information.

When presenting the rationale it is also necessary to carefully define the population, interventions, outcomes, time points, and settings on which the objectives will focus. For example, do the authors refer to a specific subgroup of the population and who are the pertinent stakeholders involved in dealing with the prevention of oral cancer? Are these stakeholders only general dentists or are they also specialists such as orthodontists, oral surgeons, periodontists etc.? And what about dental hygienists?

Further, it is necessary to explain who was involved in selecting the current research questions. Were patients or clinicians or both consulted to prioritize treatment uncertainties (Cowan 2013)?

I present some hypothetical reasons for conducting this research study:

1) Are current guidelines or systematic reviews outdated and need to be updated? If so present the evidence that they are outdated.

2) Are current guidelines or systematic reviews of poor quality and do the authors want to show the knowledge gaps? If so present evidence on the poor quality of the current guidelines or systematic reviews.

3) Do current guidelines or systematic reviews present differences in the effectiveness of methods of preventing oral cancer? If not present this evidence.

4) What is lacking in the current guidelines or systematic reviews? Maybe the current guidelines or systematic reviews only present risk factors for oral cancers, but do not present strategies to deal with them. If so present the evidence for this knowledge gap.

5) Is implementation of the current guidelines insufficient? Maybe guidelines are valid, but they do not get implemented. Possibly the barriers and facilitators to their use need to be identified and quantified. If so present the evidence for this problem etc.

OBJECTIVES

Comments on defining research questions
The objectives of this manuscript are not clear and precise. This is the result of: 1) the lack of a clear description of the rationale 2) not using a PICO format (or using elements from the PICO acronym). The use of this format is suggested by the PRISMA-P 2015 statement (Moher 2015, Shamseer 2015).

I therefore do not know which of the following PICOS (Participants, Intervention, Comparator, Outcomes, Setting) questions the authors want to address (I also consulted the section 'Main outcomes' lines 287-296 to get a better understanding of the objectives). Possibly the authors should even change their research questions completely (see my comment on asking implementation-related research questions at the end of this 'Objectives' section).

For the first objective I composed the following 'hypothetical' PIOS (Participants, Intervention, Outcomes, Setting) questions:

Option 1:
What are the methods for the assessment of risk factors of oral cancer used by dental professionals (O) on patients that visit dental practice settings (P)?

Option 2:
What methods for the assessment of risk factors of oral cancer used by dental professionals (I) on patients that visit dental practice settings (P) are considered best practice (Which are the most effective) (O)?

Option 3:
What is the quality (O) of the current methods for the assessment of risk factors of oral cancer conducted by dental professionals (I) on patients (P) that visit a dental practice setting (S)?

For the second objective I composed the following 'hypothetical' PICOS (Participants, Intervention, Comparator, Outcomes, Setting) questions:

Option 1:
What are the methods for preventing oral cancer used by dental professionals (O) on patients that visit dental practice settings (P)?

Option 2:
What methods for preventing oral cancer used by dental professionals (I) on patients that visit dental practice settings (P) are considered best practice (Which are the most effective) (O)?

Option 3:
What is the quality (O) of the current methods for preventing oral cancer conducted by dental professionals (I) on patients (P) that visit a dental practice setting (S)?

Option 4:
What is the effectiveness (O) of combined methods for preventing oral cancer when conducted by dental professionals (I) on patients (P) that visit a dental practice setting (S)?

Option 5:
What is the effectiveness (O) of combined methods for preventing oral cancer when conducted by dental professionals (I) compared with these methods conducted by physicians (C) on patients (P)?

Option 6:
What is the effectiveness (O) of communicating cancer risk (teachable moment) in the prevention of oral cancer when conducted by dental professionals (I) compared with these methods conducted by physicians (C) on patients (P)?

Option 7:
Are dental professionals (P) implementing (O) the current methods for preventing oral cancer (I)?

Option 8:
What are the barriers and facilitators (O) to the use of clinical guidelines on oral cancer (I) for dental professionals (P)(could also be interesting to include all potential stakeholder)

Note: Since outcomes of a treatment policy are preferably for the patients, I would recommend to avoid using (Line 189) 'To evaluate best practice for dental professionals'. But all depends on the decision, which research question to ask.

