# Systematic Reviews: Content Guidance

## Version 2.0

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## Acknowledgments

This updated Content Guidance is based on a report prepared by Kathleen N. Lohr, PhD, Jacqueline Amoozegar, MSPH, and Linda Lux, MPA (RTI–UNC Evidence-based Practice Center, Research Triangle Park, NC) in 2011 under Contract No. 290200710056I. The original Content Guidance was based on the PRISMA and Institute of Medicine report for reporting systematic reviews, the Methods Guide for Comparative Effectiveness Reviews, and a review of six existing Effective Healthcare Program systematic reviews. Following the Fall 2014 EPC Directors Meeting, the Guidance was revised to allow for the option of a "condensed format" based on the lessons learned from the pilot format projects and streamlined in response to feedback received over the previous three years.

# Structure and Use of the Content Guidance

This Content Guidance has a preface and 4 chapters:

- Preface: Standard or Condensed format?
- 1: Introduction
- 2: Methods
- 3: Results
- 4: Discussion.

Each chapter has a title (Ariel 18 bold) and first-level headings (Ariel 16 bold) that EPCs should use. The guidance also suggests numerous second-level heads (Ariel 14 bold). The guidance recommends that EPCs use no more than four levels of heads in any chapter, but it does not suggest what exact wording those lower-level headings might take. In some cases, the guidance offers alternatives (especially for second-level headings) to accommodate the very different needs of systematic reviews that can cover medical tests, screening and prevention, different types of therapeutic interventions, and so forth.

The actual guidance appears in tables (boxes) under the heading or subheading in questions. Where appropriate, the report provides suggested citations to a Methods Guide article (or chapter) and for the PRISMA diagram. In several places, an indented box comments on overall instructions or optional material. The aims have been to standardize what can be standardized, given the wide range of topics and issues covered by systematic reviews, and to simplify the overall organization for systematic reviews.

This guidance may not address or answer all questions that EPCs might have about a given systematic review. When in doubt, consult with the relevant AHRQ Task Order Officer. Also, when some information may be too much to present even in appendices to a systematic review (let alone in the main body of the review), consider indicating that further information is available upon request from the authors, as is sometimes done with peer-reviewed articles. The aim is to keep the total volume of the report (including appendices) to a manageable size. Please remember that this document is not a template - EPCs should not try to enter text or other materials directly into it. Finally, the products from the AHRQ EPC (and Effective Health Care) program are sure to expand and evolve over time. An increased emphasis on readability and transparency may dictate changes in how systematic reviews (or other reports) are to be produced and published. Thus, this guidance is likely to evolve over time.

# Preface: Standard format, condensed format, or hybrid?

The first consideration when planning a report is whether the topic is best suited to the standard or condensed format or a hybrid. The table below lists the key differences between standard and condensed formats.

| | Standard | Condensed |
|---|---|---|
| Number of reports | One | May be multiple |
| Report Length | Should be as concise as possible but ideally <70 pages | <30 pages each |
| Executive summary | Yes | May not be necessary, depending on topic: discuss with TOO |
| Methods | Should be concise | Strictly limited to what a reader needs to know to understand the analysis and judge its reliability; refers to protocol for all standard procedures and details |
| Tables and Figures | As appropriate | Limited to summary information, all detailed information in appendix (may include PICO, SOE domain table) |

The choice of whether to use the standard or the condensed format, or whether to adopt some elements of each should be driven by the characteristics of the topic. For example, a topic with very few studies will be much easier to explain fully in under 30 pages, and therefore an executive summary is unlikely to add more than the abstract and can be omitted. However a very complex topic may require fifty or sixty pages to explain the results, and therefore having a short executive summary that provides sufficient detail for readers to understand the results but is less daunting than the full report may be important. Similarly, some topics have key questions that can be easily split into discrete reports that stand alone (diagnosis and treatment, prevention and treatment, children and adults, etc.) while others do not (intermediate and patient centered outcomes).

The choice of what format to use should be made as soon as there is enough information. The decision should be discussed with the TOO and AE at the time of the protocol.

# 1. Introduction

*(goal <2,000 words)*

# Background

## Condition

- Briefly discuss in text the context of the condition (disease, health problem). Details might include the following (*neither a required nor a comprehensive list*), which may come from background information in the protocol, if one was developed:
  - Definition (as could be understood by an informed lay person)
  - Incidence and prevalence
  - Populations affected
  - Etiology (nature of the disease; pathophysiology; etc.)
  - Burden of disease to the individual (may include burden and costs to society)
  - Other information as needed to explain the condition and its importance.
- Use *optional* table(s) or figure(s) to describe, for example, phases, trajectory, symptoms, typical prognosis of the disease or condition.

