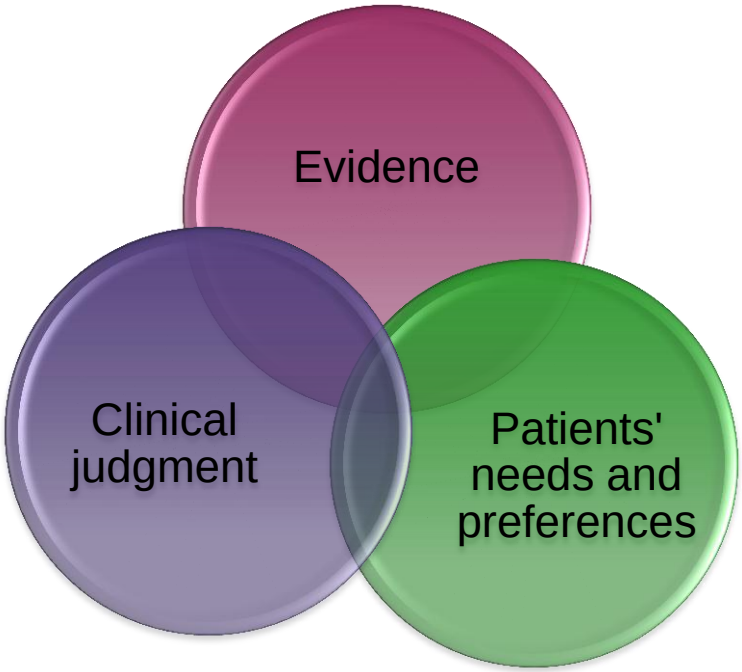
2013 Update

ADA Clinical Practice Guidelines Handbook



ADA. Center for Evidence-Based Dentistry™

American Dental Association

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1. Overview

ADA Clinical Practice Guidelines are developed through the ADA Center for Evidence-Based Dentistry (EBD Center) under the guidance of the Council on Scientific Affairs.

Instituted in 2006, the goal of the ADA Clinical Practice Guidelines program is to review and prepare clinical recommendations for dentists based on the best currently available evidence. In the first few years of the program, the clinical practice guidelines (clinical recommendations in prior terminology) were based on one or more systematic reviews of the best currently available evidence. In the current process, a *de novo* systematic review of primary studies is performed. The ADA Clinical Practice Guidelines are developed by a panel of experts who critically appraise, summarize, and interpret the body of evidence to develop practical recommendations for clinical practice. The program also identifies gaps in the scientific evidence and provides suggestions to help guide future research.

This handbook documents how the ADA develops evidence-based Clinical Practice Guidelines through a process that is:

- Objective;
- Transparent;
- With bias minimized; and
- Reproducible.

1.1 Purpose of ADA Clinical Practice Guidelines

The ADA Clinical Practice Guidelines provide clinicians with tools to help them implement evidence-based interventions. The American Dental Association defines Evidence-Based Dentistry as "an approach to oral health care that requires the judicious integration of systematic assessments of clinically relevant scientific evidence, relating to the patient's oral and medical condition and history, with the dentist's clinical judgment and the patient's treatment needs and preferences." This definition acknowledges that treatment recommendations should be individualized for each patient by his or her dentist, and that the clinician's judgment and patient preferences should be considered while planning treatment. *Evidence-based clinical practice guidelines are intended to provide guidance and should be integrated with a practitioner's professional judgment and a patient's needs and preferences. They are not standards of care, requirements, or regulations. They represent the best judgment of a team of experienced clinicians, researchers and methodologists interpreting the scientific evidence on a particular topic.*

1.2 Roles

1.2.1 Council on Scientific Affairs

The ADA Council on Scientific Affairs (CSA) oversees the Clinical Practice Guidelines program through the EBD Center. The CSA selects the topics for Clinical Practice Guidelines, provides input into the clinical questions, nominates the Expert Panelists, designates the Chair, and approves the final report. Periodic updates are provided to the CSA at council meetings.

1.2.2 Internal and External Stakeholders

Stakeholders are individuals and organizations whose activities may be affected by one or more of the recommendations or who have other legitimate reasons for providing input into the process. Stakeholders may be involved in two ways in the clinical recommendations process: as members of the expert panel or as reviewers/commentators on the final report. They will be identified with their roles in the published document. The published document will also disclose any conflicts of interest on behalf of the members of the expert panel.

1.2.2.1 Internal Stakeholders

The CSA may invite other agencies of the ADA to designate an individual to serve as a liaison of that agency with the expert panel and/or to review the final report based on mutual interest in the topic. ADA agencies whose representatives have previously helped to develop clinical practice guidelines include the Council on Access, Prevention and Interprofessional Relations (CAPIR), Council on Dental Education and Licensure (CDEL), Council on Dental Practice (CDP) and Council on Dental Benefit Programs (CDBP). That individual is responsible for keeping his or her agency informed on the project's progress. Internal stakeholders can attend meetings and voice opinions, but they are typically non-voting panel members. Although current methodological philosophy encourages the inclusion of patients or patient groups in the panel, the ADA currently relies on the liaisons to bring this perspective to the expert panel.

1.2.2.2 External Stakeholders

External stakeholders for each topic are identified by the steering committee with input from EBD Center staff and approved by the CSA Chair and Co-chair. Some will be invited to participate on the panel through their representatives. Representatives keep their organizations informed of the progress of the project. All external stakeholders will be provided an opportunity to review and comment on the final report. Representatives ensure that the stakeholders' perspectives are reflected in the final report. The final report will identify the stakeholders who participated on the Expert Panel, as well as those who reviewed the final report.

1.2.3 Co-sponsors

The ADA seeks opportunities to collaborate with other health care agencies and national and specialty organizations in the development of clinical recommendations when such collaboration will improve the acceptance and implementation of the end product by practitioners. The Center will prepare a letter of agreement covering the terms of the collaboration, including financial and staff support, and selections of panelists/chair with input from the ADA Division of

Legal Affairs. Collaborating organizations will be expected to abide by the evidence-based process as stated in this handbook.

1.2.4 End-users

ADA Clinical Practice Guidelines are primarily intended to be used by practitioners who are actively involved in patient care. When considering a topic for recommendations, CSA uses the ADA's EBD Web site to call for specific questions that practitioners would like answered on the topic. To ensure that recommendations have clinical utility and applicability, each panel will include one or more practitioners actively involved in patient care. During the review process, the panel may ask Center staff to convene a focus group of end-users to review the draft report and recommendations, subject to the availability of funding. End-user feedback will help ensure that the key messages and recommendations are relevant and appropriate.

2. Starting a Clinical Practice Guideline: Topic Selection

A flow chart in the Appendix called "Starting a Clinical Practice Guideline Project" provides a visual description of the process steps in more detail from Topic Selection through establishing the Steering Committee.

2.1 Potential topics are identified by the CSA considering member input through ADA member surveys and other ADA agencies as well as other sources.

2.2 To assess the availability of published information on a topic, Center staff performs a broad search of the literature focused on systematic reviews on the topics identified by the CSA and compiles a list of manuscripts on each topic, a list of key questions addressed in these reviews and a list of existing guidelines and recommendations on the topic published by other agencies. Systematic reviews and guidelines can be easily identified in MEDLINE through PUBMED, and additional guidelines can be identified through the National Guideline Clearing House (ww.guideline.gov) and the database of the Guideline International Network (www.g-i-n.net). Section 7.3 provides details for conducting a search for systematic reviews. Relevant randomized controlled trials can also be identified; however, the purpose of the search is to determine the state of the literature base on the topic of interest.

2.3 CSA evaluates proposed topics using the checklist set forth in Table 1. One of the issues CSA considers in selecting topics is whether there is a substantive or developing body of research or related evidence in the topic area, where plausible linkages between treatment decisions and outcomes can be demonstrated. The Center's resources are best directed to projects where there is potential for change in patient-centered outcomes based on valid scientific studies. Other topic areas with high value include those on treatments or procedures that are very common, very expensive, or complex.

NOTE: *In some situations, if a preliminary search reveals that insufficient evidence exists to address a clinical question, developing evidence-based recommendations may not be possible. However, these instances may provide value if they highlight the need for future research in the*

subject area. It is important to note that topics on which there is little evidence and conflicting opinions from experts are often ones where the profession looks for guidance. In those situations, CSA may consider using other communications vehicles, to disseminate key information to practitioners rather than through formal Clinical Practice Guidelines.

2.4 The CSA approves and prioritizes topics for clinical practice guidelines.

2.5 The CSA appoints a Chair for the clinical practice guideline topic

Table 1: Criteria for Assessing Topic Suitability for Clinical Practice Guidelines

1. Will the ADA be able to add value by issuing guidance? In particular, taking into account whether, **a) there is a substantive or developing body of research or related evidence in the topic area, where plausible linkages between treatment decisions and outcomes can be demonstrated; and/or** **b) there is a demonstrated need through member or stakeholder input for guidance by expert consensus in the absence of high quality evidence.**	☐
2. Would it be timely to provide guidance on the proposed topic? In particular, **a) would the guidance still be relevant and timely at the expected date of publication, and/or** **b) is there emerging significant professional/public concern, and/ or** **c) is this emerging as an important new area for action?**	☐
3. Would guidance promote the best possible improvement in patient care? In particular, does the topic aim to, **a) improve methods for disease prevention and/or** **b) improve methods of diagnosis, treatment and clinical management and/or** **c) address a condition which is associated with significant harm and/or** **d) address a condition, treatment, or procedure that is very common and/or** **e) address a treatment or procedure that is very expensive and/or** **f) address a treatment or procedure that is very complex.**	☐
4. Is the ADA the most appropriate source of guidance on the topic?	☐

3. Building the Expert Panel

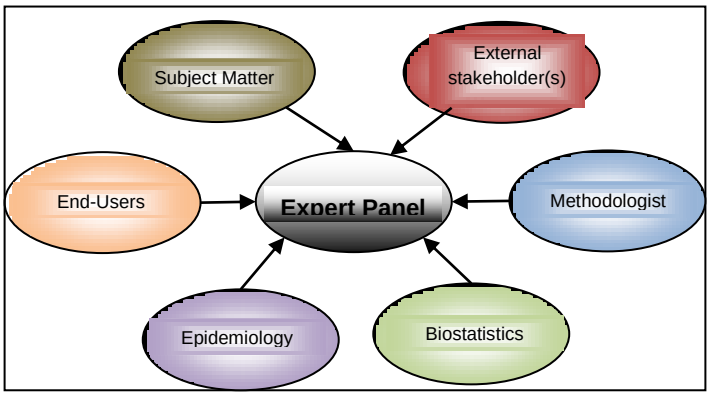


Figure 1. Composition of expert panel.

3.1 Chair

3.1.1 The CSA designates a chair, subject to the agreement of any collaborator(s).

This individual should be familiar with, though not necessarily an expert in, the management of the clinical condition and the scientific literature. The Chair should be skilled in chairing meetings, possess basic knowledge of parliamentary procedure and the proper role of the chair as a neutral facilitator, be skilled in scientific writing, have prior experience in leading expert discussions and be capable of facilitating the interpersonal aspects of group processes so that the panelists work in the spirit of collaboration with balanced contribution from all members.

3.1.2 The selection of the Chair for the panel will be based on absence of any significant conflicts of interest (currently only commercial, but intellectual conflicts may also be considered) on the topic of the project. The determination whether a significant conflict exists will be made by the Director, Center for Evidence-Based Dentistry and the Senior Vice President, Science and Professional Affairs in consultation with staff of the ADA Legal division.

3.1.3 The Chair should be capable of meeting the following commitments:

- Understand the process for developing clinical recommendations as described in this manual;
- Assist staff in planning meeting agendas;
- Participate in the Steering Committee (see below) and all its activities;
- Moderate and guide the panel during its development of clinical recommendations;
- Provide input on key decisions as required by the project;
- Ensure that the group functions effectively and remains focused;
- Encourage all members of the group to contribute to the discussions;

- Delegate assignments and integrate completed assignments and group feedback into the draft report;
- Stimulate discussion and facilitate group consensus while refraining from undue personal input; and
- Encourage constructive debate without forcing agreement.

3.1.4 The Panel Chair together with the CSA Chair and Center staff nominate Steering Committee members to the full panel, one of which is a CSA representative.

