Instructions for Authors

Instructions for Authors for the Preparation of Drafts for *IARC Handbooks* Volume 19 – Oral Cancer Prevention

These Instructions for Authors were prepared by the scientific staff of the *IARC Handbooks* programme for the members of the Working Group to guide them in preparing the first drafts before the Working Group meetings. For transparency, they are accessible to the scientific community and the general public. Authors are also provided with a detailed outline, which defines the structure of the *Handbook*. Authors are also advised to consult a recent volume of the *IARC Handbooks.*

Although the preliminary drafts are prepared by individual members of the Working Group, the final *Handbook*, including the resulting evaluations, is a consensus document that is reviewed and validated by the entire Working Group, with no individual authorship.

The Instructions for Authors were modified in 2021 to align with the Preambles to the *IARC Handbooks* as updated in October 2019, as recommended by the Advisory Group to Recommend an Update to the Preamble to the *IARC Handbooks*.

This document should be read in conjunction with the Preambles to the *IARC Handbooks*, for primary prevention and for secondary prevention, which describe the scientific principles and procedures used in developing a *Handbook*, the types of evidence considered, and the scientific criteria that guide the evaluations.

Please read these instructions carefully.

Contents

Instructions at a glance, valid for all writing assignments

Each IARC Handbook *is composed of sections that are narrative reviews and sections that are systematic reviews. When you receive your writing assignment, make sure to verify which type of review you will be asked to conduct.*

- IARC uses an online tool for draft sharing and peer review during the preparation and conduct of *Handbooks* meetings: the IARC Online Publications System (IOPS).
- For the systematic reviews, Working Group members are provided with the results of preliminary searches performed by the IARC Secretariat. PDF files of all retrieved articles are accessible on a dedicated FTP site. The searches are preliminary. It is the responsibility of each Working Group member to ensure that all relevant studies are included, that is, not all articles retrieved may be included, and Working Group members are expected to include any other informative studies they may identify.
- For the narrative reviews, the Working Group will perform searches to identify recent, representative articles and reviews of the topic. It is the responsibility of each Working Group member to ensure that a representative set of studies are included.
- It is important to search for and include data from low- and middle-income countries to the extent possible. Where data are lacking for important regions or countries, this may be noted.
- Working Group members draft text in Microsoft Word. Tables are created in Word using the templates provided where appropriate (see Annex 1). Please submit your drafts electronically via the IARC Online Publication System (IOPS).
    - Please adhere to the word limits, content description, and format indications where indicated.
    - Use of text that is a direct copy and paste from original publications is considered plagiarism and can be detected by specialized software.
- The writing assignment should be prepared before the meeting according to the deadline provided to you.

- Working Group members are expected to conduct peer reviews of other sections. Detailed information will be provided after the Working Group members have submitted their writing assignments.
- At the meeting, within subgroups, the Working Group members critically review, discuss, and revise the pre-meeting drafts and adopt the revised versions as consensus subgroup drafts. During the plenary session, each subgroup presents its drafts for scientific review and discussion, for adoption as a consensus Working Group product.
- Summaries are written in subgroups as a result of the revised subgroup drafts, and reviewed in detail during the plenary session. Summaries are the most-read part of the *Handbook* and should be finalized by the end of the meeting.

Instructions for the narrative reviews

Narrative reviews provide background information and support to the sections that lead to an evaluation. In the narrative reviews, the text should give a representative overview, and not all available data are considered comprehensively. Information is obtained from reviews, textbooks, government reports, recent research studies, and other publicly available sources, with all statements of scientific fact substantiated by a fully referenced article, report, or website.

Section 1. Oral cancer and OPMDs

Format: maximum of 1000 words for each subsection, and tables and/or figures; up to 10 pages in total

This section covers both oral cancer and oral potentially malignant disorders (OPMDs), and is composed of several subsections: descriptive epidemiology, classification and natural history, stage at diagnosis and survival, and treatment and management of the diseases. The outline of the subsections may be modified, in consultation with the IARC Secretariat.

