



Mathur, S., Conway, D. I., Macpherson, L. M.D. and Ross, A. J. (2022) Systematic overview of systematic reviews and clinical guidelines: assessment and prevention of behavioural risk factors associated with oral cancer to inform dental professionals in primary care dental practices. *Evidence-Based Dentistry*, (doi: [10.1038/s41432-022-0235-1](https://doi.org/10.1038/s41432-022-0235-1)).

This is the Author Accepted Manuscript.

There may be differences between this version and the published version. You are advised to consult the publisher's version if you wish to cite from it.

<http://eprints.gla.ac.uk/267675/>

Deposited on: 12 May 2022

Enlighten – Research publications by members of the University of Glasgow
<http://eprints.gla.ac.uk>

Systematic Overview of Systematic Reviews and Clinical Guidelines: assessment and prevention of behavioural risk factors associated with oral cancer to inform dental professionals in primary care dental practices

Sweta Mathur*¹, David I. Conway², Lorna M.D. Macpherson², Alastair J. Ross²

Sweta Mathur: mathursweta@outlook.com

David I. Conway: david.conway@glasgow.ac.uk

Lorna M.D. Macpherson: lorna.macpherson@glasgow.ac.uk

Alastair J. Ross: alastair.ross@glasgow.ac.uk

Institution: ¹Kaiser Permanente Center for Health Research, Portland, OR, U.S.A.

²School of Medicine, Dentistry, and Nursing, University of Glasgow, U.K.

*Corresponding author:

Sweta Mathur: mathursweta@outlook.com

10317 Bilston Ct, Apt 4, Saint Louis, MO-63146, USA

ABSTRACT

Aims/Objectives: Tobacco and alcohol are recognised as the major modifiable risk factors for oral cancer, the incidence of which is rising globally and predicted to increase. This paper aimed to a) appraise and synthesise best practice evidence for assessing the major behavioural risk factors for oral cancer and delivering behaviour change interventions (e.g. advice, counselling, signposting/referral to preventive services) and b) assess appropriateness for implementation by dental professionals in primary care.

Methods: A systematic overview was undertaken of systematic reviews and international clinical guidelines. This involved: systematically searching and collating the international literature on assessing oral cancer risk and delivering preventive interventions within primary care, quality appraising and assessing the risk of bias using validated tools, synthesising the evidence for best practice, and assessing application of key findings to the dental setting.

Results and Conclusions: There is clear evidence for the effectiveness of a “brief”, in-person, motivational intervention for sustained tobacco abstinence or reduced alcohol consumption, following risk factor assessment. Evidence for combined behavioural interventions is lacking. There is no firm conclusion with regards to optimal duration of brief interventions (ranged 5-20 minutes). For tobacco users, longer (10-20 minutes) and intensive (more than 20 minutes, with follow-up visits) interventions are more effective in increasing quit rates compared to no intervention; very brief (less than 5 minutes) interventions in a single session show comparable effectiveness to the longer / more intensive interventions. For alcohol users, 10-15 minutes multi-contact interventions were most effective, compared to no intervention or very brief (less than 5 minutes) intervention or intensive intervention; brief interventions of 5-minutes duration were equally effective. There is limited direct evidence from the dental practice setting (one high-quality systematic review relating to tobacco prevention and none relating to alcohol). Thus, very brief, or brief advice of up to 5 minutes, should be trialled for tobacco and alcohol respectively in a dental practice setting, after risk assessment tailored to patient motivational status. Exploring delivery by the dental team is supported, as effectiveness was generally independent of primary care provider.

Systematic review registration: PROSPERO CRD42015025289

Keywords: Oral cancer, prevention, tobacco, alcohol, primary care, dental professionals, Systematic Reviews, clinical guidelines

INTRODUCTION

The incidence of oral cancer continues to rise globally and in the UK, with a steady increase in oral cavity cancer rates and a rapid increase in oropharyngeal cancer rates in the last decade.^{1,2} In Scotland, between 2001 and 2012 there was a dramatic increase in oropharyngeal cancer cases (85%), while incidence rates remained relatively unchanged for oral cavity cancer (10% increase).² These rates are projected to increase further over the next decade, so there is a pressing need to optimise oral cancer prevention strategies.^{1,2}

There is a significant increased risk for oral cancer among lower socioeconomic groups, males, and older age groups³ and recent recognition of the role of human papillomavirus in the aetiology of oropharyngeal cancers.⁴ However, tobacco and alcohol use are recognised as the major modifiable risk factors for developing oral cancers (oral cavity and oropharyngeal cancers).^{5,6} These modifiable behaviours are also associated with a wide range of diseases affecting oral and general health and are thus denoted as ‘common risk factors’, increasing the public health benefit should they be tackled.⁷

There is therefore a clear need to implement optimal preventive interventions in dental primary care.⁸ However, there are remaining uncertainties about the best evidence for particular strategies and approaches to assessing risk, giving advice, or referral to specialist counselling or cessation services.⁸ A particular evidence gap relates to the specific form and content of such interventions (for example: tailoring to need/ assessing risk, duration, who delivers).⁸⁻¹¹ Most previous studies have been carried out in medical or community pharmacy settings^{12,13} leading to a number of items of clinical guidance.^{14,15}

Thus, the main aim of this paper was to provide a comprehensive overview of Systematic Reviews (SRs) and Clinical Guidelines (CGs) from across primary care to make recommendations for dental practice in relation to assessing/ targeting the major behavioural risk factors (tobacco smoking and alcohol drinking) associated with oral cancer and delivering preventive interventions. Specific objectives were: to assess best practice for assessing risks and facilitating behaviour change; to assess commonality and/or divergence between SR evidence and CG recommendations; to assess feasibility for the dental setting.

METHODS

The study protocol details the methodology for this systematic overview, which was registered with PROSPERO (registration number CRD42015025289) and implemented without any changes has previously been published.¹⁶ The overview was framed in accordance with the PICOS (Population, Intervention, Comparator, Outcomes, and Setting) format and findings were reported using the PRISMA statement for reporting of SRs and meta-analyses.¹⁷

Search Strategy

Search terms were identified from scoping the initial literature and from MeSH subject headings. The search was not limited to oral cancer studies so as to include interventions aimed at another clinical condition (for example, smoking cessation strategies targeting periodontal disease).¹⁸ The literature search for SRs and CGs was carried out in August 2015 and updated in August 2018, in the following electronic databases: Cochrane Library, Ovid MEDLINE, EMBASE, Web of Science, PsychINFO, PubMed, TRIP, and Google Scholar.