3.2 Steering Committee Composition and Responsibilities

The Steering Committee is generally made up of 3-5 individuals including the Chair, the CSA representative, and other members with multidisciplinary backgrounds, including at least one subject matter expert and one EBD process expert. The Steering Committee becomes a subgroup of the Expert Panel. The purpose of the Steering Committee is to facilitate the work of the panel. Steering Committee members are designated by the CSA chair in consultation with Center staff and the Chair of the Expert Panel. A flow chart in the Appendix called "Defining the Project Scope" provides a visual description of the Steering Committee's work to draft the project scope for consideration and approval of the Full Expert Panel. The work of defining the project scope and building the expert panel and can be done simultaneously.

The members of this committee will:

- Participate in all conference calls;
- Define the scope of project;
    - Format and prioritize clinical questions based on the practitioners' questions and input from the CSA;
    - Develop the analytical framework identifying all the PICO[1] elements along with the evidence links if necessary;
    - Develop the search strategy with ADA Center staff **including whether or not a full systematic review is required or if the clinical recommendations can rely on published systematic reviews**;
    - Determine methods for searching for potential harms (using included studies only or requiring a separate search)
    - Develop preliminary inclusion and exclusion criteria with any limitation to study designs;
    - Guide any questions or concerns about the strategy for meta-analysis and data synthesis.

[1] See Section 6 for further information on PICO question format (*P*atient, *I*ntervention, *C*omparator, *O*utcome)

- Identify individuals to be nominated for the expert panel based on the needs of the project, expertise of the individuals, and need to balance perspectives to be approved by the CSA.

3.3 Expert Panel

The Expert Panel is generally made up of 10 to 15 individuals, including the Chair and Steering Committee, with multidisciplinary backgrounds, possibly including representatives of external stakeholder groups, subject matter experts, EBD process experts, end-users, epidemiologists and statisticians. This diversity ensures consideration of multiple perspectives. The work of building the expert panel and defining the project scope can be done simultaneously.

3.3.1 The Steering Committee nominates panel members based on the needs of the project, expertise of the individuals, and need to balance perspectives. Internal and external stakeholder organizations are nominated.

3.3.2 The CSA, with the agreement of any collaborator(s), approves the Steering Committee's nominations. Any changes to the Steering Committee's nominations should be carefully considered to ensure that all individuals meet the needs of the project as defined by the Steering Committee. After the Council has designated the individuals to serve on an expert panel, letters of invitation will be emailed under the signature of the CSA Chair.

Subject matter experts should:

- have recognized competence in writing and publishing peer-reviewed papers;
- be currently active and respected in their field; and
- be capable of knowledgeably assessing a body of evidence when developing clinical practice guidelines.

3.3.3 Roles of the expert panelists are explained in detail in the following sections, but highlights are summarized here:

- Review the draft decisions made by the Steering Committee and discuss until consensus is achieved;
- Review and finalize the list of included studies;
- Referee any disputes that arise while screening for studies;
- Be the duplicate abstractors/quality assessors for the included studies;
- Provide input into the draft evidence profile;
- Draft preliminary evidence statements;
- Assess the strength of the body of evidence for each intervention/outcome combination;
- Assess the magnitude of benefit for each intervention/outcome combination;
- Consider potential harms of the interventions;
- Present and discuss the bodies of evidence, meta-analyses, summary of findings tables, evidence profiles, and harms with the rest of the entire panel at the face-to-face meeting;
- Prepare a draft outline of the report;

- Edit the drafts of the report until finalized.

As a member of the Expert Panel, individuals must be prepared to make the following **commitments**:

- Attend panel meeting(s) at ADA Headquarters;
- Participate in conference calls before and after the meeting;
- Review literature and critically appraise the data for panel consideration before the meeting;
- Lead discussions involving specific manuscripts during the panel meeting, as assigned;
- Write sections of the report as assigned; and
- Consider all comments received as part of the external review process and revise the report as appropriate.

Panel members are expected to keep an open mind about what the evidence shows and avoid predetermined judgments about the outcome of the process.

3.4 Conflict of Interest Procedures

This Conflict of Interest procedures support the goal of having a process by which the Center for Evidence-Based Dentistry develops Clinical Practice Guidelines that are consistent, objective, and transparent. The profession must have confidence in the integrity of the process in order to adopt and implement the outcome in clinical practice.

3.4.1 General Procedures

Individuals who are invited to serve on an expert panel must first complete the ADA's Conflict of Interest Form.

Disclosed conflicts are not confidential. Unless the individual is disqualified to serve, his or her disclosures will be shared with the other panelists and be published in the final report. Disclosure allows the ADA to maintain a transparent process and convene a balanced group.

Completed disclosure forms will be kept on file by Center staff and updated at least yearly. All persons who develop potential conflicts of interest after initial disclosure must update the Conflict of Interest Questionnaire and disclose changes by electronic means to the disclosure review committee.

Each person will be notified of the committee's ruling by Center Staff (see below).

Individuals may recuse themselves voluntarily from participation with regard to specific aspects of the processes; however, a voluntary recusal does not free a member from the obligation to disclose a conflict.

3.4.2. Procedures for Review of Completed Disclosure Forms and Rules for Action

A preliminary determination of appropriate action will be a made EBD Center staff with the Panel Chair. Consideration of the panelist's eligibility to participate and/or vote on the panel will include the following:

- Is there any question that the person has not made a full and complete disclosure?
- Is there any indication that the person may provide any clinical information that could be perceived as misleading?
- Is there any indication that the person while participating in the expert panel may improperly favor any outside entity or may appear to have an incentive to do so?
- Does the person appear to be subject to incentives that might lead to disqualifying bias?
- Is there any indication that the person's conflict may prevent him or her to meet his or her obligations to, or the objectives of, the Clinical Practice Guidelines program?
- Do the person's current engagements present any conflicts between outside interests (e.g., is he simultaneously working on projects for competing business entities, fiduciary positions with other organizations, etc.)?

The following determinations of action will be made:

- *No action*.
  No disclosure or recusal necessary and individual may fully participate in the panel's activities
- *Information disclosure to expert panel*.
  Individual must disclose potential conflict to the full panel and may fully participate in discussion and vote.
- *Information disclosure to expert panel and recusal from voting*.
  Individual must disclose potential conflict to the full panel and may fully participate in discussion but will be recused from voting.
- *Recusal from all participation*
  Individual may not be part of the expert panel.

Typically, when there are no disclosures reported, EBD Center staff will note "no action". If there are any disclosures reported besides working for a university (which is typical for panel nominees), the panel Chair, the CSA Chair or Vice-Chair, and/or the ADA's Legal Division will be consulted for further decisions.

3.5 Confidentiality

All discussions and documents should remain confidential until the final report is publically disseminated via JADA, ADA.org, EBD Web site or other communication vehicles. If panelists are provided access to embargoed manuscripts during the course of the discussions, such information should remain confidential until manuscript publication.

3.6 Continuing Education Credits

Expert panel members will receive continuing education credits for pre-assignment work (see section 8.6), and the on-site Expert Panel meeting. The number of hours of CE credit is dependent upon the hours spent in critically appraising the included literature. The learning objectives for this program are as follows:

- Apply relevant risk of bias assessment criteria to included studies;
- Evaluate the robustness of evidence in terms of strengths and weaknesses;
- Critically appraise included studies for the validity, reliability and applicability of the evidence to answer the clinical questions;
- Extract and translate important findings from a body of evidence into level of certainty in the body of evidence
- Assess the balance of benefits and harms to arrive at clinical recommendations.

3.7 Authorship Guidelines

Panelists will be given authorship credit if they satisfy the requirements of the Journal of the American Dental Association that people listed as authors are those who have made an intellectual contribution to the manuscript. All authors will be listed with their affiliations, their academic degrees and their scientific or clinical contributions to the paper. EBD Center staff will also be listed as authors according to their contribution to the manuscript. A combination of the Panel Chair, the CSA Chair, and EBD Center staff will make the final determination of authorship and may ask a panelist to provide information supporting his or her listing as an author. Individuals representing ADA internal agencies may be listed as authors based on their individual contributions.

5. Clinical Practice Guideline Development Timeline

The CSA expects Clinical Practice Guidelines to be developed within 18 to 24 months. The following timeline may be used for planning clinical recommendations. If the need for a systematic review is established prior to or during the search for literature, the time required to conduct such a review may force a longer timeline.

Table 2: Process Overview and Timeline

	Staff	Panel Chair	Steering Committee (SC)	Full-panel
	Planning and Pre-work			
Month 1	Invite Panel Chair as designated by CSA Help determine SC members Facilitate COI process for SC Invite approved SC nominees	Help determine SC members along with Center staff and CSA Chair Approve SC members along with CSA Chair after COI vetting process complete		
Month 2	Convene SC Facilitate COI process for full panel including external stakeholders	Lead SC calls	Identify and vet panelists	
Month 3	Facilitate full panel approval by CSA Invite panelists Co-develop search strategy	Lead SC calls	Develop clinical questions Develop inclusion and exclusion criteria Co-develop search strategy	
Month 4	Conduct search & screen citations by title and abstract in duplicate	Lead SC calls	Answer any questions regarding screening	
Month 5-6	Pull full text articles; screen citations by full text in duplicate	Lead SC calls	Answer any questions regarding screening; Referee included and excluded studies	
Month 7	Arrange orientation Call 1	Lead orientation Call 1	Finalize data abstraction forms Finalize critical appraisal assignments	Orient on CR process, finalize Clinical Questions, search, inclusion exclusion criteria, included and excluded studies

Month 8-11	Develop and conduct training in EBD methods for full panel			Provide input on meta-analysis strategy, procedures and grouping of data
	Arrange orientation Call 2 Organize papers by topic and determine assignment plan Abstract data Critically appraise articles Adjudicate panel and staff appraisals and data abstraction Perform draft meta-analyses if needed according to approved strategy Compile Topic Discussion Guides Distribute all materials to panel	Lead orientation call 2 Approve assignment plan Facilitate assignments Finalize meeting agenda		Orient on Critical Appraisal process and receive assignments Submit assignments (critical appraisals and data abstraction) Approve meta-analysis strategy, procedures and grouping of data
	Panel meeting			
Month 12	Facilitate discussions and attainment of consensus Collect action items important meeting conclusions	Lead discussions		Assess level of certainty in evidence Determine net benefit rating Develop evidence statements

		Distribute writing assignments (evidence profiles and rationale)		Develop draft recommendation statements and strength of recommendations
	Post-panel meeting			
Month 13-15	Compile and address action items Compile evidence profiles (benefits and harms) & rationale (balance between benefits and harms) Draft manuscript and distribute to panel			
Month 16				Review report and provide comments
Month 17	Compile comments and distribute to panel Arrange conference calls Edit document as needed	Determine need and budget for second meeting vs. continued conference calls		Finalize statements and recommendations
Month 18	Distribute revised report to full-panel	Refine report		Final review and comment
Month 19		Finalize Report		
Month 20-21	Distribute report for external review			
Month 22				Address comments from external reviewers
Month 23	Submit to CSA Compile version for Journal submission			Review final report Finalize report
Post CSA-Approval				
Month 24			Approve Journal version	

Month 25	Submit Journal version to JADA and copy edit galley proofs Compile additional dissemination materials			
Month 26	Conduct focus group to refine message and test tools (if needed)		Approve dissemination materials	
Month 27	Disseminate			

6. Forming the Clinical Questions

The Steering Committee should develop the clinical questions based on the questions identified by the CSA as well as other CSA guidance. The clinical questions should be structured in the PICO (*P*opulation, *I*ntervention, *C*omparison, and *O*utcome) format to best define the scope of the project. Further, the Committee should identify the objective of the recommendations in terms of the Provider, Patient(s), and Settings that the recommendations would address.

The Steering Committee should develop not more than four or five questions for each topic, and consider limiting the scope to 2-3 questions. Questions should reflect the concerns of the clinical practitioner. Both the benefits and harms associated with an intervention should be considered.

The Steering Committee can consider developing an analytical framework to develop the clinical questions and identify all the parts of an evidence chain (an example of a screening question is shown in Fig. 3). This framework provides a visual diagram of the linkages between population, intervention and the outcomes, and helps to identify and highlight the need for evidence between intermediate and patient-oriented outcomes. The final report may include the analytical framework.