Descriptive epidemiology: The global distribution of the diseases is described. Each subsection (Section 1.1.1 and 1.1.2) will include incidence, prevalence, and mortality; worldwide, by region, by Human Development Index (HDI), by socioeconomic status, by age, sex, ethnicity; trends, projection estimates, and susceptible populations. Regional differences and time trends are noted. Trends in the presence or absence of screening are a relevant component of this section.

Classification and natural history: The natural history from OPMDs to cancer is briefly described. Classification and histopathology of the lesions is described, referring to recent reviews or textbooks.

Stage at diagnosis and survival: Information on stage at diagnosis and survival in different settings is reviewed, with a worldwide perspective.

Treatment and management of the diseases: The main steps in management and treatment of OPMDs and cancer are given only very succinctly (200–500 words), because the *Handbooks* do not cover evaluations of treatments. Example of text:

> Treatment advice is dependent on the stage of disease. The decision about whether to administer neoadjuvant treatment is based on the stage determined by imaging. In particular, an advanced T stage in rectal cancer is an indication for neoadjuvant

> radio(chemo)therapy. Other treatment decisions are based on pathological staging. For early pT1 cancers, the risk of lymph node metastases is low and local treatment may therefore be sufficient. For a more balanced risk evaluation in those patients, additional histological biomarkers are usually included in the discussion (Bosch et al., 2013). When only tumour stage is taken into consideration, adjuvant chemotherapy is usually advised for patients with stage III disease, as well as for high-risk patients with stage II disease (Benson et al., 2004). For patients with stage IV disease, a personalized approach is chosen, which varies between the resection of limited metastatic disease and palliative systemic therapy and combinations thereof. In general, treatment decisions are made at multidisciplinary team meetings.

Section 2.1. Established risk factors

Format: 200–500 words per subsection, and 1 or 2 tables as appropriate; up to 10 pages in total

For each risk factor, present succinctly the evidence that it is associated with oral cancer and/or OPMDs, and if available the attributable fraction in those countries or regions with a high prevalence (maximum of 10 references). A summary table presenting all risk factors should be prepared. The table will include, for a given level of exposure to the risk factor, the average or pooled relative risk or a range of relative risks, with the most relevant reference (see the table template in Annex 1). Example of text:

> Physical activity reduces the risk of colon cancer (IARC, 2002; WCRF/AICR, 2017). The protective effect appears to be slightly greater for recreational activity than for occupational physical activity (Mahmood et al., 2017). Two recent meta-analyses estimated similar decreases in risk of proximal and distal colon cancers among the most physically active compared with the least active individuals (Boyle et al., 2012; Robsahm et al., 2013). In contrast, physical activity appears to be unrelated to the risk of rectal cancer (Robsahm et al., 2013; WCRF/AICR, 2017). Cohort studies have shown that the beneficial effect of physical activity is independent of body mass index (Leitzmann et al., 2015). Overall, there is a dose–response relationship with risk reduction across a wide range of the frequency and intensity of physical activity, and exercise does not need to be intense or long-lasting to have substantial benefits.

Other risk factors include: second-hand smoke, maté drinking, poor oral hygiene, dietary deficiency, chronic inflammation, mucosal trauma, and the oral microbiome.

Table template:

Risk factors

Section 2.3. Preventive agents for the development of OPMDs

This section will describe studies, if any, that assess the effect of agents in preventing the development of OPMDs, presumably in populations at high risk. This section will NOT cover the effect of agents on the regression of premalignant lesions, which would represent tertiary prevention and is beyond the scope of the *Handbooks*.

Section 3.1–3.2. Overview of the products, Prevalence of consumption of SLT/AN

Format: 2000 words and 1 table and/or figure, as appropriate

This section is organized by World Health Organization (WHO) region, limiting the description to those countries or settings where the habit is prevalent. In those WHO regions with a large diversity and high prevalence of use, the description should be by country or setting.

The section will be preceded by a short introduction of the products consumed (200–500 words), referring to recent reviews and textbooks.

Section 4.1. Screening methods

Format: 2000–3000 words for each technique or subchapter

It is important to distinguish between the screening technique and the screening procedure, i.e. between the technique itself and the way in which it is administered.