An internet search of the websites of health boards and relevant (professional, medical, dental, public health, scientific) organizations/agencies was also carried out. The bibliographies or reference lists of identified documents were also hand-searched for additional references. Experts in the area were contacted to help locate any unpublished and ongoing research as the overview proceeded to minimise publication bias. The Ovid MEDLINE search strategy is provided in the protocol¹⁶ and was adapted for other databases. Key terms were organised according to three subsets:

- Prevention (for example: advice, cessation, harm reduction, brief intervention, counselling);
- Primary care (for example: general dental practice, general medical practice, pharmacy);
- Risk factors (for example: tobacco, alcohol)

Inclusion and Exclusion Criteria

SRs or meta-analyses (of randomised and non-randomised studies) and CGs (published/e-learning) available worldwide were included in this systematic overview. Papers were included from all primary care settings (dental/medical/pharmacy) if describing in-person or face-to-face preventive interventions (including risk factor assessment, behavioural advice,

and/or signposting/referral) for tobacco and alcohol. No language restrictions were applied. Two non-English papers were translated to English with the help of Google Translate and private translation services. CGs were limited to the last 10 years (2006 to 2015). There were no date restrictions for SRs. Narrative/literature reviews and SR protocols were excluded.

Data Management and Extraction

In accordance with Cochrane review group guidance, all steps in data management (review of titles and abstracts, inclusion and exclusion decisions, data extraction, quality appraisal, assessing risk of bias, collating themes for final synthesis) were carried out independently by two members of the multidisciplinary review team (author (SM) + one of three supervisors (AR/DC/LM)), and discrepancies discussed. The data extraction form was pilot tested on a small set of papers (three SRs and three CGs) and refined to ensure sensitivity and specificity.

Quality Appraisal

In order to assess the methodological quality and risk of bias of included SRs, the AMSTAR (A MeaSurement Tool to Assess systematic Reviews) and the ROBIS (Risk Of Bias In Systematic reviews) tools were used respectively.^{19, 20} The quality of the included CGs was appraised using the AGREE II (Appraisal of Guidelines for REsearch & Evaluation II) instrument.²¹

Data Synthesis

The general frameworks for conducting narrative ('thematic') synthesis developed by the Economic and Social Research Council (ESRC) Methods Programme²², along with guidance from the Centre for Reviews and Dissemination²³, and Petticrew and Roberts²⁴ were adopted for conducting a narrative synthesis for the overview. A final integrated/combined synthesis then compared and contrasted evidence from the reviews and guidelines streams. The narrative synthesis assessed the best practice evidence by taking quality and recency of evidence into account, giving higher weighting to dental findings, and considering higher quality and more recent medical/pharmacy findings applicable in a dental practice setting - informed by the ADAPTE framework.²⁵

RESULTS

Systematic Reviews (SRs)

The search strategy retrieved 1727 potentially relevant records. Title and abstracts were screened independently by two reviewers (SM and AJR) and of these, 72 records were selected for full text review. 28 SRs were included after discussion and a few discrepancies were discussed with the wider team (DC and LM). Three additional SRs were included through hand searching of the reference lists of the 28 included SRs. Thus, finally 31 SRs were included in this overview (Figure 1). References to all included SRs is provided in Table S1. A list of excluded studies (n=44) was presented with the reasons for exclusion (Table S2).

As might be expected there was trial duplication or overlap in the included SRs, i.e. reviews included some trials in common. To address this, a list of all authors of all primary studies/trials referenced by all included SRs was created, sorted, and labelled to identify publications which appeared two or more times on the list.²⁶ Where duplicates were identified, overview results based on individual trials have been synthesised here from higher quality/ more recent SRs. This avoided overstressing the evidence-base by accumulating SR results which themselves drew from the same evidential sources, thus biasing findings. The 31 SRs reviewed a total of 171 discrete original trials of face-to-face preventive interventions in a primary care setting (i.e., after removing duplicates).

The main characteristics and findings of the included 31 SRs are presented in Table S3 (for example: target risk factors, included preventive interventions, intervention provider, study quality, type of synthesis and outcomes). Study IDs (from Table S1) are used to reference cohort SRs in the text of this paper. The included SRs were relatively heterogeneous in that they covered different primary care settings (dental/medical/pharmacy), risk factors (tobacco/alcohol) and preventive interventions (motivational interviewing/cognitive behavioural therapy). Preventive interventions also varied with respect to: duration of individual sessions; total number of sessions; follow-up visits; and provider training.

The AMSTAR scores for all SRs are included in Table S4; only two SRs met all 11 criteria in AMSTAR (SR: 1, 16). This overview identified ten high-quality SRs (score range from 8 to 11), 18 mid-quality (score 4 to 7), and three low-quality SRs (score 0 to 3). The ROBIS scores for all SRs are included in Table S5. Figure 2 shows AMSTAR and ROBIS scores. It

can be seen that high AMSTAR score SRs were correlated with low risk of bias in ROBIS and vice-versa, while risk of bias was unclear in some SRs.

In this paper, the high-quality evidence/findings are presented from all low risk of bias (low ROBIS) reviews, giving priority in the narrative data synthesis to: firstly, high-quality AMSTAR scores with low risk of bias in ROBIS (n=10); and secondly to mid-quality AMSTAR scores but with low risk of bias in ROBIS (n=5). Key findings from these high-quality SRs are shown in Table 1. There was only one high-quality SR in the dental practice setting relating to smoking cessation and no reviews at all on alcohol reduction. However, best practice recommendations have been developed from synthesising the best evidence from other primary care (medical/pharmacy) settings, which could be adapted/adopted for dental practice, along with synthesising the best quality available guidance (discussed later). There were 13 high-quality reviews (SR: 1, 2, 6, 7, 8, 10, 11, 16, 17, 22, 24, 25, 27) of preventive interventions delivered in a primary care medical or community pharmacy setting. Of these, eight SRs included trials/studies with preventive interventions solely for smoking (SR: 1, 2, 6, 8, 10, 16, 24, 27), four reviews included studies with preventive interventions for alcohol only (SR: 11, 17, 22, 25), while one review (SR 7) included studies delivering preventive interventions for both smoking and alcohol separately; none of the studies included combined interventions targeting both smoking and alcohol.

The dental review (SR 12) demonstrated the effectiveness of brief (or very brief) interventions delivered by trained dental professionals incorporating an oral examination component (compared to no intervention or usual care) in increasing tobacco abstinence rates for at least 6 months (OR=1.71, 95%CI 1.44, 2.03; n=14 trials) among cigarette smokers and smokeless tobacco users. The effect was stronger in the adult smokers (OR=2.38, 95%CI 1.70, 3.35; n=5 trials) compared to smokeless tobacco users (OR=1.70, 95%CI 1.36, 2.11; n=6 trials). Though the review showed no additional benefit of intensive intervention (gauged by number of personal contact) over brief intervention, there was a lack of reporting of effect sizes comparing both. The dental review (SR 12) concluded that: “Differences between the studies limit the ability to make conclusive recommendations regarding the intervention components that should be incorporated into clinical practice, however, behavioural counselling (typically brief) in conjunction with an oral examination was a consistent intervention component that was also provided in some control groups.”