Comments on defining items

Various items have not been defined, i.e., Dental professionals (Do they include dental hygienists, oral surgeons and other specialists or only general practitioners), best practice, dental practice settings (university clinics, private practice, national health service systems etc.)

Comment on the broad-spectrum character of the research questions
The broad-spectrum character of both research questions of this protocol will make it difficult to handle. I suggest to split this manuscript in 2 separate papers: One for methods for assessing risk factors of oral cancer and one for methods to prevent oral cancer.

Comment on sociodemographic factors

In line 190: The adjunct 'taking into account the sociodemographic factors' should be excluded from the objectives, unless a specific group is excluded based on such factors. Sociodemographic factors can be explored later in subgroup analyses to assess whether dispersion of outcomes depends on such variables.

Comment on exclusion of a subgroup

In the 'Discussion' section (Line 347) the authors write: 'This study will identify best practice for oral cancer risk factor assessment and preventive interventions for dental professionals. This study will exclude early detection, screening and examination, as we (in the University of Glasgow Dental School) are undertaking another study assessing best practice for oral cancer early detection, screening and examination.

This issue of excluding a specific subgroup has not been presented prior to the Discussion and requires additional explanation.

Comment on prioritizing research uncertainties

This paper covers oral cancer, which is a serious health condition. Great scrutiny is necessary to design a research protocol that prioritize treatment uncertainties. A variety of stakeholders (patients, carers, clinicians, and researchers) should be consulted to identify these uncertainties and to develop adequate research questions.

Comment on asking implementation-related research questions

In lines 196-202 the authors explain that this systematic review will be used to explore the views of dental teams in Scotland on oral cancer prevention guidelines (e.g. evaluation of current knowledge, and barriers and facilitators to implementing guidelines). In that case implementation-related research questions could be more indicated. For example: undertaking a systematic review that identifies and quantifies barriers and facilitators to the use of oral cancer guidelines (prioritizing uncertainties).

METHODS
Comment on fine-tuning of sentences

1) The sentence starting in line 205 needs to be fine-tuned

2) In the sentence starting in line 208 the authors write that they followed the PRISMA-P recommendation. They should refer to this document as the PRISMA-P 2015 statement. The verb 'follow' is not appropriate. Indeed they consulted this document, but many important items were not considered by the authors.

ELIGIBILITY CRITERIA

Comments on subdividing the eligibility criteria in domains

The PRISMA P-2015 statement divides the study and report characteristics in various domains (Shamseer 2015). I recommend to adopt this framework of domains, because it improves the transparency of the eligibility criteria and facilitates future updating of the systematic review. The current description of the eligibility criteria needs to be expanded and fine-tuned. These issues are further explained under here.

Comment on study designs

A more thorough description of eligible clinical guidelines and systematic reviews is indicated. Definitions of eligible clinical guidelines should be provided. The word 'guideline' in the title does not mean that the publication is indeed a guideline (Rosenfeld 2013). Next to the AGREE instrument also The Conference on Guideline Standardization (COGS) checklist can be used to assess the validity of a clinical practice guideline (Shiffman 2003).

The eligibility of systematic reviews that include non-randomized studies should be further explained. Quality issues of such systematic reviews should be described. Are both primary and secondary outcomes of systematic reviews that address the research questions of this protocol eligible? etc.

In the sentence starting in line 217 the authors write 'The included systematic reviews will contain evidence for the effectiveness of interventions delivered in primary care (medical and dental) for preventing oral cancer via addressing risk factors. This sentence implicates that only systematic reviews that address the secondary objectives of this protocol will be eligible. What about systematic reviews that address the first objective 'Methods to assess risk factors for oral cancer'?

Comments on participants
A clear description of eligible participants is necessary. In the current eligibility criteria, no information is provided on the type of participants. For example are all age groups eligible?

Comments on interventions

Define oral cancer screening and define the context. Describe which methods for assessing risk factors for oral cancer are eligible. Describe which preventive methods for oral cancer are eligible. Eligible interventions are not described in this section.