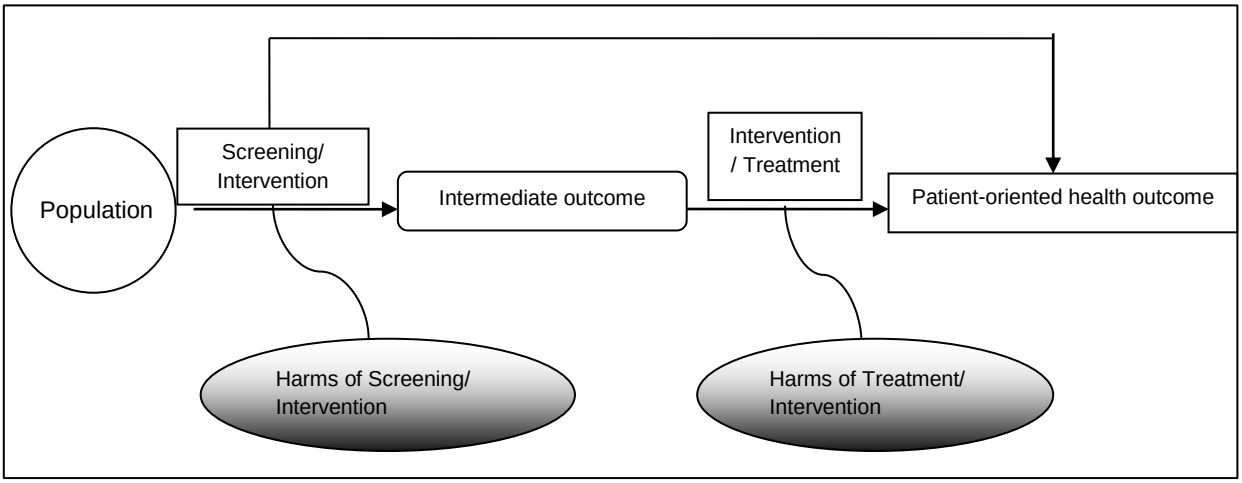


Figure 3: Analytical framework of an evidence chain

6.1 Selecting Outcomes Measure(s)

Specific outcome measures should be identified in framing the clinical questions to facilitate more efficient screening of the literature as well as determining which data will be used to evaluate the effect of the intervention in any meta-analyses. If more than one outcome measure will be chosen, these need to be ranked by the steering committee as to their relative importance (critical for decision making, important but not critical for decision making, low importance for decision making)[b]. Note that to date, cost has not typically been included when making clinical recommendations.

The Committee will need to identify all relevant health outcomes in order to effectively weigh the risks and benefits of an intervention. This includes potential harms or adverse events that may occur with the intervention of interest.

In some instances, the Steering Committee may choose to include surrogate or intermediate measures to assess health outcomes. This should be noted and supporting reasons discussed in the final report. Typically, surrogate outcomes should only be used when there is strong biologic plausibility for a causal connection with the true health outcome and when patient-oriented outcomes are not available in the literature. When multiple health outcomes are being considered, the panel should document the relative importance given to each outcome in making a recommendation for or against an intervention or procedure.

If surrogate or intermediate outcomes are included in the key questions, it is recommended that additional questions to establish associations to complete the entire chain of evidence should be considered for inclusion (i.e. the population, intervention and health outcome should be linked in establishing an evidence-based recommendation) if appropriate.

6.2 Setting Inclusion / Exclusion Criteria

Inclusion and exclusion criteria are established before a search is begun. In some instances, additional criteria may be established after the screening has begun. In such instances the report should clearly indicate which criteria were established *a priori* and which were added later. Historically, for clinical recommendations concerning interventions, those products that are not commercially available in the United States have been excluded, although the final decision is up to the expert panel.

Issues to consider include the study design(s) to be included. For example, are only randomized controlled trials (RCTs) eligible for inclusion, or can non-randomized controlled trials also be eligible? For some topics, the literature base of RCTs may be very small or nonexistent. Also, some clinical questions such as those regarding diagnostics may be answered by observational studies.

[b] Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, Alderson P, Glasziou P, Falck-Ytter Y, Schünemann HJ. GRADE guidelines: 2. Framing the question and deciding on important outcomes. J Clin Epidemiol 64 (2011) 395-400.

In general, systematic reviews of RCT's and individual RCT's constitute the highest level of evidence. Although developing recommendations based on the highest level of evidence is desirable, RCT's are not always available. In such circumstances, the ADA Clinical Practice Guidelines strive to be all-inclusive and analyze the current best evidence on a specific clinical question.

When determining if the study design yields the highest level of research possible, the following hierarchy of evidence (modified from the Oxford scale) may be used as a general guide. The highest level of research design is based on the type of clinical question (e.g. etiology or prevention or diagnosis etc.). Note: This table has been reproduced in its entirety. However for the purposes of ADA Clinical Practice Guidelines, the table merely provides a guide to the hierarchy of levels of evidence based on the type of clinical question in order to assess the risk of bias. The Classification levels and the quality criteria in the footnotes do not apply to our processes.

Table 3: **Hierarchy of Evidence: Adapted from the Oxford System**[c]

Level	Therapy/Prevention, Etiology/Harm	Prognosis	Diagnosis	Differential Diagnosis/Symptom Prevalence Study
1a	SR of RCTs	SR of inception cohort studies	SR of Level 1 diagnostic studies	SR of prospective cohort studies
1b	Multiple RCTs	Individual inception cohort study with ≥ 80% follow-up;	Validating[4] cohort study with good [5] reference standards;	Prospective cohort study with good follow-up[7]
1c	All or none[1] or single RCT	All or none case-series	Absolute SpPins and SnNouts[6]	All or none case-series
2a	SR of cohort studies	SR of either retrospective cohort studies or untreated control groups in RCTs	SR of Level 2b and better diagnostic studies	SR of 2b and better studies
2b	Individual cohort study, including low quality RCT	Retrospective cohort study or follow-up of untreated control patients in an RCT;	Exploratory cohort study with good [5] reference standards;	Retrospective cohort study, or poor follow-up
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies
3a	SR of case-control		SR of 3b and better	SR of 3b and better

[c] NOTE: The Oxford Center for EBM is updating its rating scale, which can be accessed at http://www.cebm.net/index.aspx?o=5653

	studies		studies	studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population
4	Case-series, and poor quality cohort and case-control studies [2]	Case-series and poor quality prognostic cohort studies [3]	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards

1 Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.

2 By poor quality cohort study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.

3 By poor quality prognostic cohort study we mean one in which sampling was biased in favor of patients who already had the target outcome, or the measurement of outcomes was accomplished in <80% of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors.

4 Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are 'significant'.

5 Good reference standards are independent of the test, and applied blindly or objectively applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study.

6 An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis.

7 Good follow-up in a differential diagnosis study is >80%, with adequate time for alternative diagnoses to emerge (e.g. 1-6 months acute, 1 - 5 years chronic).

6.3 Selecting Meta-Analysis Criteria and Summary Statistics

Prior to starting the project, the method of data summarization should be established. Those familiar with the literature on the topic of interest should have insight into the following issues. Alternatively, the Steering Committee can review related systematic reviews and RCTs to gather information on the data that are available so that decisions can be made. As the last resort, after the screening process has been completed and prior to performing the statistical analyses, a discussion should be held to formulate an analysis strategy.

Typically, a random effects model with inverse-variance approach is utilized. For continuous outcomes, a choice of mean difference, standardized mean difference, or other measure (such as prevented fraction) must be made. The mean difference is the absolute difference between two groups in a

clinical trial.[d] The standardized mean difference divides the absolute difference by the standard deviation to account for the different scales used in the included studies.[e] The choice is determined by whether or not the outcomes are expected to be reported on the same scale. When the outcomes are reported on the same scale, the mean difference (or difference in means) approach is used.

If the standardized mean difference is used, the panel may want to agree upon a relative scale to interpret the magnitude of benefit. Several approaches for interpreting magnitudes of effect from standardized mean differences are described in the Cochrane Handbook (see Chapter 12.6):

1. The first is based on rules of thumb*: "0.2 represents a small effect, 0.5 a moderate effect, and 0.8 a large effect (Cohen 1988). Variations exist (for example, <0.40 = small, 0.40 to 0.70 = moderate, >0.70 = large). Review authors might consider including a rule of thumb in the Comments column of a 'Summary of findings' table. However, some methodologists believe that such interpretations are problematic because patient importance of a finding is context-dependent and not amenable to generic statements."*[f]
2. *Re-expressing SMDs by transformation to odds ratio (Chapter 12.6.3)*
3. *Converting SMDs to NNTs (Table 12.6.a)*
4. *Re-expressing SMD by converting to a familiar instrument (Chapter 12.6.4)*

The Generic Inverse Method may also be used when adjustments utilizing a correlation coefficient are required to calculate the difference between the treatment and control groups. Other issues requiring discussion are the need for sub-group analysis, and if needed, identification of the sub-groupings; the need for statistical adjustments for split-mouth trials, and if so, what correlation coefficients to use; and the need for other statistical adjustments such as for cluster trial designs. Other statistical issues to be discussed include the need for sensitivity analysis, and if needed, what conditions should be analyzed and how the results should be reported. These decisions preferably should be made *a priori*. Note that sub-group analyses should not be over-interpreted since they are essentially observational in nature.

7 Searching for Evidence

No single source or electronic search will yield all the evidence. To locate all relevant evidence, a search strategy should incorporate a number of sources, including several relevant electronic databases. Hand-searching of relevant sources is typically performed, but the specific process should be discussed and approved by the Steering Committee. The Steering Committee needs to decide whether or not to include grey literature (abstracts of relevant scientific meetings, printed

[d] See Cochrane Handbook, http://www.cochrane-handbook.org/, Chapter 9.2.3, accessed 9-4-12.
[e] See Cochrane Handbook, http://www.cochrane-handbook.org/, Chapter 9.2.4, accessed 9-4-12.
[f] See Cochrane Handbook, http://www.cochrane-handbook.org/, Chapter 12.6.2, accessed 9-4-12.

bibliographies/reference lists, direct communication with researchers and expert practitioners in the field, and other sources).

7.1 Literature Sources

7.1.1 Published Evidence – Systematic Reviews and Clinical Studies

Center staff searches for published evidence by performing electronic literature searches using a variety of databases including MEDLINE and the Cochrane Library. MEDLINE is accessed through PubMed--the U.S. National Library of Medicine's free search engine and hand searches of relevant articles. At the orientation call, Center staff asks the panel about other literature that they may be aware of that could provide relevant evidence and meets the inclusion criteria. Note that including publications in languages other than English will require a language translation strategy.

The Steering Committee determines if additional search strategies, such as those stated below, are necessary:

- other databases such as the Institute of Medicine, , the evidence reports sponsored by the Agency for Healthcare Research and Quality (AHRQ), the Health Technologies Assessment database, EMBASE, CINAHL, and subject-specific databases
- hand searching relevant journals
- hand-searching references of relevant articles, particularly recent systematic reviews
- searching for unpublished material such as theses and dissertations

7.1.2 Background Information – Ongoing Trials and Other Guidelines

Staff should also provide the panel with background information about ongoing trials and evidence-based guidelines from other organizations. The Cochrane Central Register of Controlled Trials (part of the *Cochrane Library*) contains references to more than 218,000 clinical trials that have been identified though database and hand searching. The Database of Clinical trials (http://www.clinicaltrials.gov), the WHO International Clinical Trials Registry platform (http://www.who.int/trialsearch/) and the NIH CRISP database (http://crisp.cit.nih.gov) also contain references to ongoing trials. If the panel believes an ongoing study or studies will have significant impact on the Clinical Practice Guidelines, the panel may choose one of two options: 1) delaying publication of the Clinical Practice Guidelines until the study is published in a peer-reviewed journal; 2) moving forward with Clinical Practice Guidelines based on existing published evidence and considering additional evidence at the next update of the report; or 3) note in the publication that ongoing studies exist.

Center staff should provide guidelines and recommendations on the same topic from other agencies as background material for the Expert Panel's consideration. However, these documents are not considered as part of the evidence-analysis process.

7.1.3 Gray Literature

Some expert panels may wish to search the gray literature. Advantages of searching gray literature include minimization of publication bias. Disadvantages include additional time and resources as well as the need to determine *a priori* the methods that will be used to critically appraise these types of publications. If the decision is made to search the gray literature, identification of the sources and methods of searching should be planned as well as a strategy for critical appraisal.