The nine high-quality medical practice reviews show that theory-based ‘brief’ interventions (motivational interviewing in particular) delivered by primary care professionals in a single session, following an assessment of a patient’s smoking status, are effective (compared to no intervention or simple advice) in increasing smoking cessation rates. The lack of precise reporting of intervention duration and number of sessions (brief intervention described as 5-20 minutes) somewhat limited the inferences regarding duration of sessions that can be drawn. It was reported that although longer interventions (10-20 minutes) were more effective in increasing quit rates, even very brief interventions of as little as 2-minutes have also been shown to be effective (RR 1.66, 95% CI 1.42 to 1.94). There was a small additional benefit of more intensive interventions (more than 20 minutes, and more than one follow-up visits) compared to brief (or very brief) interventions (RR 1.37, 95% CI 1.20 to 1.56). Interventions were reported to be effective if delivered by a primary care professional with minimal training in theory-based approaches, however, effect sizes were not reported to compare interventions delivered by professionals without training. Moreover, the exact training characteristics to deliver the intervention require better reporting and clarification by future researchers. Additional components (i.e., written materials, self-help aids) were reported to support behavioural advice, however, again, effect sizes were not reported to compare interventions ‘with’ versus ‘without’ supporting materials. Furthermore, this overview shows a lack of trials reporting effect sizes for referral pathway compared with behavioural advice for smoking cessation in primary care settings.

All high-quality SRs for reducing alcohol consumption established that brief (10-15 minutes) multi-contact (two or more follow-up visits over a year) motivational interventions were most effective (consumption decreased by 3.6 drinks per week from baseline; 95% CI, 2.4 to 4.8 drinks/wk) (SR 11); interventions of up to 5 minutes duration were also reported to be effective in equally higher quality review (mean difference: -38 grams/week, 95% CI: -54 to -23) (SR 17). Intensive interventions were also reported to be effective, however, where compared, the reported effect rates were smaller for intensive compared to brief interventions (non-significant; SR 11). There was little evidence for the effectiveness of very brief (less than 5 minutes) interventions in reducing alcohol consumption (5-8% increased abstinence in very brief versus 7-12% in brief intervention) (SR 11).

The effective brief advice was supported by written materials or self-help manuals, however, comparison of intervention ‘with’ and ‘without’ supporting materials was lacking. We found an overall lack of studies reporting on local referral pathways for reducing alcohol consumption and their effectiveness compared to brief interventions or usual care (referral to specialist services was indicated in cases of alcohol dependence only). And there was limited evidence on whether signposting or formally referring to specialist services would be more effective for ensuring patients attended or were followed up.

Lastly, this overview showed a lack of combined interventions for smoking and alcohol (only isolated interventions were reported).

Clinical Guidelines (CGs)

The search strategy retrieved 2477 potentially relevant records through database searches and 12 additional records were identified through organization or health board website searches. All included records were screened (title and abstract) and of these, 59 records were selected for full text review. Finally, 26 CGs were included in this overview (Figure 3), references to which are provided in Table S1. The reference lists of the included CGs were hand searched for any relevant CGs (and SRs) to be included in this overview. Some of the referenced SRs (which met our inclusion criteria) in the included guidelines were already included in this overview (SR: 1, 6, 8, 12, 16, 27). A list of excluded guidelines (n=32) was presented with the reasons for exclusion (Table S2).

Included CGs were from different countries/regions across the world: Australia, Europe, India, New Zealand, United Kingdom, and United States. Table S6 presents the various recommendations made about the assessment of major risk factors and delivering behavioural preventive interventions for each of the included CGs (n=26), along with target risk factors, and target users for these guidelines.

The quality of all included CGs was assessed using the AGREE II instrument (Table S7); there were 11 high-quality guidelines (score 6 or 7), 15 mid-quality guidelines (score ranged from 3 to 5), and no low-quality guidelines (score of 1 or 2). As with the SR synthesis, high-quality recommendations are synthesised here, with preference given to recency of publication and the level of evidence for particular recommendations within high-quality guidelines. Data duplication, i.e., previous guidelines or SRs (used for developing guidelines)

was also considered while presenting findings. The key recommendations from high-quality CGs are presented in Table 2.

Of the 11 high-quality guidelines, there was only one guideline (CG 11) which provided recommendations for delivering behavioural preventive interventions delivered exclusively in a primary care dental setting. This guideline was developed by the *Scottish Dental Clinical Effectiveness Programme* (SDCEP) and met all criteria in AGREE II. This guidance presented clear and consistent advice to support dental professionals to deliver preventive interventions for both smoking (or smokeless tobacco) and alcohol (Table 2). Overall, it is recommended that practitioners record a patient's smoking (or tobacco use) status as part of social history, assess patient's risk levels, and offer very brief opportunistic advice (for a few minutes). It is further recommended to offer information on 'quit-lines' or local stop smoking services. However, not all recommendations made are supported by research evidence. For alcohol, practitioners should assess a patient's alcohol consumption (using screening tools), and follow this with very brief advice/discussion to outline and discuss the possible harmful effects of excessive alcohol consumption, and then recommend that patients visit their general medical practitioner for further advice and help. However, there is no research evidence reported to support these recommendations. Thus, further guidance is required (supported with evidence) regarding delivering effective behavioural alcohol intervention in a dental practice setting.

The remaining 10 high-quality guidelines (CG: 1, 2, 5, 12, 14, 17, 18, 21, 22, 23) included interventions delivered in a primary care medical or community pharmacy setting (Table 2). Five of these guidelines (CG: 17, 18, 21, 22, 23) also included dental professionals as their target users. For smoking cessation, it is recommended to ask, assess, and record a patient's tobacco use status in the clinical records, and offer an opportunistic 'brief' tailored intervention to all smokers (or tobacco users) by a trained primary care provider (although no evidence to support effectiveness of training), to increase abstinence rates; with some guidelines recommending very brief intervention – but this had little evidence base. Intensive interventions (more than 20 minutes) have a small additional effect on quit rates (in line with SR evidence; Table 1). Again, the duration of effective interventions recommended ranged from as little as 3 minutes to 20 minutes or even more, thus making it difficult to determine a precise specification of the intervention duration. It is further recommended, if the patient is willing to quit, to make referral to quit-line services (proactive support) for further help

which were reported to be effective along with brief intervention and pharmacotherapy to increase abstinence rates (RR 1.29; 95% CI: 1.20–1.38). Thus, the recommendations seem to be much stronger from CGs regarding referral to cessation services than came through from SRs in the medical practice setting. In addition, it is recommended that primary care providers support advice with feedback, written materials, and follow-up support, however, again there is no direct evidence to support its effectiveness.

For alcohol reduction interventions in primary care medical practice, the recommendation is that practitioners ask, assess, and record an adult patient's alcohol use in the clinical records. Use of validated screening tools (for example, AUDIT, AUDIT-C, CAGE) is recommended for assessing alcohol risk levels. Following alcohol risk assessment, a brief (10-15 minutes) multi-contact intervention (two or more sessions) delivered by a trained provider is most effective. Very brief interventions of less than 5 minutes are also recommended, but the evidence reported is weaker compared to the longer interventions to support this recommendation. Where needed, for example if patient is dependent on alcohol, referral to specialist alcohol treatment services is recommended. Advice should be supported with written materials, self-help materials, and/or goal-setting. However, research evidence for the latter is lacking.