## Diagnosis Strategies *or* Treatment Strategies *or* Prevention Strategies

(heading as appropriate to the topic)

- Briefly describe the clinical interventions being compared; give only enough detail to make clear to key clinical and nonclinical stakeholder audiences what the comparison interventions are and briefly introduce issues about them—*for example (neither a required nor a comprehensive list):*
  - The current available interventions (those being compared; perhaps meaningful alternatives that are not being compared)
  - For treatments, what interventions are —standardll practices (presumably including comparators), or ones recommended by existing clinical practice guidelines (authoritative standards of care or usual practice)
  - For diagnostic (medical) tests, the gold standard for diagnosis, if any
  - Variations in use that may be relevant to availability, acceptability, outcomes, or costs
  - Outcomes (e.g., perceived benefits and harms) generally associated with the interventions being compared
  - Potential advantages or disadvantages of the interventions being compared (e.g., ease of use, access, cost, invasiveness, patient preference, use of other resources or tests) and/or the potential added value of proposed interventions.

*Optional*

- Use *optional* tables to document interventions reviewed in the systematic review, especially in lieu of text conveying the same information. *For example*:
  - Table n. Drugs approved for use in the United States—generic and brand names, labeled indications, important pharmacologic/pharmacokinetic information, etc.
  - Table n. Usual dosing range and frequency of administration for adults, children, special populations, etc.
  - Table n. Behavioral interventions used for this condition—name of intervention (if is a specific type or variant); types of providers or settings; provider and/or patient (caregiver; family) training needed, if any; relationship to other interventions; combinations; etc.
  - Table n. Types of operative or other procedures used for this condition
  - Table n. For procedures, medical tests, medical devices—manufacturers, regulatory status, types of providers and settings; provider and/or patient (caregiver; family) training, phase of diffusion; relationship to other interventions; combinations of interventions; etc.
  - Use *optional* figure, if helpful, to describe sequencing of diagnosis and/or treatment.

# Scope and Key Questions

## Scope of the Review

- Briefly indicate in text what the systematic review covers in general terms. Use the general idea of Populations, Interventions, Comparators, Outcomes, Timeframes, and Settings (PICOTS). Mention here if any entity (e.g., federal agency) is a partner in funding the systematic review.
- Might mention here what the systematic review will not cover.
- Briefly note briefly the reasons for doing this review now. If known, note how this systematic review will complement or supplement any similar reviews recently published or under way (but do not describe in any detail here). *For example* (*neither required nor comprehensive*):
  - Controversy or uncertainty about the topic
  - Level of uncertainty associated with use of these interventions and their expected benefits or harms
  - Ongoing difficulty or complexity of related clinical or policy decisions
  - Consequences of such uncertainty or complexity for decision-making or confusion about preventing, diagnosing, treating, or managing the condition
  - Confusing or conflicting literature
  - Relevant literature not in one place.
- Briefly note the relevance of the systematic review to specific clinical decisionmaking or policymaking dilemmas or steps important to target audience(s) or stakeholders. Note that review questions should address items noted in this section. *For example* (*neither required nor comprehensive*):
  - Weighing benefits and harms for patients
  - Taking patient preferences into account
  - Targeting specific populations
  - Clarifying applicability to medical (primary, specialty) practice
  - Documenting burden to the health care system, society (including costs, if relevant)
  - Facilitating coverage or reimbursement decisions.

## Key Questions

- Include the Analytic Framework Figure in this section and briefly describe or explain it
- Label it to depict where each key question falls. The AHRQ topic development and refinement guidance has an illustration, but the analytic framework should be designed and described to help readers understand the logic of the analysis, from populations through to important health (or other) outcomes, including patient-important outcomes, that the systematic review will cover.
- Develop alt text in a separate document for 508 compliance.
- Give the full (exact) wording of each key question
- Check that key questions here map to those in protocol to a reasonable degree (changes from originally posted Key Questions are acceptable and modifications of KQs in protocol may also be acceptable)
- Ensure here (if not true of Key Questions in protocol) that they are comprehensible—e.g., avoid complex lead-ins and use correct English (grammar; punctuation).