7.2 Search Strategy

The Steering Committee is responsible for developing the search strategy with input from staff of the EBD Center staff and the ADA Library. The committee may adopt a single search string for the topics or multiple strings for each question. Additional separate search strategies may be necessary for systematic reviews and Clinical Studies. It is important to document the exact search strategy to facilitate updating the recommendations and maintain transparency of the process. When developing the search, strategies presented within the systematic reviews and other guidelines identified during the preliminary literature search may provide additional keywords that can be included. For more details on how to develop a search strategy, see Appendix 16.2.

Note that a different type of search may be required when addressing harms/adverse events depending on the decision of the expert panel on how to collect this evidence, since these types of outcomes are historically reported as case reports. Past projects have collated adverse event reports from included articles and supplemented these with general knowledge on commonly used medications from the FDA's website.

7.3 Protocol for Identifying and Screening Articles

One member of the Center staff will conduct the search and, along with the list of citations, document the number of citations retrieved and the date of search. The list of citations will be shared with a second staff member. These two staff members will serve as reviewers and screen the citations based on:

- Relevance to questions
- Inclusion and exclusion criteria

When applying the criteria the reviewers should err on the side of inclusion and include the article if there is any doubt whether it satisfies the criteria. A representative from the Steering Committee or a third staff member will act as referee in cases where there is a discrepancy between reviewers. The entire screening process should be independently documented by the reviewers to ensure a systematic approach. As a final step, the Steering Committee will approve all inclusions and exclusions.

7.3.1 Protocols for Searching and Screening

There are two steps to the protocol for conducting the literature search and screening articles for inclusion/exclusion. The steps are based on whether or not the clinical question has been addressed in the literature and whether or not systematic reviews will be considered as a suitable

foundation for the clinical recommendations. The current methods utilize the protocol for finding primary studies. The protocol of finding systematic reviews is provided for general information.

Protocol for identifying trials (primary evidence):

1. Using the search strategy developed by the committee and any additional key words identified in the systematic reviews, conduct a search for clinical trials/studies on human subjects using Pubmed at http://www.ncbi.nlm.nih.gov/pubmed/. Repeat using any other agreed upon databases.
2. Record a) the number of titles obtained; b) the date of the literature search; and c) search strategy used. It is useful to conduct the searches while logged into My NCBI and save the results for backup.
3. Combine results from different databases into Endnote (excluding duplicates) if possible
4. Share the list of citations with the second reviewer
5. Screen the titles and abstracts of the citations and select publications for potential inclusion (two reviewers working independently) and exclusion
6. Typically combine all included articles from both reviewers for screening by full text
7. Convert the full text citations into an Excel spreadsheet for capturing screening results including reasons for exclusion
8. Obtain full text articles
9. Divide full text between two reviewers or alternatively one staff screens for inclusion/exclusion and a panel member reviews the decisions
10. Determine if included or excluded, and if excluded, provide a reason in the Excel sheet
11. Compare results between reviewers and calculate agreement statistics to include in the final report
12. One member of the Steering committee or another staff member will adjudicate the disagreements between reviewers

Protocol for finding systematic reviews:

1. Perform a literature search for **systematic reviews** using PubMed http://www.ncbi.nlm.nih.gov/entrez/query/static/clinical.shtml
2. Record a) the number of titles obtained; b) the date of the literature search; and c) keywords used.
3. Convert the search results into an Excel spreadsheet for capturing screening results.
4. Share the list of citations with the second reviewer
5. Screen the titles and abstracts of the citations and select publications for inclusion (two reviewers working independently) with reasons for exclusion
6. Compare results between reviewers and calculate agreement statistics and include in the final report
7. One member of the Steering committee or one staff member will adjudicate the disagreements between reviewers

8. Obtain full texts of the selected titles and affirm that the publications are systematic reviews AND are relevant to the clinical questions with relevant outcomes reported. In case of discrepancy, request the Steering Committee to referee.
9. Record the number of systematic reviews included
10. Group the systematic reviews based on the clinical questions
11. Assess the clinical question, inclusion and exclusion criteria and **quality of the search** within the most recent systematic review.
12. In consultation with the Steering committee, determine if the systematic review can be used as the primary source document.
    a. If so, proceed with critical appraisal of the systematic review according to an agreed upon tool such as AMSTAR.
    b. In some cases, the systematic review may be used as a starting point, and an abbreviated literature search to capture the most recent literature search only can be conducted. In this case, proceed to the second protocol, which involves PubMed search using specific search dates and terms identified through examining the systematic review.
    c. It is most likely that the systematic review either does not exactly match the clinical question, is not of high quality, or that no systematic reviews were identified. In these cases a full systematic review is required to form the foundation of the clinical recommendations. The second protocol describes the literature search procedure for clinical trials.

7.3.2 Saving Search Strategies and Results

Search strategies can be saved in MyNCBI via PubMed and rerun to retrieve any references recently added to the database. The Auto Alert (SDI – Selective Dissemination of Information) feature allows the reviewer to save the search strategy and have the system e-mail the new references found each time the database is updated or at regular intervals.

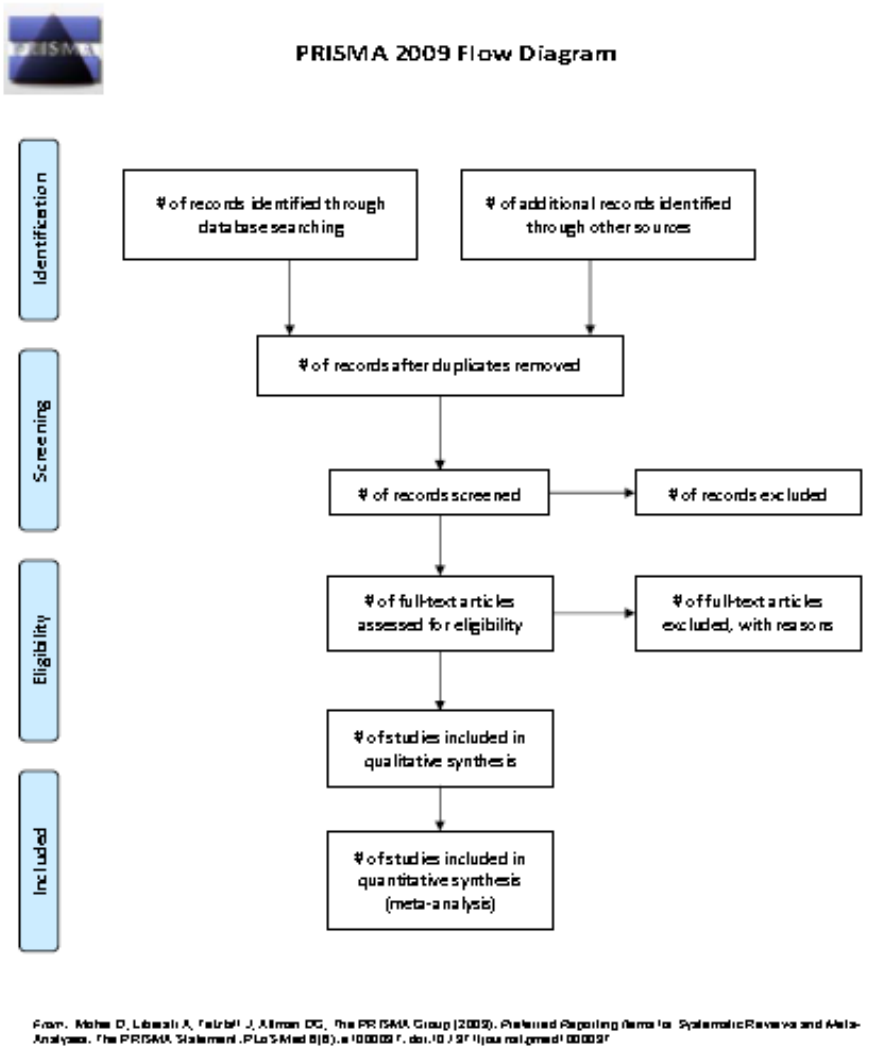
7.3.3 Literature Retrieval and Screening

All articles that have not been excluded at the title/abstract stage need to be retrieved for assessment at the full text stage. The ADA library may assist in obtaining articles. Articles that are not available through the ADA library or interlibrary loan may need to be purchased directly from the publisher. Full text screening is to be performed independently and in duplicate. All reasons for exclusion at this stage need to be recorded in the Excel screening spreadsheet.

Inclusion and exclusion criteria are established before a search is begun. In some instances, additional criteria may be established after the screening has begun. In such instances the report should clearly indicate which criteria were established *a priori* and which were added later.

7.3.4 Documenting and Reporting Literature Screening Results (PRISMA)

A flow diagram of the literature search and screening process is to be developed according to the PRISMA statement (http://www.prisma-statement.org/). A template is available in RevMan[g] for this purpose. At a minimum, the flow diagram should list the number of records identified through database and other searching, the total number of records after duplicates were removed, the number of records excluded after screening by title and abstract, the number of articles excluded after full text review, the number of articles included in qualitative review(s), and the number included in quantitative review(s).



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

[g] Review Manager (RevMan) [Computer program]. Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

8. Preparing for the Panel Meeting

Center staff will schedule orientation teleconference(s) and/or webinar(s) with the full panel. Topics for discussion at the orientation(s) include:

- Introduction of panel members
- Introduction to the ADA Center for EBD staff
- Introduction to the Clinical Practice Guidelines Program
- Roles and responsibilities of panelists, including chair and steering committee
- Commitment
- Conflict of interest
- Confidentiality
- Review of clinical (PICO) questions
- Details of the search
- Finalization of the inclusion and exclusion criteria
- Introduction to the literature
- Critical appraisal process and quality assessment of studies
- Pre-assignments
- Introduction to data abstraction forms (see Appendix 16.5 & 16.6)
- Training in assessing risk of bias (critical appraisal)

The handbook should be distributed as background to the conference call background on the process.

The following procedures should be completed prior to the panel meeting: 1) adjudicated data extraction; 2) adjudicated critical appraisal; 3) meta-analysis by intervention and outcome; 4) completion of Topic Discussion Guides.

9. Critical Appraisal and Data Abstraction of Individual Studies

A data extraction and critical appraisal spreadsheet will be developed for the project. Previous spreadsheets can be reviewed to determine what, if any, modifications need to be made for each specific project dependent on the subtleties of the literature. The panelists will need to identify critical items regarding study conduct, outcomes measures, and domains to consider for risk of bias that would be prudent to summarize across all studies.

9.1 Spreadsheet Development and Piloting

Ideally, the spreadsheet should be piloted by several panel members along with Center staff on a few randomly selected articles to determine if modifications are necessary to the spreadsheet prior to rolling it out to all panelists for all included articles. The panel can consider if they want to measure the agreement between reviewers.

9.1.2 Data Extraction

Cochrane's checklist of items for data collection / data extraction (available at: http://www.cochrane-handbook.org/ Table 7.3.a) is a good foundation for data extraction items to be considered:

Table 4: Items for data collection. Items without parentheses should normally be collected in all reviews; items in square brackets may be relevant to some reviews and not others.

Source

- Study ID (created by review author).
- Report ID (created by review author).
- Review author ID (created by review author).
- Citation and contact details.

Eligibility

- Confirm eligibility for review.
- Reason for exclusion.

Methods

- Study design.
- Total study duration.
- Sequence generation*.
- Allocation sequence concealment*.
- Blinding*.
- Other concerns about bias*.

Participants

- Total number.
- Setting.
- Diagnostic criteria.
- Age.
- Sex.
- Country.
- [Co-morbidity].
- [Socio-demographics].
- [Ethnicity].
- [Date of study].

Interventions

- Total number of intervention groups.

For each intervention and comparison group of interest:

- Specific intervention.
- Intervention details (sufficient for replication, if feasible).
- [Integrity of intervention].

Outcomes

- Outcomes and time points (i) collected; (ii) reported*.

For each outcome of interest:

- Outcome definition (with diagnostic criteria if relevant).
- Unit of measurement (if relevant).
- For scales: upper and lower limits, and whether high or low score is good.

Results

- Number of participants allocated to each intervention group.

For each outcome of interest:

- Sample size.
- Missing participants*.
- Summary data for each intervention group (e.g. 2×2 table for dichotomous data; means and SDs for continuous data).
- Estimate of effect with confidence interval; P value.
- Subgroup analyses.

Miscellaneous

- Funding source.
- Key conclusions of the study authors.
- Miscellaneous comments from the study authors.
- References to other relevant studies.
- Correspondence required.
- Miscellaneous comments by the review authors.