Again, as with SRs, none of the CGs recommended offering combined interventions for tobacco and alcohol.

Data synthesis

Most of the high-quality SR evidence and CG recommendations were in accordance with each other, i.e., guidelines were based on the review evidence (Table 1 and 2). However, there were some areas where evidence and guidance were lacking, for example, there were no validated screening tools reported for assessing a patient's tobacco use status in all high-quality reviews and guidelines. This has implications for the use of tobacco risk assessment tools in a primary care practice. In addition, high-quality reviews and guidelines in the dental practice setting were lacking with regard to evidence of effectiveness of interventions for reducing alcohol consumption. All the high-quality advice for alcohol came from the primary care medical practice settings. Thus, there is a need for more studies to evaluate the effectiveness of behavioural alcohol interventions in a primary care dental practice setting.

Overall, the integrated findings from this overview identified that risk factor assessment is an important first step in any prevention intervention (i.e., questions must be asked to assess the risk levels or dependence). Regarding tobacco cessation intervention, it was found that an appropriate intervention would be to offer an in-person brief motivational, tailored intervention, delivered by dental professionals, in a single session, following an assessment of a patient's tobacco use status (risk levels) and incorporating an oral examination component. Although longer (10-20 minutes) and intensive (more than 20 minutes, with follow-up visits) interventions have shown to be effective in increasing quit rates compared to shorter interventions, very brief (less than 5 minutes) interventions also showed comparable effectiveness to the longer brief or intensive interventions.

For alcohol drinkers, after assessing the patient's alcohol use or dependence (using validated screening tools), a brief motivational, tailored intervention, delivered by dental professionals, could be offered to motivate alcohol users to reduce consumption in a dental practice setting. A brief 10-15 minutes multi-contact intervention was the best recommended intervention in medical practice reviews and guidelines for helping alcohol users to reduce consumption; brief interventions of 5 minutes duration were also reported to be equally effective. Thus, very brief (less than 5 minutes) or brief advice (of up to 5 minutes), should be trialled for tobacco and alcohol respectively in a dental practice setting (considering feasibility and effectiveness as reported in reviews and guidelines), tailored to patient motivational status. Exploring use of the dental team is supported, as effectiveness was generally independent of primary care provider (i.e., general practice physician or nurse).

DISCUSSION

This study was novel in synthesising evidence from both SRs and CGs for undertaking a risk factor assessment and delivering preventive interventions for major behavioural risk factors associated with oral cancer (tobacco and alcohol). The overview went beyond the review and trial evidence, and contributed to the knowledge by developing a robust framework for integrated or combined evidence synthesis (narrative 'thematic') across these information sources, addressing review/guideline quality, recency and duplication. Reported findings were based on a much greater body of research in the primary care medical practice setting compared to the limited research undertaken in the dental practice setting. Informed by the ADAPTE framework,²⁵ which provides a systematic approach to adapting guideline developed in one setting for use in another setting, the high-quality evidence and

recommendations in the primary care medical/pharmacy setting in this overview were adapted to develop recommendations relevant to the dental practice setting.

This overview describes transferrable best practice from medical practice settings for dental professionals who interact with smokers (or tobacco users) in the clinical setting. The results from another overview study by Ramseier and Suvan,¹⁰ that aimed to improve periodontal health, supports these findings, and showed the effectiveness of tobacco use cessation interventions in the primary care dental practice. The effect size reported in the study by Ramseier and Suvan¹⁰ was similar to that reported in this overview (OR 2.38; 95% CI 1.70–3.35) with regards to increased odds of quitting tobacco. However, it failed to report the type of intervention, optimal length, and frequency of interventions for effective tobacco cessation; and showed a need for further research in this field.¹⁰ A similar lack of dental evidence was reported in reviews and guidelines included in this overview study, i.e., insufficient number of studies to determine the specific support measures delivered by dental professionals to provide an increased effectiveness beyond brief advice.^{9, 18}

Dental professionals are in an ideal position to provide brief alcohol advice to their patients. Despite, this opportunity, there is a lack of studies developing and evaluating alcohol brief interventions in a dental practice setting. Moreover, studies have reported various barriers to the successful implementation of these brief interventions in a dental practice, some of the barriers reported in previous feasibility studies being: lack of knowledge, skills, confidence, and time, and even doubts about the effectiveness of counselling.²⁷⁻³⁰ The lack of evidence supporting the effectiveness of brief alcohol reduction interventions in primary care dental practices, in comparison to other primary care medical practice settings, has been reported in other existing literature.^{10, 31, 32}

As discussed in the study protocol, multiple risk factors need to be considered for oral cancer prevention, as tobacco and alcohol in combination magnifies the risk for oral cancer. However, combined interventions were almost completely lacking in this overview. Other existing reviews and guidelines have also reported a similar lack of evidence focusing on the most effective approach to deal with multiple behaviours (for example, if someone smokes, and consumes alcohol above recommended limits).^{33, 34} The question thus remains: whether these behaviours should be approached in sequence or in combination, and how this should be decided? Hence, further investigation is needed to address this large gap in knowledge

about the effectiveness of multifactorial or combined interventions, incorporating both smoking and alcohol advice in a primary care setting, including dental practice.

Strengths and limitations

This extensive overview involved a systematic literature search (international literature, no language restriction, and grey literature search for CGs). The systematic search was not limited to “oral cancer” and “dental setting”, thus the overview did not rule out good guidelines and/or evidence on how to assess risk and deliver prevention for tobacco/alcohol, that may be aimed at another clinical/medical condition (e.g., lung cancer, periodontal or cardiovascular disease).^{18, 35, 36} A robust quality appraisal was carried out to assess the methodological quality of included SRs (AMSTAR and ROBIS), and CGs (AGREE II) independently by two reviewers, and discrepancies discussed with the wider team. This helped to ensure the rigour of findings. Moreover, the duplication of trials in all included SRs, and duplication of guidelines and reviews within all included CGs was addressed, i.e., none of the findings were synthesised twice, thus strengthening the robustness of the overview synthesis.

One of the main study limitations concerned the limited number of SRs in the dental practice setting, which resulted in restrictions and in extrapolating findings from other settings (medical/pharmacy) to the dental practice setting. The heterogeneity among study populations, settings and outcomes were explored as an integral part of data synthesis, but as this work was not meta-analytic, a narrative synthesis approach was used to address the applicability of findings across, professional groups and/or patient behaviours. Interpretation and recommendations were limited by lack of consensus in definitions of brief, very brief, and intensive interventions. Additionally, there was limited information provided on many occasions regarding details of interventions covered.