All known methods used (screening or adjunct) are described to the extent to which they are used or depending on the availability of information. Information may be tabulated (e.g. for data on test performance). The technical aspects and the state-of-the-art application of the method are described concisely, highlighting:

- equipment and staff expertise;
- technical quality control;
- screening performance (ability of test to detect cancer and to distinguish cancer from non-cancer conditions); and
- host factors affecting screening performance.

Section 4.1.5 on Emerging technologies describes methods that may be available in some countries but are not yet in routine use, methods for which there are not enough data available to make an evaluation, or methods that are still under development.

For the most important, relevant, and/or mature methods, this section is typically organized similarly to the sections for methods for which an evaluation is conducted; for emerging methods that are still in development, the text briefly presents the detection method and its most recent developments.

This section may contain tables, for example for comparing the methods described with respect to key features and patient considerations, or to present the performance in detecting neoplasia.

Table template:
Test performance

Section 4.2. Availability and use of oral cancer screening activities

Format: up to 5 pages in total; 500–1000 words and 1 table per region

The following aspects are summarized, if available:

- policies and guidelines for, and regulation of, screening;
- type of screening offered (e.g. opportunistic screening, pilot, organized population-wide programme), standard diagnostic procedures;
- screening modalities most commonly used or recommended; and
- extent of population coverage and participation rates.

Results may be summarized in tables, in particular for those countries where there are sufficient data.

Table templates:
Population-based organized screening programmes
Opportunistic screening

Section 4.5. Risk-based model

Format: 500–1000 words and 1 table

This section describes the emerging approach of screening based on the risk of the population. Environmental as well as personal host factors are taken into consideration for establishing a risk score.

Instructions for the systematic reviews

Sections that lead to evaluations of the preventive effects of the intervention(s) will follow the principles of a systematic review, and specific instructions apply.

These sections follow a comprehensive, critical review that presents, for each intervention (primary prevention or screening intervention), all of the pertinent studies on efficacy and effectiveness, and identifies the level of evidence for the cancer-preventive effects. The length of the section will be determined by the number of studies reviewed.

This includes the following sections:

- Section 2.2. Effectiveness of reducing/quitting exposure in reducing cancer/precancer incidence
- Section 2.3. Preventive agents for the development of OPMDs
- Section 3.3. Interventions to reduce consumption of smokeless tobacco/areca nut (SLT/AN)
- Section 4.3. Determinants of participation in screening
- Section 4.4. Effectiveness of screening and early diagnosis

Interventions may include: population/community-based, youth-targeted based, other subpopulation-based, mass media-based/social marketing campaigns, and dental practice-based.

1. Comprehensive searches of the literature and selection of studies

A systematic preliminary search and selection of articles has been or will be performed for all review questions that will lead to evaluations.

2. Screening and organizing the results

The IARC Secretariat provides to the Working Group member the articles (in PDF format) for the studies from these preliminary searches.

The Working Group member performs a full-text review of all the retrieved articles for relevance to the evaluation.

The searches are preliminary. It is the responsibility of each Working Group member to ensure that all relevant studies are included, that is, not all articles retrieved may be included,

and Working Group members are expected to include any other informative studies that they may find.

The epidemiological (experimental or observational) studies may report data on the following outcomes (as applicable):

- Beneficial effects: reduction in risk of incidence, reduction in risk of mortality, shift in disease stage, other measures of screening effectiveness; the effects may also be reported in sub-analyses (e.g. according to invitation or participation, age range);
- Adverse effects: false-positive and false-negative findings, overdiagnosis (likelihood of unnecessary treatment), short- and long-term side-effects, psychological factors;
- The balance of benefits and harms;
- Cost–effectiveness: by setting, development index, age range, etc.

3. Description of the characteristics and results of the included studies

The Working Group member extracts the relevant data in a standardized manner. Tables include the information needed to assess study quality. The text highlights the characteristics of the studies and the key results, and presents the major strengths and limitations of the study. Information given in the tables does not need to be repeated in the text.