*Full description required for standard items in the 'Risk of bias' tool (see Chapter 8, Section 8.5).

9.1.3 Assessment of the Risk of Bias: The Cochrane Risk of Bias Tool

The risk of bias (individual study quality) is independently assessed by at least one panelist in combination with one EBD Staff Member prior to the panel meeting.

It is suggested that the panel adopt the Cochrane Risk of Bias tool for assessing the quality of individual studies.
The tool is based on the following summary of the most common sources of bias: http://www.cochrane-handbook.org/ Table 8.4a and shown in its entirety as Table 5. The tool is available at: http://www.cochrane-handbook.org/ Table 7.3.a.

Table 5: A common classification scheme for bias

Type of bias	Description	Relevant domains in the Collaboration's 'Risk of bias' tool
Selection bias.	Systematic differences between baseline characteristics of the groups that are compared.	• Sequence generation. • Allocation concealment.
Performance bias.	Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest.	• Blinding of participants and personnel. • Other potential threats to validity.
Detection bias.	Systematic differences between groups in how outcomes are determined.	• Blinding of outcome assessment. • Other potential threats to validity.
Attrition bias.	Systematic differences between groups in withdrawals from a study.	• Incomplete outcome data
Reporting bias.	Systematic differences between reported and unreported findings.	• Selective outcome reporting (see also Chapter 10).

The assessment of risk of each domain is expressed simply as 'Low risk', 'High risk' or 'Unclear risk' of bias. The panel can decide whether or not to assign a summary assessment for each study individually (which may facilitate sensitivity analyses with respect to study conduct), but at a minimum, there needs to be a summary assessment of each study/outcome combination. This is because there may be separate conduct and reporting for each outcome in a singular study. The panel should also give thought as to which of the domains are key domains that could affect the confidence in the results of the study, and whether the potential for bias will tend to overestimate or underestimate the true intervention effect. These key domains will play a dominant role in assessing the level of certainty in the body of evidence as a whole (more details in described in Section 10).

9.2 Processes

9.2.1 Panel Pre-Assignments

Center staff should distribute included studies among the Panelists for critical appraisal and data extraction at least eight weeks before the Expert Panel meeting. Panelists should be provided the data abstraction forms to complete and submit to Center staff at least four weeks prior to the panel meeting. Data abstraction and critical appraisal should always be performed in duplicate.

Note that it may be beneficial to assign groups of studies based on intervention to panel members rather than assigning studies randomly. This facilitates decision-making throughout the document development process.

9.2.2 ADA Staff Responsibilities

In parallel with the Panelists completing critical appraisal and data extraction, ADA EBD Center staff also complete the same task independently. Prior to the panel meeting, an ADA EBD Center Staff member who did not do the primary data extraction and critical appraisal will adjudicate the duplicated abstracted information, possibly by discussing the details with either or both reviewers.

After the data and risk of bias assessments have been adjudicated, the data will be combined as necessary for the project. This may entail conducting several meta-analyses. Center staff will prepare Topic Discussion Guides and distribute them to the Panelists prior to the Panel meeting. These Topic Discussion Guides serve to summarize the salient information, provide a format for group discussion at the meeting, and provide a format to capture group decisions. An example is provided in the Appendix.

9.3 Non-Interventional Questions or Using Study Designs at Higher Risk of Bias

Some clinical questions relate to topics other than interventions, such as diagnostics. In these cases, the highest evidence may be observational studies. Further information can be found at the Oxford Centre for Evidence Based Medicine (www.cebm.net), the Cochrane Diagnostic Test Accuracy working group[h], and the QUADAS 2 tool for quality assessment of diagnostic accuracy studies[i]. General criteria for assessing study designs other than RCTs are listed in the three figures below.

Generally, a “low risk” study meets all of the criteria. An “unclear risk” study fails to meet (or it is unclear that it meets) at least one criterion, but does not have a “fatal flaw.” “High risk” studies have at least one fatal flaw.

[h] http://srdta.cochrane.org/handbook-dta-reviews

[i] Whiting PF, Rujtes AWS, Westwood ME, et al. QUADAS-2: A revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 155[8]:529-536 (2011).

Criteria for Case-Control Studies:

- Accurate ascertainment of cases
- Nonbiased selection of cases/controls with exclusion criteria applied equally to both
- Response rate
- Diagnostic testing procedures applied equally to each group
- Measurement of exposure accurate and applied equally to each group
- Appropriate attention to potential confounding variables

Low risk of bias	Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate equal to or greater than 80 percent; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables.
Unclear risk of bias	Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rate less than 80 percent or attention to some but not all important confounding variables.
High risk of bias	Major selection or diagnostic work-up biases, response rates less than 50 percent, or inattention to confounding variables.

Criteria for Cohort Studies:

- Initial assembly of comparable groups
- consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination)
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- All important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intention to treat analysis for RCTs.

Low risk of bias	Comparable groups are assembled initially and maintained throughout the study (follow-up at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention to confounders in analysis.
Unclear risk of bias	Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for.
High risk of bias	Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention.

Criteria for Diagnostic Studies: • **Screening test relevant, available for primary care, adequately described** • **Study uses a credible reference standard, performed regardless of test results** • **Reference standard interpreted independently of screening test** • **Handles indeterminate results in a reasonable manner** • **Spectrum of patients included in study** • **Administration of reliable screening test**	
Low risk of bias	Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100) broad-spectrum patients with and without disease.
Unclear risk of bias	Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients.
High risk of bias	Has fatal flaw such as: Uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size or very narrow selected spectrum of patients.

10. Panel Meeting Objectives

One of the main objectives for the Expert Panel meeting is to review the evidence to determine the level of certainty in the evidence for each question posed by the panel. The ADA follows the USPSTF general procedures as shown in Table 6 to identify the level of certainty as High, Moderate, or Low. The table describes the definition of each level of evidence as well as factors that may limit the confidence in the evidence and estimates of effect. The table is modified slightly to include items from the GRADE[j] approach, which has been adopted by the Cochrane Collaboration as well as many other organizations responsible for developing systematic reviews.

[j] Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 64 (2011): 401-406.

Table 6. Level of Certainty in the body of evidence included within this systematic review.*

Level of Certainty in Effect Estimate	Description
High	**The body of evidence usually includes consistent results from well-designed, well-conducted studies in representative populations. This conclusion is unlikely to be strongly affected by the results of future studies**. This statement is strongly established by the best available evidence.
Moderate	**As more information becomes available, the magnitude or direction of the observed effect could change, and this change could be large enough to alter the conclusion.** This statement is based on preliminary determination from the current best available evidence, but confidence in the estimate is constrained by one or more factors, such as: • the limited number or size of studies; • plausible bias that raises some doubt about the results; • inconsistency** of findings across individual studies; • imprecision in the summary estimate; • limited applicability due to the populations of interest; • evidence of publication bias; or • lack of coherence in the chain of evidence.
Low	**More information could allow a reliable estimation of effects on health outcomes.** The available evidence is *insufficient* to support the statement or the statement is based on extrapolation from the best available evidence. Evidence is insufficient or the reliability of estimated effects is limited by factors such as: • the limited number or size of studies; • plausible bias that seriously weakens confidence in the results; • inconsistency** of findings across individual studies; • imprecision in the summary estimate; • gaps in the chain of evidence; • findings not applicable to the populations of interest; • evidence of publication bias; or • a lack of information on important health outcomes.

*Adapted from the United States Preventive Services Task Force system with modifications from the GRADE approach
**Inconsistency of findings is a concept incorporating direction of effect, similarity of point estimates, overlapping of confidence intervals, and statistical heterogeneity, which typically originates from methodological heterogeneity.

10.1 Factors to Evaluate

The level of certainty (quality) of a body of evidence is based on the extent to which there is confidence in the estimate of the effect. Each outcome is considered separately by assessing the body of evidence. Five domains are included in the assessment of the quality of the body of evidence for each outcome. These domains are:

1. Risk of bias (limitations of the evidence)
2. Applicability of evidence
3. Inconsistency or unexplained heterogeneity of results
4. Imprecision (wide confidence intervals)
5. High probability of publication bias

The Cochrane Handbook Chapter 12.2.2 describes each of these domains in detail. A synopsis is provided herein:

10.1.1 Summary Assessment of Risk of Bias Across Studies

The summary assessment depends on a judgment of the relative importance of different domains and the potential of the domain to affect the estimate of the effect. The reasoning behind the judgments should be transparently explained. The following Table 7 (modified from http://www.cochrane-handbook.org/ Table 12.2.d) lists considerations for the summary assessment of risk of bias for all studies across domains for each outcome. The summary assessment should be reported in the Evidence Profile.

Table 7: Approach for summary assessment of the risk of bias for each important outcome across domains and across studies

Across all studies and domains	Interpretation	Considerations	Summary assessment of risk of bias for all studies
Most information is from studies at low risk of bias for all key domains.	Plausible bias unlikely to seriously alter the results.	No apparent limitations.	Low risk of bias.
Most information is from studies at low risk of bias for all key domains and low or unclear risk of bias for non-key domains.	Plausible bias unlikely to seriously alter the results.	Potential limitations are unlikely to lower confidence in the estimate of effect.	Low risk of bias.
Unclear risk of bias for one or more key domains and the remaining domains low risk of bias	Plausible bias that raises some doubt about the results.	Potential limitations are likely to lower confidence in the estimate of effect.	Unclear risk of bias
Most information is from studies at unclear risk of bias for all key domains and unclear or high risk of bias	Plausible bias that raises some doubt about the results.	Crucial limitation for one criterion, or some limitations for multiple criteria, sufficient to lower confidence in the estimate	Unclear risk of bias

for non-key domains.		of effect.	
The proportion of information from studies with high risk of bias for one or more key domains is sufficient to affect the interpretation of results.	Plausible bias that seriously weakens confidence in the results.	Crucial limitation for one or more criteria sufficient to substantially lower confidence in the estimate of effect.	High risk of bias

10.1.2 Applicability

Applicability refers to the extant the evidence is directly related to the question of interest. For example, the question may ask about topical fluoride use in adults, but all the evidence is on children. Another example would be if the question asks about treatments A versus B, but evidence exists only for A versus placebo and B versus placebo. Another consideration is whether the evidence is generalizable, for example, if all the evidence on an intervention is from populations with no comorbidities, and the question of interest relates to a primary care population. Downgrading of evidence for applicability could be considered by the panel. All judgments are recorded in the evidence profile.

10.1.3 Inconsistency or Unexplained Heterogeneity of the Results

Consistency refers to similarities in point estimates, extent of overlap of confidence intervals, and statistical criteria such as tau, the p-value of tau, and I^2. Sub-group analysis may explain some inconsistency, but note that these analyses are only observational in nature. Sources of inconsistency include clinical or methodological differences between trials. Downgrading of evidence for large and unexplained inconsistency should be considered by the panel, especially in cases where some studies show substantial benefit and others show no effect or harm (rather than only gradations in effect size) [Guyatt et al. 2011][k]. All judgments are recorded in the evidence profile.

10.1.4 Imprecision (Wide Confidence Intervals)

Wide confidence intervals can arise when the totality of evidence consists of few studies and few participants. Confidence intervals are reported in the Evidence Profile, but the level of certainty can be downgraded for this. For example, the summary estimate may show a large mean benefit, but because if imprecision, the confidence interval may cross the line of no effect.

10.1.5 High probability of Publication Bias

One way to assess publication bias is to look for asymmetry in the funnel plot or using Egger's statistic if possible. As a rule of thumb, tests for funnel plot asymmetry should be used only when

[k] Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 7. Rating the quality of evidence – inconsistency. J Clin Epidemiol. 64 (2011):1294-1302.

there are at least 10 studies included in the meta-analysis, because when there are fewer studies the power of the tests is too low to distinguish chance from real asymmetry [Sterne et al. 2011][l].

Inclusion of gray literature decisions may alleviate publication bias. Clinicaltrials.gov can be investigated for the presence of unpublished studies or unreported outcomes.

10.2 The Evidence Profile

The evidence profile summarizes the number and study designs of the included studies (by outcome), and then lists in tabular form if there are any serious concerns in each of the domains for quality (risk of bias, consistency, precision, applicability, and probability of publication bias) and the overall determination of the level of certainty in the evidence. The final column lists the summary effect measure result. An example is shown in Table 8.

Table 8. Evidence profile.