Furthermore, there was very limited evidence available in terms of effect sizes for some interventions that both the SRs and CGs were to some extent recommending. This included referral to specialist services and the use of patient educational materials such as posters and leaflets. Thus, this heterogeneity (and limited information) constrained the ability to make conclusive recommendations regarding which components of behavioural preventive interventions should be incorporated into primary care practices.

CONCLUSION

In conclusion, this overview shows a lack of direct evidence from the dental practice setting (one high-quality SR relating to tobacco prevention and none relating to alcohol). However, relatively strong evidence and recommendations from other primary care (medical/pharmacy) settings were identified and synthesised, which could potentially be adapted and adopted by dental professionals. Thus, very brief or brief advice of up to 5 minutes, should be trialled for tobacco and alcohol respectively in a dental practice setting, after risk assessment tailored to patient motivational status. Exploring delivery by the dental team is supported, as effectiveness was generally independent of primary care provider.

Supplementary Files

Table S1: References to studies included in this overview

Table S2: List of excluded studies at the full-text screening stage with reasons for exclusion

Table S3: Characteristics and main findings from all included Systematic Reviews (n=31)

Table S4: AMSTAR scores for included Systematic Reviews (n=31)

Table S5: ROBIS scores for included Systematic Reviews (n=31)

Table S6: Recommendations from all included clinical guidelines (n=26) about oral cancer risk factor assessment and delivering preventive interventions

Table S7: Quality scores of clinical guidelines for the six domains of the AGREE II Instrument (D 1–D 6) and the overall quality

Abbreviations

AGREE II: Appraisal of Guidelines for Research & Evaluation II; AMSTAR: A Measurement Tool to Assess Systematic Reviews; CG: Clinical Guideline; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SDCEP: Scottish Dental Clinical Effectiveness Programme; SR: Systematic Review.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

SM wrote the first draft of the manuscript, with feedback from other authors. SM, AJR, DIC and LMDM participated in the study design, development, refinement of the methodological

approach, quality appraisal, and synthesis. All authors contributed to revising manuscript, and all authors read and approved the final manuscript.

Acknowledgements

The project has received funding from NHS Education for Scotland and the Glasgow Dental Educational Trust. The study is ethically approved by the University of Glasgow College of Medical, Veterinary & Life Sciences Ethics Committee. We gratefully acknowledge the input and feedback provided by John Gibson, Andrea Sherriff, Heather Worlledge-Andrew, and Naeema Al-Balushi. The views expressed are those of the authors and not necessarily those of any of the funders or organizations they represent.

REFERENCES

1. Shield KD, Ferlay J, Jemal A, Sankaranarayanan R, Chaturvedi AK, Bray F, et al. The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. *A Cancer Journal For Clinicians*. 2017;67(1):51-64.
2. Conway DI, Purkayastha M, Chestnutt IG. The changing epidemiology of oral cancer: definitions, trends, and risk factors. *British Dental Journal*. 2018;225:867.
3. Winn D, Lee YC, Hashibe M, Boffetta P. The INHANCE consortium: toward a better understanding of the causes and mechanisms of head and neck cancer. *Oral Diseases*. 2015;21(6):685-93.
4. Gillison ML, Chaturvedi AK, Anderson WF, Fakhry C. Epidemiology of human papillomavirus-positive head and neck squamous cell carcinoma. *Journal of Clinical Oncology*. 2015;33(29):3235.
5. IARC. International Agency for Research on Cancer working group on the evaluation of carcinogenic risks to humans. Tobacco smoke and involuntary smoking v.83: World Health Organization; 2004.
6. IARC. International Agency for Research on Cancer monographs on the evaluation of carcinogenic risks to humans. Alcoholic drinking v.96. Lyon: World Health Organization; 2007.
7. Sheiham A, Watt RG. The common risk factor approach: a rational basis for promoting oral health. *Community Dentistry and Oral Epidemiology*. 2000;28(6):399-406.

8. Petersen PE. Oral cancer prevention and control—the approach of the World Health Organization. *Oral oncology*. 2009;45(4):454-60.
9. Carr AB, Ebbert J. Interventions for tobacco cessation in the dental setting. *Cochrane Database of Systematic Reviews*. 2012;6:CD005084.
10. Ramseier CA, Suvan JE. Behaviour change counselling for tobacco use cessation and promotion of healthy lifestyles: a systematic review. *Journal of Clinical Periodontology*. 2015;42 Suppl 16:S47-58.
11. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *The Lancet*. 2003;362(9391):1225-30.
12. Kaner EFS, Dickinson HO, Beyer FR, Campbell F, Schlesinger C, Heather N, et al. Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database of Systematic Reviews*. 2009;4(CD004148):CD004148.
13. Lindson-Hawley N, Thompson Tom P, Begh R. Motivational interviewing for smoking cessation. *Cochrane Database of Systematic Reviews [Internet]*. 2015; 3(3). Available from: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006936.pub3/abstract>.
14. WHO. WHO framework convention on tobacco control: report of the first sub-regional awareness raising workshop: Kathmandu, Nepal, 18-19 March 2004: Regional Office for South-East Asia: World Health Organization; 2004.
15. WHO. Public health problems caused by harmful use of alcohol: Report by the Secretariat. Geneva: World Health Organization; 2005.
16. Mathur S, Conway DI, Worlledge-Andrew H, Macpherson LMD, Ross AJ. 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. *Systematic Reviews*. 2015;4(1):1.
17. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine*. 2009;151(4):264-9.
18. SDCEP. Prevention and treatment of periodontal diseases in primary care: Dental Clinical Guidance. Dundee: Scottish Dental Clinical Effectiveness Programme. Evidence-based dentistry. 2014;15(3):1-116.
19. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BioMed Central Medical Research Methodology*. 2007;7(1):10.

20. Whiting P, Savović J, Higgins JP, Caldwell DM, Reeves BC, Shea B, et al. ROBIS: a new tool to assess risk of bias in systematic reviews was developed. *Journal of Clinical Epidemiology*. 2016;69:225-34.
21. Consortium ANS. AGREE Next Steps Consortium. The AGREE II instrument (electronic version) 2009 [Available from: <http://www.agreetrust.org>].
22. Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, et al. Guidance on the conduct of narrative synthesis in systematic reviews: A product from the ESRC Methods Programme. Version 1. 2006.
23. CRD. Systematic reviews: CRD's guidance for undertaking reviews in health care: York: University of York NHS Centre for Reviews and Dissemination; 2009.
24. Petticrew M, Roberts H. Systematic reviews in the social sciences: a practical guide: Blackwell Publishing (John Wiley & Sons); 2008.
25. Collaboration A. The ADAPTE process: resource toolkit for guideline adaptation (version 2.0). Guidelines International Network ([wwwg-i-nnet](http://www.g-i-n.net)). 2009.
26. Dijkers M. Duplicate publications and systematic reviews: problems and proposals. *KT Update: An e-newsletter from the Center on Knowledge Translation for Disability and Rehabilitation Research*. 2018;6(2):2.
27. Macpherson LMD, McCann MF, Gibson J, Binnie VI, Stephen KW. The role of primary healthcare professionals in oral cancer prevention and detection. *British Dental Journal*. 2003;195(5):277-81.
28. Shepherd S, Young L, Clarkson JE, Bonetti D, Ogden GR. General dental practitioner views on providing alcohol related health advice: an exploratory study. *British Dental Journal*. 2010;208(7):5.
29. Amemori M, Michie S, Korhonen T, Murtomaa H, Kinnunen TH. Assessing implementation difficulties in tobacco use prevention and cessation counselling among dental providers. *Implementation Science*. 2011;6(1):50.
30. Yusuf H, Tsakos G, Ntouva A, Murphy M, Porter J, Newton T, et al. Differences by age and sex in general dental practitioners' knowledge, attitudes and behaviours in delivering prevention. *British Dental Journal*. 2015;219:E7.
31. Dyer TA, Robinson PG. General health promotion in general dental practice - the involvement of the dental team. Part 1: a review of the evidence of effectiveness of brief public health interventions. *British Dental Journal*. 2006;200(12):679-85.