This is particularly important, because in the discussion (line 347) the authors write: 'This study will identify best practice for oral cancer risk factor assessment and preventive interventions for dental professionals. This study will exclude early detection, screening and examination, as we (in the University of Glasgow Dental School) are undertaking another study assessing best practice for oral cancer early detection, screening and examination.

These sentences could imply that the authors want to exclude a particular subgroup of interventions. This should be defined in the eligibility criteria for interventions.

Comments on outcomes and timing

Eligible outcomes and endpoints important for decision making should be described and carefully defined.

Comments on the setting

Are there restrictions to the setting? Do the authors plan to include patients visited in private dental clinics, university clinics, through national health systems etc?

Comments on the language

Explain how language issues are dealt with. How do the authors plan to translate non-English guidelines and systematic reviews?

INFORMATION SOURCES

Comment on information sources for systematic reviews

The authors present a list of electronic databases for identifying systematic reviews, but information sources for the Grey literature are not presented. And what about searching Google
Scholar ? Issues to search MEDLINE through Pubmed or Ovid need to be discussed with an information specialist. There are advantages and disadvantages connected to both interfaces.

Comments on information sources for clinical guidelines

The authors present a list of electronic databases for identifying systematic reviews, but guidelines also need to be searched in other locations. The authors listed only 5 mostly UK based institutes that could provide additional guidelines. However, all databases consulted for the identification of clinical guidelines should be listed a priori in the protocol. Additional databases identified during the actual search process for the systematic review should be listed post-hoc in the final systematic review and should be labeled as 'post hoc'. It could be helpful to consult articles with similar objectives and assess which databases were consulted to find guidelines.

Under here I have listed some useful databases for guidelines that should be expanded upon by the authors of this protocol:


* American College of Physicians Clinical Practice Guidelines. [online] Available from: www.acponline.org/clinical_information/guidelines/guidelines/

* ADA Center of Evidence-Based Dentistry. [online] Available from: www.ebd.ada.org


* WHO programmes and projects. [online] Available from: http://www.who.int/entity/en/

* Institute for Clinical Systems improvement. [online] Available from: https://www.icsi.org/guidelines__more/
SEARCH STRATEGY

As described under 'Objectives', the authors did not use the PICO format for managing their clinical question. This acronym facilitates the identification of pertinent keywords. The authors have selected prevention, primary care, and risk factors as their 'Key terms'. But why not using 'oral cancer' as one of the building blocks of the search strategy since this is the health condition of interest?

DATA MANAGEMENT AND SELECTION PROCESS

Comment on duplicate publications

Authors should explain how they assess and deal with multiple publications of the same research data.

Comment on contacting authors

Authors should present a protocol for contacting authors in the case of uncertainties about the eligibility of an article.

DATA EXTRACTION

Comments on missing items

The authors combined 3 items of the PRISMA-P 2015 statement: Data collection process (Item 11c), Data items (Item 12), and Outcomes and prioritization (Item 13) into 1 item and named it 'Data extraction'. Important items were inappropriately eliminated during this fusion. I will list some of them under here.

Comment on data extraction operators

In the sentence starting in line 280, the authors write 'Data will be extracted from the included studies independently by two investigators (SM + 1 of AR/DC/LM), and using a pre-agreed template.

I would recommend to work with the same data operators for all data extraction procedures at all times.

Comment on data extraction form
I recommend to carefully define each extracted item in the data extraction form. This initially takes a lot of time, but significantly speeds up the data extraction procedures and reduces discussions and disagreements between reviewers. The PRISMA-P2015 statement under Item 12 addresses this issue as: 'List and define all variables for which data will be sought' (Shamseer 2015).

Comment on contacting authors

Authors should present a protocol for contacting authors in the case of uncertainties about data items in eligible studies.

Comment on the choice of the main outcomes

Authors should present a separate subheading titled as 'Outcomes and prioritization' (Item 13 of the PRISMA-P2015 statement). The authors should probably present their outcomes as primary and secondary outcomes.