Therapy and Outcome	Level of certainty assessment							Level of Certainty	Effect measure
	Quantity of evidence		Risk of bias	Consistency	Precision	Applicability	Publication bias		(e.g. Mean difference)
	No. Studies	No. participants							

10.3 Drafting Preliminary Evidence Statements

Evidence statements are brief (one or two sentences) statements that summarize the evidence. Evidence statements should be clear, concise and specific. Each evidence statement is paired with an explicit statement of 1) whether or not there is a benefit using the intervention or diagnostic technique and 2) the level of certainty in the estimate of the effect.

10.4 Drafting Preliminary Clinical Practice Guideline Statements

10.4.1 Language

After the panel has finalized the evidence statements and determined the level of certainty, it drafts the recommendations. Recommendations are written in a clear, concise and direct manner. They should guide the practitioner on how the current evidence on a topic may be applied to a patient's treatment. Each recommendation is based on evidence statements, supported with publication references. Expert Panels may choose to stratify recommendations based on criteria such as risk factors, age, population, etc. if warranted by the evidence and/or if such stratification would make the recommendations easier to understand.

The essential components of each recommendation should include[m]:

[l] Sterne JAC, Egger M, Moher D, Cochrane Bias Methods Group. Chapter 10: Addressing reporting biases. In: Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0. available at: http://handbook.cochrane.org/: The Cochrane Collaboration; March 2011.

- *when* (i.e. under what specific conditions)
- *who*
- must, should, may/can (should reflect the level of certainty within the evidence and the grade for the strength of recommendation)
- do *what*
- to *whom*

10.4.2 Consensus / Expert Opinion Recommendations

If there is insufficient or inconclusive evidence, the panel may choose to not make a recommendation for or against an intervention or make recommendations based on consensus opinion. This method should be conspicuously noted in the report. Further, if achieving consensus among experts for developing consensus-based recommendations, a simple vote may be taken by the Chair and the result recorded in the report. The vote should be conducted by secret ballot or other robust consensus development procedure.

10.4.3 Assessing Benefits vs. Harms and the Judging the Strength of the Recommendation

After the recommendation has been drafted, a process is used to arrive at the strength of the recommendation (Table 9).

First, the level of certainty in the evidence and the summary estimate of effect from the evidence profile are used in this process. The level of certainty in the evidence determines the row of Table 9 that is under consideration.

In the case of low certainty, the clinical recommendation is given a strength of "expert opinion" (either for or against use). It is important to note that topics on which there is little evidence and conflicting opinions from experts are often ones where the profession looks for guidance. ***Note:*** *If an entire project is found to be lacking evidence, CSA may consider using other communications vehicles to disseminate key information to practitioners rather than through formal Clinical Practice Guidelines.*

Next, the panel needs to discuss and come to a consensus about the balance between the benefit (estimate of effect from the meta-analysis, which could actually be negative or no benefit) and any potential harms that have been identified by the panel through conducting the systematic review. The panel must decide of the three options: 1) the benefits clearly outweigh the harms; 2) the benefits and harms are closely balanced OR there is uncertainty in the estimate of the balance; or 3) the harms clearly outweigh the benefits.

[m] Rosenfeld RM and Shiffman RN. Clinical practice guideline development manual: A quality-driven approach for translating evidence into action. Otolaryngology – HNS (2009) 140, S1-S43.

Once the balance between benefits and harms has been decided, the intersection of the level of certainty in the evidence row and the harm/benefit balance column indicates the final strength of the recommendation, which is either a) strong; b) in favor; c) weak; d) expert opinion for; e) expert opinion against; or f) against. Table 10 lists definitions of the strengths of the recommendations. Table 11 shows the color coding that has been adopted to facilitate communicating the strength of the recommendation.

Table 9: Balancing Level of Certainty in the benefit estimate with potential for harms*

Level of Certainty	Net Benefit Rating		
	Benefits outweigh potential harms	*Benefits balanced with potential harms*	*No benefit or potential harms outweigh benefits*
High	Strong	In Favor	Against
Moderate	In favor	Weak	Against
Low	Expert Opinion For¥ or Expert Opinion Against¥		

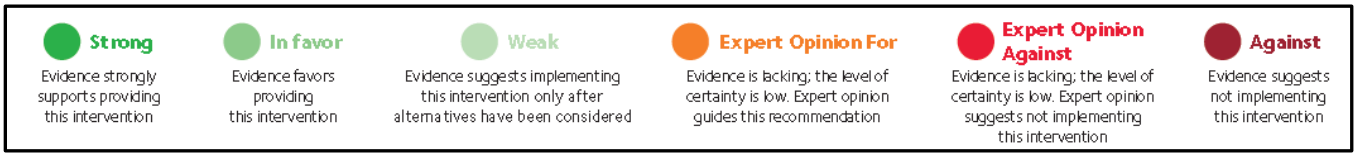
¥The USPSTF system defines this category as insufficient evidence and makes I-Statements. They do not make recommendations when the level of certainty in the evidence is low.

Table 10: Definitions for the strength and direction of recommendations are as follows:*

Recommendation strength	Definition
Strong	Evidence strongly supports providing this intervention
In Favor	Evidence favors providing this intervention
Weak	Evidence suggests implementing this intervention after alternatives have been considered.
Expert Opinion For¥	Evidence is lacking; the level of certainty is low. Expert Opinion guides this recommendation
Expert Opinion Against¥	Evidence is lacking; the level of certainty is low. Expert Opinion suggests not implementing this intervention
Against	Evidence suggests not implementing this intervention or discontinuing ineffective procedures

*Adapted from the USPSTF system
¥The USPSTF system defines this category as insufficient evidence and makes I-Statements. They do not make recommendations when the level of certainty in the evidence is low.

Table 11. Clinical recommendation strength color coding



10.4.4 Clinical Recommendation Summaries

Clinical Recommendation Summaries summarize the strengths and weaknesses of the evidence in terms of benefits and harms. An accurate, explicit Clinical Recommendation Summary offers the readers and the panelists the most compelling argument to accept a recommendation strength. The rationale provides information on the panels' interpretation of the balance between benefits and harms and the reasons for the recommendations. The following is an example of a Clinical Recommendation Summary:

Example. SRP versus no treatment or supragingival debridement:

- Level of certainty: High
- Benefit: Yes
  - Overall net gain in clinical attachment (Mean difference, MD) =0.66 [95% CI: 0.39, 0.93] mm (improvement)
- Adverse events or harms: Possible pain the day of or the day after treatment, possible increase in dental hypersensitivity within a week. Rarer chance of fever or myalgia.
- Benefit-harm assessment (net benefit rating): Benefits of SRP outweigh potential for harm
- Strength of clinical recommendation: Strong

11. Panel Meeting Logistics

The following procedures occur at the panel meeting and are presented for each intervention of interest according to the Topic Discussion Guides (an example is in the Appendix):

1. Review data abstractions for included articles
2. Review meta analyses / assessment of evidence of benefit for each outcome
3. Assessment of level of certainty in estimates of effect for each outcome
4. Evidence statements language and evidence profile development
5. Assessment of harms
6. Draft clinical recommendations statements
7. Strength of the recommendations
8. Recording of values/tradeoffs/ benefit vs. harms

Each Expert Panel member or team along with Center staff will present to the rest of the panel the studies that were assigned to him/her by reviewing the abstracted data and the meta-analyses. The full panel will discuss the information and make the necessary judgments to complete the Topic Discussion Guides, including the evidence profiles, the draft evidence statements, and draft clinical recommendation strengths for the question(s) assigned to him/her. A consensus method is used to achieve majority agreement.

Current gaps in the chain of evidence (if an analytical framework is used) or otherwise the body of evidence are documented as research questions to encourage future research on the topic.

12. Procedures for Voting During Development of the Report

At the discretion of the Chair of the expert panel, votes may be taken for major procedural and methodological decisions, for final recommendations, and for statements about clinical practice implications. Voting procedures include the following:

- Votes are taken by voice or hand, without secret ballots.
- Votes are recorded as yes, no, abstain, or absent. Individuals recused by reason of potential conflict of interest are recorded as recused and do not vote.
- If at all possible, a quorum of the panel should be present for all official votes (at least two-thirds of eligible members (those not specifically recused for disclosed conflicts), including the chair). It is noted that at times due to scheduling conflicts it may not be possible for a quorum of panelists to be present for all voting sessions.
- In votes that are less than unanimous, there will be no minority reports. At the discretion of the chair the results of the vote may be included in the final report as a means of explaining the uncertainty within the evidence and the different possible interpretations based on professional and value judgments.

13. Writing the Report

ADA Staff writes a **draft report** after the completion of the Expert Panel meeting. This draft document serves as an "organizational memory" to document all the important discussions that emerged at the meeting. The draft report can be circulated amongst the expert panel to ensure representativeness to the discussions and decisions that were made at the face-to-face panel meeting.

The **full report** is developed in the months following the Expert Panel meeting, and is a comprehensive document that provides transparency and information to the end users, and includes details regarding methods, evidence, and rationale supporting the recommendations. The sections of the report may be organized by the following subhead titles.

- Abstract
- Scope and Purpose (target condition or procedure, target patient, target provider and setting, expected implementation outcomes)
- Introduction
- Definition of terms, if needed
- Clinical Question
- Methods (including search documentation, data synthesis and analysis, grading, review process, conflict disclosures, funding source)
- Evidence Statements with references and level of certainty

- Clinical Recommendations; Strength of the recommendation; Clinical recommendation summaries
- Rationale for recommendations (balance between benefits and harms – "Discussion")
- Clinical Implications (Conclusion)
- Implementation needs (including potential obstacles to implementation)
- Table for suggested future research topics
- List of additional full panel members who participated but were not authors; and peer reviewers
- [if desired: Implementation plan]
- Update plan
- Acknowledgements
- List of excluded studies and reasons at full text stage

To facilitate consistency between evidence statements for different sections of the report, it may be useful to compile an evidence profile across interventions as well as a table of evidence statements. An example of the latter follows in Table 12:

Table 12. Example of evidence statement summary format

Level of certainty and balance of benefits to harms for each topical fluoride agent reviewed in this report				
AGENT	**AGE GROUP (years) OR DENTITION**	**EVIDENCE STATEMENT**	**LEVEL OF CERTAINTY**	**NET BENEFIT RATING**
2.26% fluoride varnish	Under 6	There is a benefit of 2.26% fluoride varnish application at least twice per year for caries prevention.	Moderate	Benefits outweigh potential harms
	6-18	There is a benefit of 2.26% fluoride varnish application at least twice per year for caries prevention.	Moderate	Benefits outweigh potential harms
	Root caries	There is a benefit of 2.26% fluoride varnish application at least twice per year for root caries prevention in adults.	Low	Benefits outweigh potential harms

Panelists contribute to writing the report. ADA EBD Center staff along with the panel Chair lead the effort in drafting, developing and finalizing the report with input from the full panel. To facilitate completion of the manuscript, conference calls likely will be needed with panel members and the full panel to finalize decisions and manuscript contents.

Branding requirements include:

- Header – ADA Center for EBD logo should be at a minimum 0.25" from the edge of the paper; 0.5" margins are ideal.
- The only font that is brand-compliant is Arial. Bold, italic, and size can be used to provide emphasis where needed.
- All colors used should be brand palette colors (colors are noted as Red/Green/Blue) for Word, Powerpoint and on-screen uses:

    1. Green: 51/153/51
    2. Chocolate Brown: 124/77/58
    3. Blue: 51/102/204
    4. Red: 200/16/46
    5. Yellow: 240/179/35
    6. Yellow-orange: 240/179/35
    7. Orange: 242/101/34
    8. Purple: 85/67/126
    9. Mulberry (reddish-purple): 153/51/102

The above apply to **all** text, including tables, graphs, and charts.

14. External Review

Clinical Practice Guidelines undergo internal and external review to ensure scientific accuracy, clarity, and clinical usefulness. External reviewers include: 1) clinical content experts, who are asked to review the document to verify the completeness of the literature review and to ensure clinical sensibility; 2) experts in systematic reviews and/or guideline development, who are asked to review the method by which the recommendation was developed; 3) potential users of the recommendations, who are asked to judge their usefulness; and 4) stakeholders who may be affected by the recommendations, including but not limited, to third party-provider trade organizations. The expert panel as well as Center staff nominate and select external reviewers. A PDF file of the manuscript (helpful if line numbers are included) is provided to the external reviewers with explicit instructions to provide written comments along with justifications for requested change(s). After all comments have been received, Center staff compiles the comments and schedules conference calls with the panel members to discuss comments and determine if changes in the manuscript are needed, and if so, what the changes are. Currently, no feedback is provided to the external reviewers with respect to how their comments were addressed; however, all comments should be considered by the expert panel although they need not be accepted. External reviewers are acknowledged in the manuscript.