32. McAuley A, Goodall CA, Ogden GR, Shepherd S, Cruikshank K. Delivering alcohol screening and alcohol brief interventions within general dental practice: rationale and overview of the evidence. *British Dental Journal*. 2011;210(9):E15.
33. Goldstein MG, Whitlock EP, DePue J. Multiple behavioral risk factor interventions in primary care. Summary of research evidence. *Am J Prev Med*. 2004;27(2 Suppl):61-79.
34. NICE. Behaviour change: individual approaches. Public Health guideline (PH49). England: National Institute for Health and Clinical Excellence; 2014.
35. Fiore MC, Jaen CR, Baker TB, Bailey WC, Bennett G, Benowitz NL, et al. Treating tobacco use and dependence: 2008 update. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service: Clinical Practice Guideline; 2008 May 2008. Report No.: 0749-3797.
36. NICE. Alcohol-use disorders: preventing harmful drinking. Public Health guideline (PH24). England: National Institute for Health and Clinical Excellence 2010. Report No.: 1904671268.

Figure 1: PRISMA four-phase flow diagram - for included Systematic Reviews

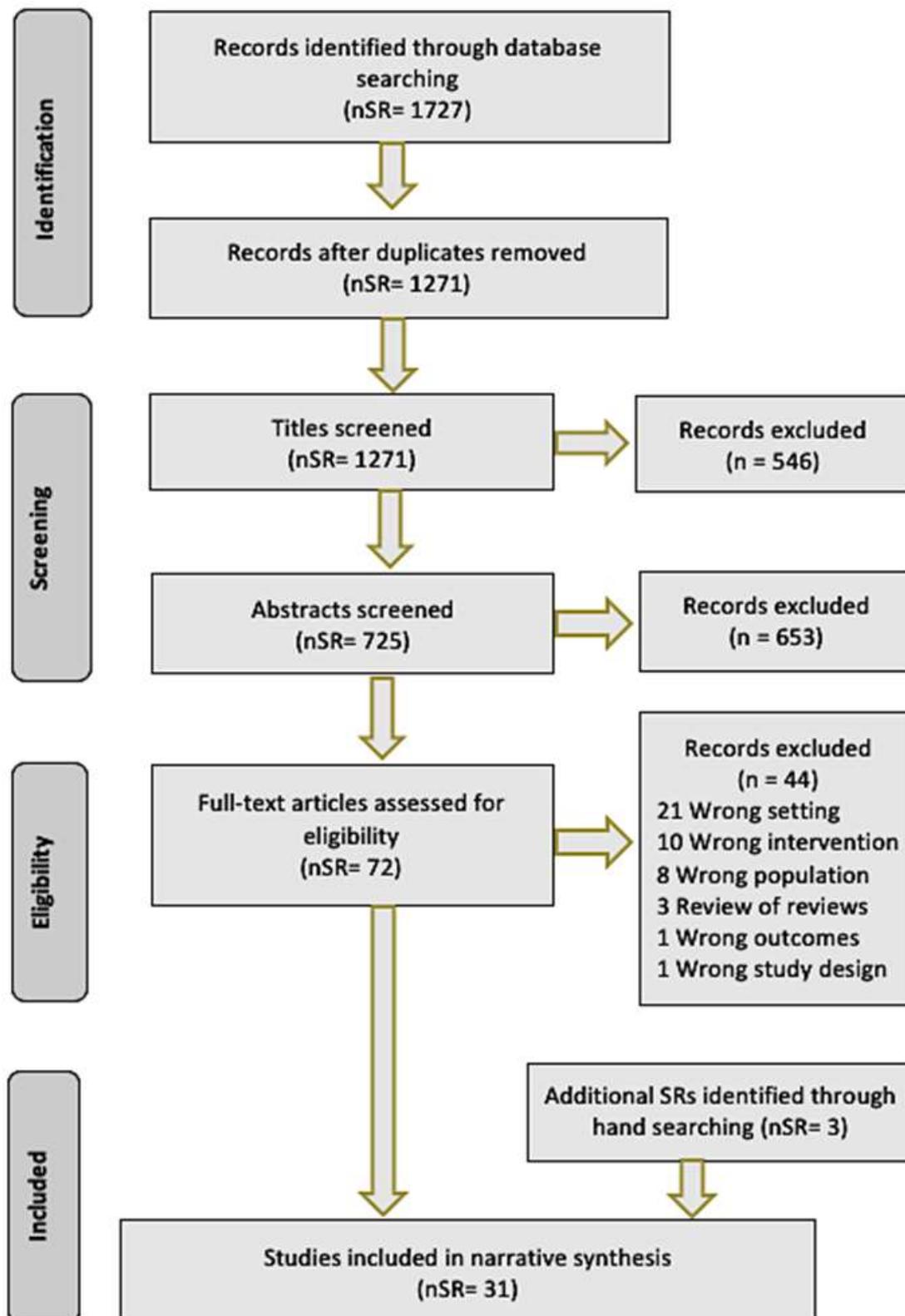
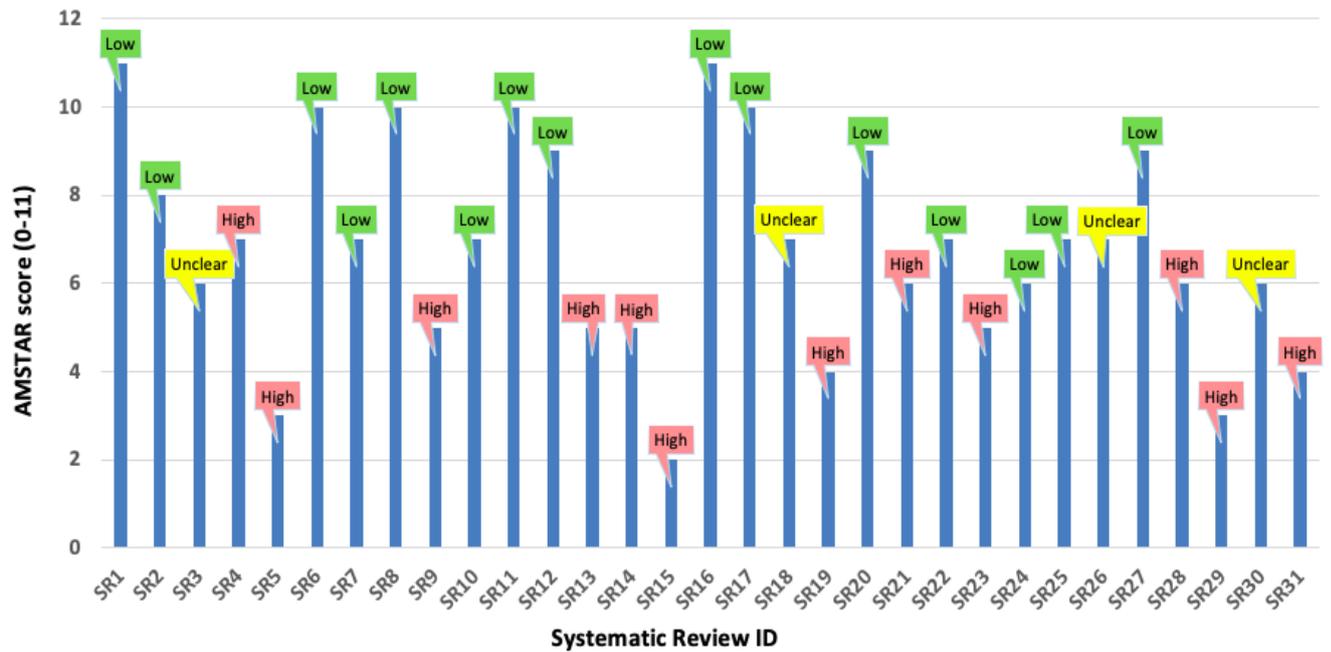