Tables

Study design and relevant numerical results of all included studies are presented in tabular format. Each type of study has a table template to enable comprehensive reporting of the pertinent information in a standardized manner.

Table templates for randomized controlled trials:

RCT design

RCT results

Meta-analyses of RCTs

Table templates for observational studies:

Observational studies – Cohort studies

Observational studies – Case–control studies

Text

Included studies are described succinctly, providing essential information about the study (design, location, number of subjects) and the key results (risk estimate, 95% confidence interval). Example of description:

> The United Kingdom Flexible Sigmoidoscopy Screening Trial (UKFSST) was a randomized controlled trial of once-only screening with sigmoidoscopy (Atkin et al., 2010). Men and women aged 55–64 years who were registered with participating general practices in the United Kingdom were eligible for the trial, provided they had no history of colorectal cancer, adenomas, or inflammatory bowel disease, had a life expectancy of at least 5 years, and had not received a colonoscopy or sigmoidoscopy in the previous 3 years. Eligible subjects (368 142) were first sent a questionnaire asking whether they would participate in a randomized controlled trial of colorectal cancer screening. Those who agreed to participate were then randomized in a 2:1 ratio to the control arm or the intervention arm of the trial. Subjects in the intervention arm underwent baseline sigmoidoscopy with polypectomy. Those with polyps meeting any of the following criteria were referred for colonoscopy: ≥ 10 mm in diameter, ≥ 3 adenomas, tubulovillous or villous histology, high-grade dysplasia, malignancy, or ≥ 20 hyperplastic polyps above the distal rectum. Trial enrolment began in November 1994 and was completed in March 1999. A total of 170 432 individuals were randomized, and after exclusions for deaths and previous colorectal cancer, 170 038 were included in the analysis (112 939 in the control arm and 57 099 in the intervention arm); 50.0% were women. The participation rate in the baseline screening was 71%; of those screened, 5% underwent follow-up colonoscopy, of whom 85% subsequently entered a surveillance programme.

The level of detail should be proportional to the importance of the study in the context of all the studies presented. Information given in the tables does not need to be repeated in the text unless it is especially important for interpreting the results. Risk estimates and 95% confidence intervals should be provided for the main results, without description of statistical significance. *P* values for trend may be reported when available.

Multiple publications on the same study population may result from (i) inclusion in independent studies of overlapping populations, or (ii) successive follow-ups of a single cohort. In these situations, only the most recent, most comprehensive, or most informative report should be reviewed in detail in the text and tables. Other publications will be, in case

(i), briefly noted in the text and in the Comments field in the table, and in case (ii), listed in the Reference field in the table.

Less informative studies may be listed briefly, giving key characteristics and results of the study, or as an aggregate of related studies.

For each study or group of studies, an expert assessment of the strengths and limitations as well as important points of interpretation should be indicated in square brackets [e.g. inadequate duration, underpowered study, lead time bias, contamination of non-screened group] and/or in the Comments field in the tables.

Subsections describing a number of studies may have a brief introduction describing the included literature and the reasons for exclusions, if any, and highlighting important issues of interpretation. Example of an introduction:

> This section summarizes findings from the randomized controlled trials on the effects of sigmoidoscopy on colorectal cancer mortality, colorectal cancer incidence, and all-cause mortality. All relative risks and hazard ratios are from intention-to-treat analyses, unless otherwise stated. For per-protocol analyses, the United Kingdom Flexible Sigmoidoscopy Screening Trial (UKFSST) and the Screening for Colon and Rectum (SCORE) trial reported adjusted relative risks derived using the Cuzick method (Cuzick et al., 1997). The Norwegian Colorectal Cancer Prevention (NORCCAP) trial reported per-protocol 10-year risk differences using an instrumental variable approach; these were converted to relative risks to obtain a comparable metric to that reported for the other trials. The Prostate, Lung, Colorectal, and Ovarian Cancer Screening (PLCO) trial did not report per-protocol analyses.