Comments on the main outcomes were presented previously under the objectives. As explained earlier, I feel that the authors should simplify their research objectives and focus on 1 objective at a time. I therefore suggest the following options for topics or others

1) A protocol for a systematic review on methods for the assessment of risk factors of oral cancer

2) A protocol for a systematic review on methods for the prevention of oral cancer

3) A protocol for the assessment of the quality of clinical guidelines for oral cancer

4) A protocol for the assessment of implementation issues of clinical guidelines for oral cancer (e.g., quantifying the knowledge-to-action gap, identifying and quantifying barriers and facilitators to the implementation of clinical guidelines for oral cancer etc.)

Comment on defining the main outcomes

Besides listing the primary and secondary outcomes they should also be described in sufficient detail and with clear definitions and rationale (Shamseer 2015).

RISK OF BIAS (QUALITY) ASSESSMENT
Comment on risk of bias assessors

In the sentence starting in line 299, the authors write 'Quality assessment of the included clinical guidelines and systematic reviews will be carried out, again independently by two investigators (SM + 1 of AR/DC/LM)'. I would recommend to work with the same data operators for all data extraction procedures and all risk of bias assessments at all times.

Comment on the risk of bias assessment in systematic reviews using ROBIS

Since bias is a key fundament on which the validity of a research study is based, it is necessary (besides using the AMSTAR tool) to assess the risk of bias in systematic reviews using the ROBIS tool (Whiting 2015). Since this is a new tool, I recommend the authors to discuss this issue with the editors.

DATA SYNTHESIS

Comments on missing items

As in the section 'data extraction' the authors combined 3 items of the PRISMA-P 2015 statement: Data synthesis (Item 15), Meta-biases (Item 16), and Confidence in cumulative estimate (Item 17) into 1 item and named it 'Data synthesis'. Important items were inappropriately eliminated during this fusion. I will list some of them under here.

Comment on guidance for a narrative systematic synthesis

As suggested in the PRISMA-P 2015 statement (Shamseer 2015) authors should consult the guidance from the Centre for Reviews and Dissemination (CRD 2009), and the publications by Greenhalgh et al. (2005) and Popay et al. (2006). The current section 'Data synthesis' should be expanded based on these publications. Authors should list what data they want to present in the summary and findings tables and in which order. Authors should outline how risk of bias is dealt with. For example authors could plan a priori to exclude systematic reviews based on low quality evidence. Heterogeneity should be defined a priori, i.e. variables that could cause diversity should be listed and defined. Strategies for dealing with heterogeneity should also be described etc. Variables to consider for narrative subgroup analyses and sensitivity analyses were also not listed.

Comment on dealing with information from different sources

Since information in clinical guidelines is based on systematic reviews, a significant overlap of data sources (risk of duplicate bias) will probably be identified. How do the authors plan to deal
with this issue? They should present data from clinical guidelines and systematic reviews separately and should then assess where overlap has occurred. These strategies should be described in detail.

Actually the authors could also choose to only conduct a systematic review of systematic reviews and use clinical guidelines for another purpose for example: (1) to find potential missed systematic reviews (2) as background documents to structure the synthesis and the discussion.

Comment on the confidence in the cumulative estimate

The authors do not describe how they will assess the strength of the body of evidence. The outcomes from the ROBIS tool will play an important role in this assessment (Whiting 2015).

DISCUSSION

Comment on the exclusion

In (Lines 345-351) the authors write: 'This study will exclude early detection, screening and examination, as we (in the University of Glasgow Dental School) are undertaking another study assessing best practice for oral cancer early detection, screening and examination'.

However, this issue should have been presented in the eligibility criteria with the rationale.

Comments on the strengths and weaknesses of this manuscript

The authors should indicate the strengths and weaknesses of this manuscript and the rationale.

REFERENCES USED IN THIS PEER-REVIEW

Cowan 2013


CRD 2009

Greenhalgh 2005


Lewis 2015


Moher 2015


Popay 2006


Rethman 2010


Rosenfeld 2013

Shamseer 2015

Shiffman 2003

Whiting 2015

Level of interest
Please indicate how interesting you found the manuscript:

An article of importance in its field

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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