Figure 2: Graphical representation of both AMSTAR and ROBIS scores



*Blue vertical bars in the figure represent the AMSTAR scores (which ranges from 1-11) and low/high/unclear written in boxes are ROBIS scores.

Figure 3: PRISMA four-phase flow diagram - for included clinical guidelines

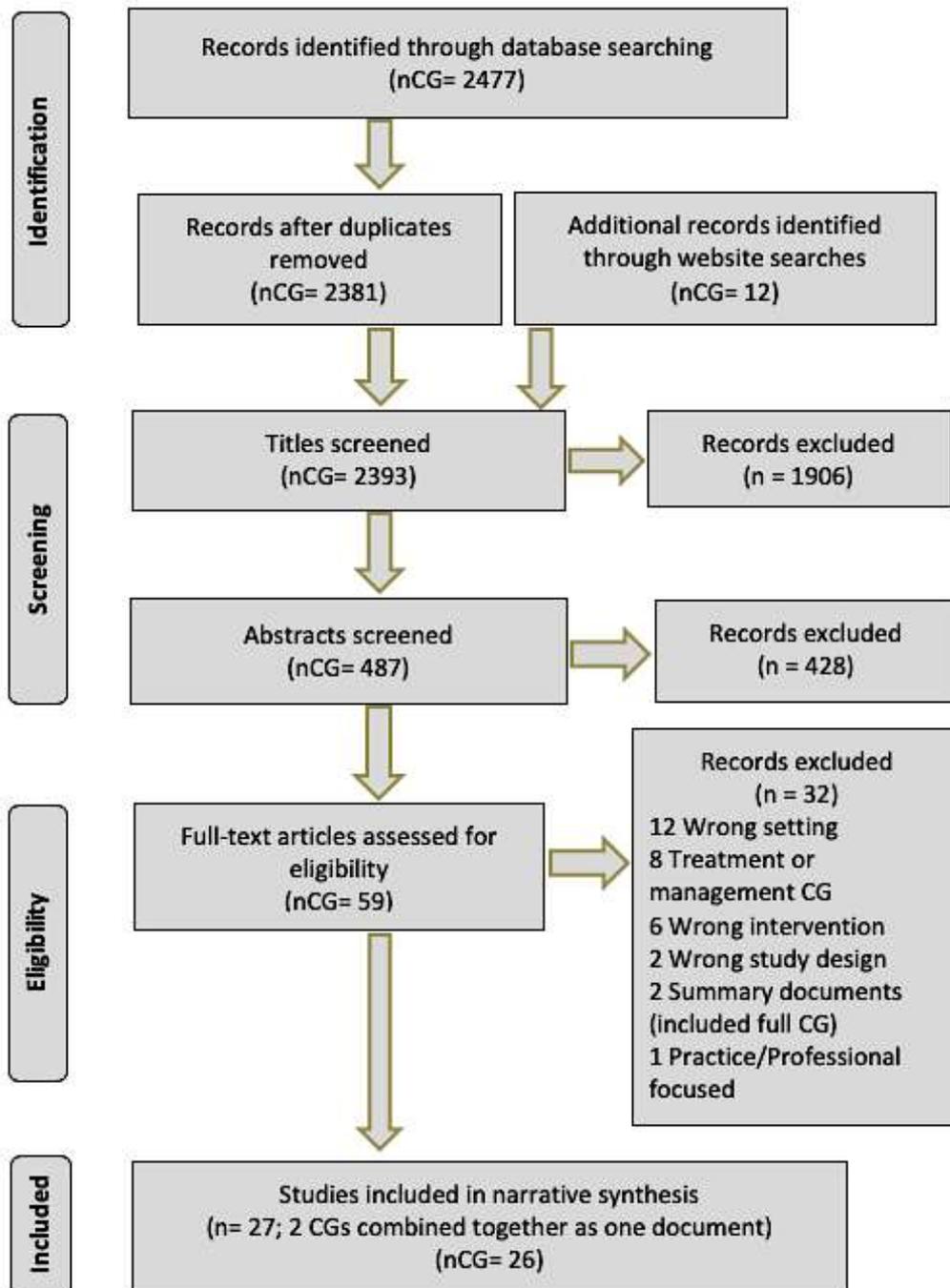


Table 1: Best practice (high-quality) evidence for smoking cessation and alcohol reduction interventions in the Systematic Reviews (SRs)

Dental Practice Setting						
Preventive Interventions for Smoking		Strength of evidence (based on effect size)	SRs supporting evidence	Preventive Interventions for Alcohol	Strength of evidence (based on effect size)	SRs supporting evidence
<u>Ask/ Assess</u>	Use patient's charts, medical records or health questionnaires to determine tobacco use status and at-risk groups	Weak	SR 12	None		
	Record findings from oral examination and relate to patient's tobacco use	Strong	SR 12			
<u>Advise/ Arrange</u>	Brief (or very brief) behavioural advice > No intervention	Strong	SR 12	None		
	Personalised (tailored) feedback from the oral examination as to the oral effects of tobacco use	Strong	SR 12			
	Intensive intervention > brief intervention	Weak	SR 12			
	Effectiveness of interventions delivered by trained professionals (effect sizes not reported)	None	SR 12			
<u>Assist/ Referral</u>	Brief advice plus quit-line referral > simple brief advice to quit (only one trial reported 3.3% quit rate)	Weak	SR 12	None		