4. Evaluation of study quality

The Working Group member reviews the included studies and evaluates their quality on the basis of considerations such as the study design, methodology, and reporting of results, as described in Part B, Section 5 of the Preamble to the *IARC Handbooks* – Secondary Prevention (summarized in the text box below). Studies that are considered uninformative are excluded from the evaluation, and the reasons for such exclusion may be explained at the beginning of the chapter (e.g. “Studies reporting … have been excluded because ….”). For each included study, the Working Group member highlights the major strengths and weaknesses, as [comments in square brackets] in the text and as Comments in the table. To guide the process, specific risks of bias are reported using the standardized form provided.

Study quality assessment checklist

- How do you rate the clarity in describing the study design and its implementation?
- How do you rate the completeness of reporting of all other key information about the study and its results?
- Has the study been designed and conducted in a manner that would minimize selection bias and other forms of bias?
- Has the screening intervention been assessed in a way that was not related to outcome status?
- Is the study population of sufficient size to obtain precise estimates of effect?
- Is there sufficient elapsed time from intervention to measurement of outcome for an effect, if present, to be observable?
- Is there an adequate intervention contrast?
- Are there relevant and well-defined time windows for intervention and outcome?
- Is the outcome measure (incidence of cancer, mortality from cancer, or an intermediate outcome) appropriate for the screening intervention and the cancer type under consideration?
- Are the methods used to assess the intervention adequate (including validity and reliability)?
- Is the likelihood (and direction) of present bias, if any, in the measure(s) of association due to intervention measurement error or misclassification?
- Did the authors take into account, in the study design and analysis, potentially confounding variables, including co-exposures, that could influence the occurrence of the outcome and may be related to the intervention of interest?
- Did you identify other potential sources of bias (reporting bias, etc.)?
- Are the statistical analysis methods used adequate?
- Are the statistical methods able to obtain unbiased estimates of intervention–outcome associations, confidence intervals, and test statistics for the significance of measures of association?
- Are the methods used to address confounding, including adjusting for matching when necessary and avoiding treatment of probable mediating variables as confounders, appropriate?

Summaries

Format: about 10–15 pages in total

The summaries are written during the meeting and concisely recapitulate the data reviewed in the main sections. Each subgroup is responsible for writing a summary of the data they reviewed.

Summaries are the most-read sections in the entire volume. Therefore, it is extremely important to provide essential and relevant information but remain concise.

The summaries should not contain information about studies or other elements that have not been mentioned in the main text.

Summaries must be understandable by the lay public. Technical jargon should be avoided. Reference citations are useful in developing the summaries but will be removed in the final version. Therefore, information such as the geographical location or the name of the study should be given to enable the reader to identify a study.

Summaries of sections with systematic reviews

A concise summary should be provided of the epidemiological studies considered to be of adequate quality for use in making the evaluations for the beneficial and adverse effects. Those studies considered to be uninformative and not used in making the evaluations should not be included in the summary.

A statement should be made about the type and number of studies (randomized controlled trials, cohort studies, case–control studies) and whether an association was found between the intervention and the decreased incidence of or mortality from cancer, and under which circumstances. Any limitations should be mentioned.

Summaries of sections with narrative reviews

The length of each summary will depend on the length of the corresponding main text and the direct relevance of the topic to the evaluations.

Annex 1. Table templates

Section 2.1. Risk factors

Table 2.1.x Established risk factors for oral cancer and associated relative risk

Risk factor	Level of exposure	Range of RR or RR (95% confidence interval)	Reference

Section 2.1.x Effectiveness of reducing exposure in reducing cancer or precancer incidence (individual studies, to be used when no recent review is available). Please use a separate table for each exposure.