After the manuscript has been approved by the panel, Center staff presents the final documents to the CSA for approval. Upon approval, staff submits the manuscript or an executive summary of the manuscript to *JADA* for publication. A chairside guide is also developed to assist in implementation efforts. ADA EBD Center staff work with ADA's graphic designers, member-based focus groups, and expert panel member to develop appropriate chairside tools.

15. Disseminating Clinical Practice Guidelines

Several modes of dissemination may be considered for disseminating Clinical Practice Guidelines. Available resources are directed to maximize reach to target audiences.

- Posting on ebd.ada.org
- JADA publication of an executive summary
- Submission to the National Guideline Clearinghouse
- Chair-side tools
    - Note that the following are the branded colors for each recommendation strength:

Strength of recommendation	Branded color (Red/Green/Blue) and transparency
Strong	Green (51/153/51); 0%
In favor	Green (51/153/51); 30%
Weak	Green (51/153/51); 60%
Expert opinion for	Orange (242/101/34); 0%
Expert opinion against	Red (200/16/46); 0%
Against	Red-brown (164/52/58); 0%

- Communication through *ADA News*, e-communications, Champions Newsletter
- CE courses
- Seminar presentations – ADA CE Seminar Speaker Series
- Panel member presentations at ADA annual session and other regional or national dental meetings
- Consumer brochures
- Multimedia tutorials

16. Updating Clinical Practice Guidelines

Every five years (or when new information/data make it necessary) Clinical Practice Guidelines will be reaffirmed or revised. Center staff repeats the search to determine if a recommendation requires revision. When updating a Clinical Practice Guideline, the new search should use the last search date used to develop the previous recommendation. Findings should be presented to the Steering committee for consideration. If no new evidence is found, the repeated search date should be documented and the unchanged recommendation should be reaffirmed. If new evidence pertaining to one or more key questions is identified, the panel may be convened via teleconference

or an in-person meeting to review the new evidence, update the existing evidence, recommendation statements and grades. Before being disseminated, all reaffirmations and revisions in the report are approved by the panel, followed by the CSA.

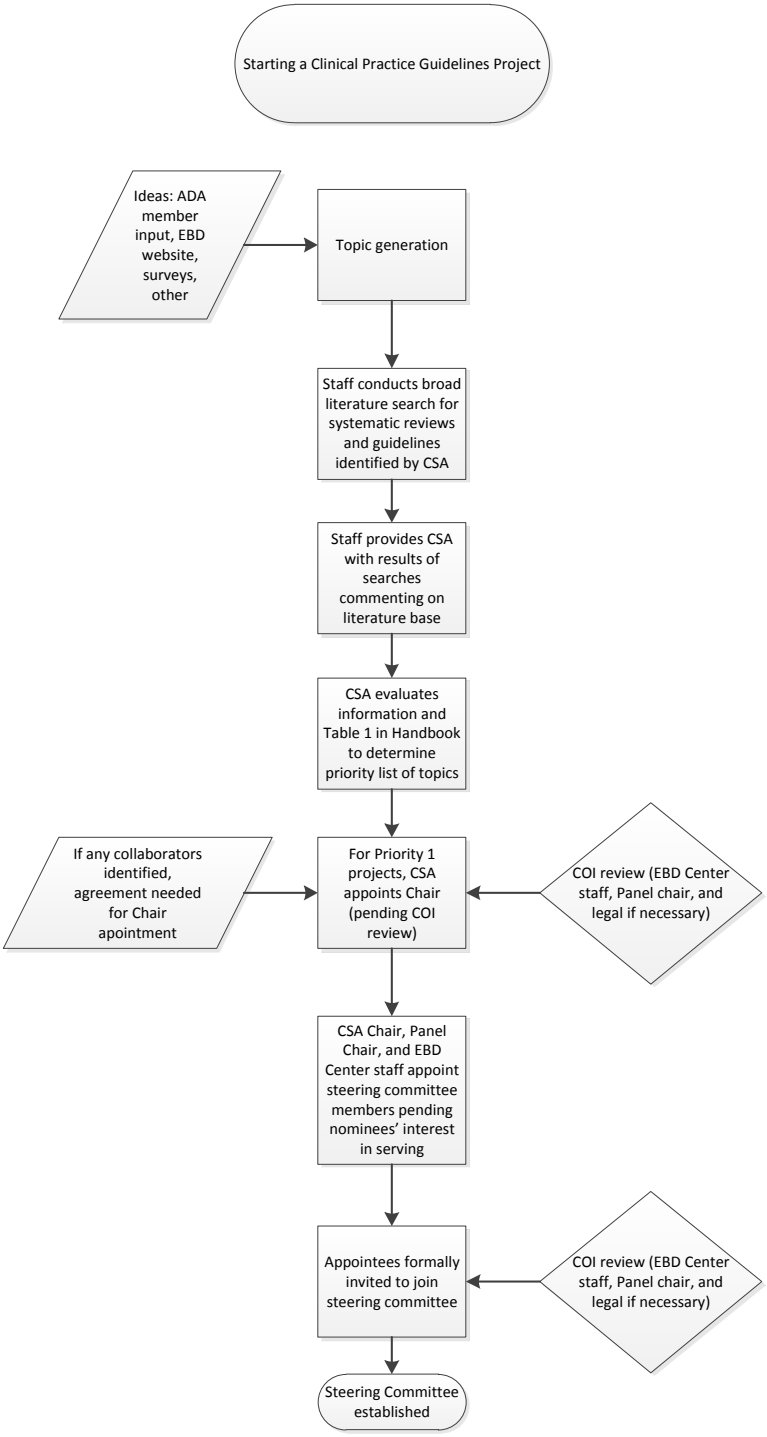
Version History

2013 / Updated by Dr. S. L. Tracy and peer reviewed by Drs. James Bader, Derek Richards, Robert Weyant, and Helen Worthington. Approved by the Council on Scientific Affairs in November 2013.

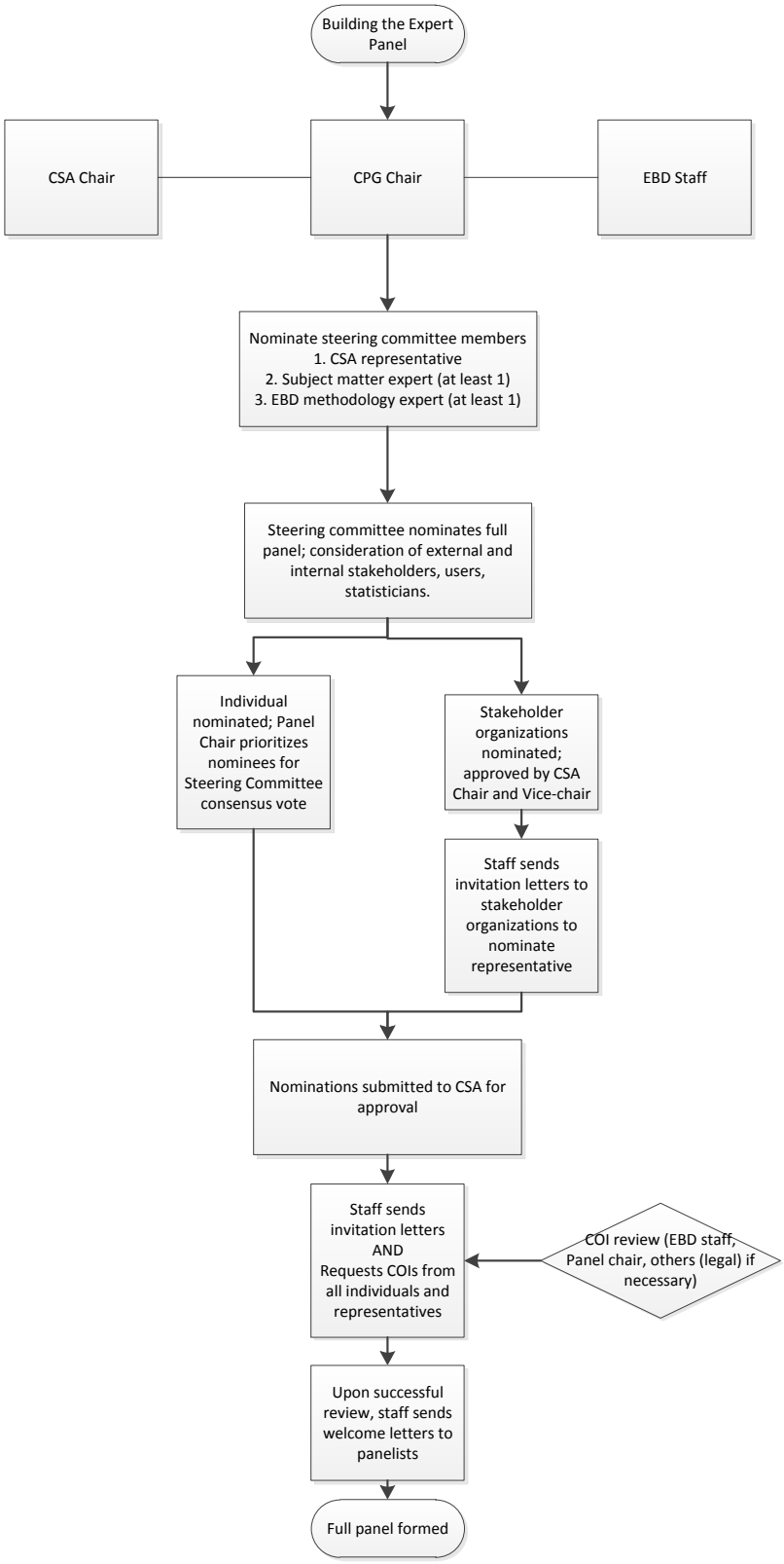
2011 / First version: We would like to thank Drs. James Bader, John Stamm and Kent Kroenschild for identifying a suitable system for grading evidence and strength of recommendations. In addition, we would like to thank the following scientific experts for reviewing the handbook and providing their valuable input: Drs. Robert Weyant, John Gunsolley, James Bader, Amid Ismail, Richard Niederman, Derek Richards, Asbjorn Jokstad, Joseph Matthews, A.S. Blinkhorn, Murray Thompson, Grant Townsend, Helen Whelton and Svante Twetman.

Appendices

Flow chart 1: Process to start a clinical practice guideline project



Flow chart 2: Process to build the expert panel



Invitation Letter – Example 1

DATE

[Click here, & type recipient's name and address]

Dear [Click here & type recipient's name]:

The American Dental Association Council on Scientific Affairs (CSA) cordially invites you to participate in an Expert Panel Workshop on <XXXXX>.

The three-day workshop will begin <XXXXX> at 1 p.m. and will adjourn <XXXXX> at 3 p.m. The workshop will be held at ADA Headquarters, which is located at 211 E. Chicago Ave., Chicago.

As an Expert Panel member, you would analyze current evidence and help develop specific recommendations for oral cancer screening. The panel's input will be used to help shape the Council's clinical recommendations and all panel members will receive authorship credit for the report, which will be submitted to *JADA*.

This is an extraordinary worthwhile undertaking--one that has the potential to impact patient care for years to come. In that light, we truly hope that you will share your time and expertise. Examples of evidence-based clinical recommendations developed by the ADA on other oral health topics are available at http://www.ada.org/prof/resources/ebd/clinical.asp.

The ADA will cover your travel expenses and hotel accommodations for two nights. We expect panel members' overall commitment to the project would last about one year and may include attendance at a second workshop, conference calls and participation in drafting sections of the CSA report.

Xxx, will call you to determine if you are able to accept this invitation. She may also be reached at 1-800-621-8099, extension x or via e-mail at x. We sincerely thank you for sharing your time and expertise in this important endeavor.

Sincerely,

Chair, Council on Scientific Affairs

Literature Searching

This section adapted from the New Zealand Guideline Group handbook.