Medical Practice Setting						
Preventive Interventions for Smoking		Strength of evidence (based on effect size)	SRs supporting evidence	Preventive Interventions for Alcohol	Strength of evidence (based on effect size)	SRs supporting evidence
<u>Ask/ Assess</u>	Assess and record patient's smoking status	Strong	SR: 1, 2, 6, 7, 8, 10, 16, 24, 27	Assess and record patient's alcohol consumption levels (moderate or dependence), using validated screening tools – to determine treatment options	Strong	SR: 7, 11, 17, 22, 25
	Details of smoking assessment, for example, duration, frequency, or type (cigarette, cigar, pipe).	None				
<u>Advise/ Arrange</u>	Theory-based or structured interventions > Simple advice or message to quit	Strong	SR: 1, 2, 7, 8, 16, 24, 27	Behavioural interventions (face-to-face tailored advice/counselling) > No intervention or usual care	Strong	SR: 7, 11, 17, 22, 25
	Brief (or very brief) motivational interventions > No intervention	Strong	SR: 1, 2, 6, 7, 8, 10, 16, 24, 27	Brief (5-20 minutes) interventions > no intervention or very brief or intensive intervention	Strong	SR: 11, 17, 22
	Intensive interventions (more than 20 minutes) > Brief interventions (small but significant benefit)	Moderate	SR: 1, 6, 7, 8	Multiple sessions > single sessions	Strong	SR: 11, 17
	Single sessions > multiple sessions	Strong	SR: 1, 7, 8	Intensive (more than 20 minutes) > brief intervention	Weak	SR 11
	Physician > nurses or counsellors (reported in only two small trials)	Weak	SR: 1	Very brief (less than 5-minutes) > brief intervention	Weak	SR 11
	Training received by providers > no training (effects not reported)	None		Primary care providers (physician, nurses, health educator) > research personnel	Strong	SR: 11
	Effectiveness of additional components: written materials or self-help aids (effect sizes not reported)	None		Training received by providers > no training (effects not reported)	None	
				Additional components to support: written materials or self-help manuals (effects not reported)	None	

<u>Assist</u> <u>(Referral)</u>	Brief advice (3-5minutes) plus referral to cessation services > Brief advice only (effect sizes not reported)	Weak	SR 8	Referral to specialized treatment services (outcomes for effectiveness not reported)	None	
--	--	------	------	---	------	--

“>” greater-than sign – used to show greater effects

Table 2: Best practice (high-quality) recommendations for smoking cessation and alcohol reduction interventions in the clinical guidelines (CGs)

Dental Practice Setting						
Preventive Interventions for Smoking		Strength of recommendation (based on supported evidence)	CGs supporting recommendation	Preventive Interventions for Alcohol	Strength of recommendation (based on supported evidence)	CGs supporting recommendation
<u>Ask/ Assess</u>	Ask and record patient's smoking (or tobacco use) status as part of social history	Strong	CG 11	Ask, assess and record patient's average daily/weekly alcohol consumption as part of social history	Weak	CG 11
	Assess patient's risk levels, and their interest in stopping smoking	Strong	CG 11	Use shorter versions of validated screening tools (AUDIT-PC, FAST)	Weak	CG 11
<u>Advise/ Arrange</u>	Offer brief or very brief opportunistic interventions	Strong	CG 11	Very brief advice - outline the possible harmful effects of excessive alcohol consumption (no details provided, e.g. duration, number of sessions, training)	Weak	CG 11
	Brief interventions should be tailored to meet individual needs	Strong	CG 11			
	Advice supported with educational materials or online support	Weak	CG 11			
<u>Assist/ Referral</u>	Offer smokers (or tobacco users) 'Smokeline' numbers or information on local smoking cessation services	Weak	CG 11	Refer patients to general medical practitioner for further advice and help	Weak	CG 11
				Provide online support (e.g. visit "Alcohol Focus Scotland" website)		

Medical Practice Setting						
Preventive Interventions for Smoking		Strength of recommendation (based on supported evidence)	CGs supporting recommendation	Preventive Interventions for Alcohol	Strength of recommendation (based on supported evidence)	CGs supporting recommendation
<u>Ask/ Assess</u>	Ask and record every patient's smoking (or tobacco use) status, and update regularly (at every visit or at least annually)	Strong	CG: 1, 2, 5, 12, 14, 17, 18, 22, 23	Ask, assess, and record patient's alcohol consumption levels (moderate or dependence), using validated screening tools – to determine treatment options	Strong	CG: 1, 14, 21
	Assess nicotine dependence (by asking amount smoked)	Weak	CG: 12, 18, 23			
	Assess readiness to change and their interest in receiving further help	Strong	CG: 1, 2, 5, 12, 14, 17, 18, 22, 23			
<u>Advise/ Arrange</u>	Offer brief or very brief tailored intervention to increase tobacco abstinence rates	Strong	CG: 1, 5, 12, 14, 17, 18, 22, 23	Offer behavioural (face-to-face) structured interventions to all patients with excessive alcohol consumption	Strong	CG: 1, 2, 14, 21
	Intensive interventions (over multiple sessions) more effective than brief intervention (small additional effect)	Moderate	CG: 1, 5, 12, 18, 23	Brief (10-15-minutes) multi-contact (two or more sessions) interventions were recommended to be most effective	Strong	CG: 1, 14, 21
	Educational materials to support advice	Weak	CG: 1, 5, 12, 18, 23	Very brief intervention (less than 5 minutes) or intensive interventions (more than 20 minutes)	Weak	CG: 1, 14
	Intervention delivered by any member of the primary care team	Strong	CG: 1, 2, 5, 12, 14, 17, 18, 22, 23	Additional components to support advice: written information or self-help materials, goal-setting	Weak	CG: 1, 2, 14, 21
	Training received by providers to deliver effective intervention	Weak	CG: 14, 17, 18, 22, 23	Intervention delivered by any member of the primary care team	Strong	CG: 1, 2, 14, 21
		Strong				

	Behavioural advice plus pharmacotherapy effective to increase abstinence rates		CG: 1, 5, 12, 18, 23	Training received by primary care providers (evidence not reported to support effectiveness)	Weak	CG: 1, 2, 14, 21
<u>Assist/Referral</u>	Make referral to quit-line services (proactive support), as part of brief intervention	Strong	CG: 12, 18, 23	Make referral to specialist alcohol treatment services (for alcohol dependence)	Weak	CG: 1, 14, 21