Table 2.x Effectiveness of reducing exposure in reducing cancer or precancer incidence

Reference Location (country)	Study population	Study description: number of participants, study period, follow-up period	Oral cancer or precancer end-point	Number of cases/deaths	RR (95% confidence interval)	Interpretation/Comments

Section 3.3. Interventions to reduce consumption of smokeless tobacco/areca nut (SLT/AN)

Table 3.3.x Interventions to reduce consumption of SLT/AN

Reference **Country**	**Study design**	**Intervention arm**	**Control arm**	***Outcome measure:*** **Efficacy of intervention**	**Comments/Interpretation**

Section 3.3.5. Interventions with outcomes other than reduction in consumption of SLT/AN

Table 3.3.x Interventions with outcomes other than reduction in consumption of SLT/AN

Reference **Country**	**Type of intervention/study design**	**Intervention arm**	**Control arm**	***Outcome measure:*** **Efficacy of intervention**	**Comments/Interpretation**

Section 4.1. Test performance (individual studies or meta-analyses)

Table 4.1.x Performance of [test] for detection of oral cancer and OPMDs [for individual studies]

Reference	Test used Outcome (cancer/OPMDs)	Sensitivity (%)	Specificity (%)	Comments

Table 4.1.x Performance of [test] for detection of oral cancer and OPMDs [for meta-analyses]

Reference	Number of studies	Number of lesions	Outcome measured (cancer/OPMDs)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)

Table 4.1.x Comparison of technologies

Technology	Advantages inherent to technology	Disadvantages inherent to technology	Advantages for screening	Disadvantages for screening	Sensitivity	Specificity	Costs for screening	Costs for assessment	Relevance to screening	Current state of development

Section 4.2.1. Population-based organized screening programmes

Table 4.2.x Policies and practice in countries with established oral screening programmes

Country, region	Start year	Target age (years)	Screening method	Follow-up	Interval (years)	No. of screening tests per year	Invitation coverage (%)	Examination coverage (%)	Participation rate (%)	References

Section 4.2.2. Opportunistic screening

Table 4.2.x Policies and practice in countries with opportunistic oral screening

Country or region	Screening method	Performed by	Interval (years)	Population targeted	Examination coverage (%)	Reference

Section 4.3. Studies (RCTs) of interventions to increase participation in screening

Table 4.3.x Randomized trials of interventions to increase participation in oral cancer screening

Reference	Country	Screening modality	Intervention arm	Control arm	Outcome

Section 4.4. Effectiveness of screening and early diagnosis (RCT design)

Table 4.4.x Characteristics of the randomized trials of the efficacy of oral cancer screening

Trial, country	Randomization	No. of participants	Accrual period for screening		Age at entry (years)	Intervention	No. of examinations/tests	Screening interval (years)	No. of rounds	Attendance at first round (%)	Determination of end-point
			Invited group	Control group							

Section 4.4. Effectiveness of screening and early diagnosis (RCT results)

Table 4.4.x Results of the randomized trial of the efficacy of oral cancer screening

Trial, country References	Age (years) at enrolment/screening	Mean duration of follow-up (years)	No. of subjects	Cancer mortality per 100 000 person-years (no. of cancer deaths) in screened/control group	RR	95% CI

Section 4.4. Effectiveness of screening and early diagnosis (Meta-analyses of RCTs)

Table 4.4.x Meta-analyses of studies of the efficacy/effectiveness of oral cancer screening

Reference	No. of studies	Age at entry (years)	Population (thousands)		Cancer deaths		RR	95% CI
			Screened	Control	Screened	Control		

Section 4.4. Effectiveness of screening and early diagnosis (Observational studies – Cohort studies)

Table 4.4.x Cohort follow-up studies of the effectiveness of oral cancer screening

Reference Location	Cohort description: number of participants, screening period, source of screening data, follow-up period, and source of follow-up data	Established programme: year of start, screening age, screening interval	Accrual and follow-up periods Person-years	Oral cancer or precancer end-point and incidence/death age ranges	Number of cases/deaths	Cancer incidence/ mortality RR (95% CI)	Adjustments	Comments

Section 4.4. Effectiveness of screening and early diagnosis (Observational studies – Case–control studies)

Table 4.4.x Case–control studies of the effectiveness of oral cancer screening

Reference Location	Screening age and interval, participants included	No. of cancer deaths source, time period for cancer deaths, years of diagnosis; proportion of eligible participants included	Screening exposure; age of included participants	No. of controls, source, whether same source population as cases, matching variables, alive at date of death or diagnosis of case	Linkage or use of screening, cancer registry, death databases; data items available	Adjustments	Cancer mortality OR (95% CI)	Comments