PUBMED

General tips for searching in PubMed

1. Use the MeSH database to find the proper indexed term(s) to match your search
2. The "Details" tab can be very useful in understanding the results of your search. It will show the way that the database mapped your terms, and also reveal any errors in the construction of your search strategy

Increasing sensitivity on PubMed – when there too few hits

- Automatic Term Mapping is the default search that matches the query against MeSH

(exploded), Journals, Phrase list and Author index. Automatic Term Mapping can be 'turned off' by the use of truncation symbol e.g. heart attack* or by entering a field descriptor e.g. [AU]

- Avoid truncation and wildcards eg infection* will retrieve infection/s/ious but not infection

control (because * turns off the automatic mapping function)

- Increase the use of "OR"

Use synonyms, spelling variations, abbreviations.Combine with OR e.g. esthetic OR aesthetic, pediatric OR paediatric.

- Decrease the use of "AND"
- Check for LIMITS
- Try NOT animal [MeSH] – instead of limit to human

Increasing precision – when there are too many hits

- Increase the "AND"
- Use additional terms
- Use NOT to remove unwanted references (noise). Choose narrow terms e.g. NOT animal will remove any reference where the word is used in the text - NOT animal [MeSH] is better
- Limits –use the limits available in PubMed - year of publication/age group/language
- Fields - limit your query to a specific field(s) e.g. "Yang YL" [AU]

Search Filters in PUBMED

Clinical Queries - use these built in filters to retrieve the types of reference that you require.

Medline Ovid

The information is generally applicable to Medline searches (not through Ovid).

A sensitive search strategy should be used initially to locate all the relevant information on any given topic. Following this relevant search filters or limits must be applied to improve the precision.

General tips for searching in Ovid:

1. Use “Advanced Search” for the most control over your search.

2. Pay careful attention to the mapping of your search terms. It is easy to miss relevant items. Use the “exp” function when in doubt.

Increasing sensitivity (where there are too few hits)

- Subject Headings/Trees

Medline assigns index terms/subject headings to the references (indicated by / after the word). This controlled vocabulary assists the searcher to obtain information by reducing the chances that differences in terminology may cause the searcher to miss valuable information. Subject headings are arranged in a tree structure with broad headings over more specific headings. Subheadings should not be used in a sensitive search.

- Scope notes (*i*)

These state the definition of the subject heading as used in the database, the year the heading was introduced, other related subject headings and possible synonyms for text-word searching.

- Explode

A command which causes the database to search on the given subject heading and the heading(s) beneath it on the tree. Indexers are instructed to use the most specific index term possible so if you search on ‘dentistry/’ you will miss the references indexed ‘asthma in children/’ unless you use ‘exp dentistry/’

- Textword Searching

This is also known as free text searching where the database is asked to search for a word in the text fields – usually title & abstract (and sometimes subject heading fields). Use the suffix .tw with your search term, eg. “oral cancer.tw”

- Truncation and Wildcards

This is another tool to increase sensitivity. When searching for information on pregnancy the use of the text term periodont$ will retrieve references including periodontal, periodontitis, periodontology

- Adjacency

Many databases include a phrase list of words that commonly occur together which the database searches as a phrase, e.g. blood pressure. When searching for phrases which may not be on the phrase list, the use of the adjacency command increases the sensitivity by retrieving reference in which both words appear, but not necessarily consecutively or in the order specified by the searcher, e.g. acute adj3 haemorrhage.tw will retrieve acute subarachnoid haemorrhage, but acute haemorrhage.tw will not

- Boolean ‘OR’

Combining truncated text word search terms OR exploded MeSH terms on the same topic will give the best sensitivity

- Pearl growing – a technique for improving search sensitivity.

Review results of preliminary search, look at the references retrieved so far, and the associated MeSH terms. Identify new terms previously overlooked, new spellings, word endings, broader/narrower MeSH terms. Modify the search strategy to incorporate the new terms.

Increasing precision (where there are too many hits)

- Boolean AND

Combining groups of terms related to different aspects of the question with AND will give a result set in which both aspects of the question are addressed e.g. (exp mouth neoplasms/ or oral cancer.tw) and (diagnosis/

- Boolean NOT

This can be used to remove a narrow group of references that are not required. Eg searching on non drug therapy for oral cancer try exp mouth neoplasms/ NOT dt.fs)

- Quality filters

There are many validated search filters that are designed to select specific types of study design. These can be added to a search on a given topic e.g. in order to identify relevant randomised controlled trials about asthma, one could do a sensitive search on asthma and add a quality filter for therapy. Filters of different sensitivity and specificity are available but filters are generally more sensitive than limits.

- Limits

Databases enable searchers to limit the search to e.g. year(s) of publication, specified page groups, specified languages, publication types, human etc. In Medline, limit to English is not always required because many non-English references in Medline have an English abstract.

Limit to publication type may miss relevant references because this term is relatively new and inconsistently applied.

Search filters for Medline Ovid

Developed by: CASPFEW Institute Of Health Sciences, University of Oxford, UK, & Health Information Research Unit McMaster University, Canada.

Diagnosis sensitivity filter 1. exp "sensitivity and specificity"/ 2. sensitivity.tw. 3. di.xs. 4. du.fs. 5. specificity.tw. 6. or/1-5	**Diagnosis specificity filter** 1.exp "sensitivity and specificity"/ 2. (predictive and value$).tw. 3. #1 or #2
Therapy sensitivity filter 1. randomized controlled 2. dt.fs. 3. tu.fs. 4. random$.tw. 5. or/1-4	**Therapy specificity filter** 1. (double and blind$).tw. 2. placebo.tw. 3. 1 or 2
Prognosis sensitivity filter 1. incidence/ 2. exp mortality/ 3. follow-up studies/ 4. mo.fs. 5. prognos$.tw.	**Prognosis specificity filter** 1. prognosis/ 2. survival analysis/ 3. 1 or 2

6. predict$.tw. 7. course.tw. 8. or/1-7	
Etiology or Harm sensitivity filter 1. exp cohort studies/ 2. exp risk/ 3. (odds and ratio$).tw. 4. (relative and risk).tw. 5. (case and control$).tw. 6. or/1-5	**Guidelines sensitivity filter** 1. guideline.pt 2. practice guidelines/ 3. all guideline$.tw 4. all recommend$.tw 5. Consensus.tw 6. Standards.tw 7. or/1-6
Etiology or Harm specificity filter 1. case-control studies/ 2. cohort studies/ 3. 1 or 2	**Guideline specificity filter** 1. Guideline.pt 2. Exp guidelines/ 3. Health planning guidelines/ 4. Or/1-3

Template for Clinical Question

	Question	Identify PICO elements	Identify outcome measures
1		P:* I: C: O:	
2			
3			
4			
5			

*** Identify provider and setting to ensure applicability of literature**

Note: Be conscious of the choice of true, patient-oriented health outcomes and surrogate or intermediate outcomes.

Systematic review data abstraction form

Reviewers:

1. Summary

Author	
Publication Year	
Title	
Journal	
Clinical Questions	
Designs of included studies	
Number of included studies	
Population(s) assessed	
Intervention/Screening Assessed	
Controls/ Standards	
Outcome(s) measured	
Inclusion/Exclusion criteria	
SR Conclusion	
Funding	

2. Quality of the Systematic Review (See Page 29)

Criteria assessed	Yes	No	Can't answer
Comprehensiveness of sources considered			
Comprehensive search strategies			
Standard appraisal of included studies			
Validity of conclusions			
Recency			
Relevance			

How would you rate the quality of the study? Good/ Fair/ Poor

3. **Applicability of evidence**

   PLEASE ADD NOTES

4. **EVIDENCE APPLICATION**

a. Which of the following Clinical Questions does this review provide evidence for?

	Provides evidence	May be used to extrapolate evidence	Unrelated
1			
2			
3			
4			
5			

5. **KEY FINDINGS**
6. **Strengths and Weaknesses of evidence**
7. **DRAFT EVIDENCE STATEMENT**
8. **NOTES & COMMENTS**

INCLUDE STUDY FOR FULL PANEL CONSIDERATION? YES /NO

Examples of clinical studies data abstraction forms (in Excel)

Citation: Author, Year	Abstraction													
	PICO question number addressed	Country	Special population? (e.g. smokers) and other data regarding inclusion - exclusion criteria for patients and teeth	Severity of disease (e.g. refractory, mild, moderate)	Test subject age (mean, median, range as described)	Control subject age (mean, median, range as described)	Control	Control Dose/ duration/ frequency/ timing if applicable	Test (typically adjunct)	Test (typically adjunct) Dose/ duration/ frequency/ timing including simultaneous/ before/ after	Was standard counseling mentioned as part of control treatment?	Trial design (split mouth / parallel group / cross over)	Duration of study	Adverse events reported

Citation: Author, Year	Clinical Attachment Level Data																							
	Outcome measure	Time period for data presented in this abstraction (as close to 9 months as possible)	Other time periods for which data are available	No. Sites treated per mouth / No. sites averaged per tooth	Test sample size Baseline	Test mean Baseline	Test SD or SE (list value) Baseline	Test sample size at end of test period	Test mean at end of test period	Test SD or SE (list value) at end of test period	SD or SE?	Mean difference TEST (final-baseline)	Mean SD (or SE) difference, TEST	Control sample size Baseline	Control mean Baseline	Control SD or SE (list value) Baseline	Control sample size at end on test period	Control mean at end of test period	Control SD or SE (list value) at end of test period	SD or SE?	Mean difference CONTROL (final-baseline)	Mean SD (or SE) difference, CONTROL	Caries data	Statstical analysis notes

Example of critical appraisal form (in Excel)

Domain:	Selection bias				Performance bias						Detection bias		Attrition bias		Reporting bias	
	Random sequence generation		Allocation concealment		Masking of participants		Masking of personnel		Were the groups treated the same except for the intervention?		Masking of outcomes assessment		Incomplete outcome data (Include percent lost to follow-up) ≤10% low; 11-20% unclear; >20% high		Selective reporting	
Citation: Author, Year	Support for judgment	Review author's judgment	Support for judgment	Review author's judgment	Support for judgment	Review author's judgment	Support for judgment	Review author's judgment	Support for judgment	Review author's judgment	Support for judgment	Review author's judgment	Support for judgment	Review author's judgment	Support for judgment	Review author's judgment

Example: Topic Discussion Guide

Nonsurgical Treatment of Chronic Periodontitis Expert Panel Meeting

February 27-March 1, 2013

ADA. Center for Evidence-Based Dentistry™
Clinical Question:
PART A: CONSENSUS ON LEVEL OF CERTAINTY
1. Summary of evidence (list studies)
Panel comments/concerns regarding the studies:
2. Quantity (number and size) of evidence Comment here on any issues concerning the quantity of evidence available on this topic and its methodological quality.
Number of studies Number of test subjects___ Number of control subjects_
3. Assessment of risk of bias (flaws in study design or methods) of evidence as a whole (see critical summary sheet and TOOL 1) Comment here on the major concerns regarding risk of bias, if any.
4. Applicability Comment here on the extent to which the evidence is directly applicable to a US population.

5. Consistency (see meta-analysis below)

Comment here on the degree of consistency demonstrated by the available of evidence. Where there are conflicting results, indicate how the group formed a judgment as to the overall direction of the evidence. Comment on the statistical heterogeneity, if applicable (Note: Statistical heterogeneity is a portion of the assessment of inconsistency and is defined as I^2<50% is low; 50<I^2<75% is moderate; I^2>75% is high)

6. Publication bias? (yes or no)

Comment here if there is evidence of publication bias. Use Egger's plot or other information that is available.

ASSESSMENT: □ Yes □ No

PART A: LEVEL OF CERTAINTY: □ High □ Moderate □ Low

PART B: Magnitude of Net Effect

7. Clinical impact

Comment here on the potential clinical impact that the intervention in question might have – e.g. size of patient population; magnitude of effect; balance of risk and benefit

a. **Draft Meta-Analysis**

b. **Magnitude of effect**

c. Adverse events assessment

d. Balance of benefits vs. harms/adverse events

8. Other factors

Indicate here any other factors that you took into account when assessing the evidence base including relative benefit vs. other management options or resource implications

Part B: Magnitude of net effect: □ Substantial □ Moderate □ Small □ Zero/negative

Part C: Generating the clinical recommendation

9. Clinical recommendation

Active language; who should do what to whom under what circumstances

Statement:

Part C:

Strength of recommendation: □ Strong □ In favor □ Weak □ Expert Opinion for

□ Expert Opinion against □ Against