# Organization of This Report

**Note: This is an *optional* section, useful especially for very complex systematic reviews.**

- Indicate very briefly what can be found in the remaining chapters (particularly if the systematic review has multiple results chapters).
- Consider listing all appendices in order so that they can be called out in any order in subsequent chapters.
- If a list of abbreviations and acronyms, and/or a glossary, is developed for the systematic review, indicate where these elements can be found (e.g., in front of report following the Table of Contents, in a specific chapter, or following references).

# 2. Methods

*(Goal <2,000 words)*

- Give a 1-2 sentence introduction to the methodological approach.
- Language along the following lines may be helpful (*example*):

The methods for this systematic review follow the AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* (available at http://www.effectivehealthcare.ahrq.gov/methodsguide.cfm )and the PRISMA checklist *. See the review protocol (insert link) for full details.

*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/journalpmed1000097.

## Topic Refinement and Review Protocol

- Mention *very* briefly that the EPC (and the Scientific Resource Center if the SRC did the topic development) engaged in a public process to develop and refine the topic and its Key Questions and to develop a draft and final protocol for the entire systematic review process.
- Language along the following lines may be helpful (*examples):*

Initially a panel of key informants gave input on the key questions (KQs) to be examined; these KQs were posted on AHRQ's EHC website for public comment in [month year] for 3 weeks and revised in response to comments. We then drafted a protocol for the systematic review and recruited a panel of technical experts to provide high-level content and methodological expertise throughout the development of the review. The finalized protocol is posted on the EHC website at XXXX. The PROSPERO registration is XXX.

*or*

The topic of this report and preliminary key questions arose through a public process involving the public, the EPC [or the Scientific Resource Center (SRC) for AHRQ's EHC program if they did topic development], and various stakeholder groups (www.effectivehealthcare.ahrq.gov/aboutUs/stakeholder.cfm). Investigators from the ABC Evidence- based Practice Center then refined the questions in consultation with a Technical Expert Panel (TEP).

- May want to add a description of the disciplines and fields represented by the key informants and the TEP *(optional)*.
- For the final (not draft) report, may also want to note where the Key informants and TEP are listed (e.g., front matter).

# Literature Search Strategy

## Search Strategy

- Explain the literature search strategy (e.g., names of required and additional databases, inclusive dates [months/years], including any interim updates of searches).
- Specify details when different searches were done for different key questions.
- Mention role of librarian and/or information specialist and, if true, that searches were peer reviewed.
- Indicate that exact search strings are in Appendix A (or whatever appendix is appropriate).
- Indicate if any more details are in other appendices, such as how study designs were classified if this is a major element of the searches themselves.
- Describe gray literature searches, if any.
- Mention hand searching reference lists, journal tables of contents, etc.
- Describe acquisition and use of FDA documents, Scientific Information Packages (SIPs), Federal Register Notice, etc.
- Describe use of trial registries, if any.
- Mention if the EPC contacted (or tried to contact) authors of studies to get additional or unpublished information.

## Inclusion and Exclusion Criteria

- Use one (or more) tables to document the inclusion and exclusion criteria overall or for specific key questions. *For condensed version, may summarize key criteria in the text and refer to a PICOTS table in the appendix.*
- Insofar as appropriate for text or tables, introduce here (or below) the relevant PICOTS.
- Explain all potentially controversial decisions. *Examples may include*: use or no use of various types of observational studies; setting a minimum sample size; use or no use of non-English studies; inclusion or exclusion of specific geographic areas; limited search dates; and other considerations appropriate to the topic.
- If gray literature or existing systematic reviews (or similar documents) are sought, describe (text or tables) any inclusion and exclusion criteria (or decision rules) for these materials.

## Study Selection

- Describe briefly the process for title and abstract review (or title review, then abstract review) and full-text review. Use descriptive language, rather than Phase 1/2 or Stage 1/2 terminology.
- Explain how dual review was done.
- Mention any other quality control mechanisms in this process **or refer to protocol**.
- Cite the appendix that lists articles excluded (at full-text review stage) with reasons for exclusion.
- If review forms for titles/abstracts or full-text articles are in an appendix, cite it.
- Consider being specific as to which reference manager software was used (as with citing statistical packages). *Optional*

## Data Extraction

- Describe the quality assurance mechanisms used and how disagreements were resolved, refer readers to the protocol for details, and note any deviations from the protocol.
- If data extraction forms are included in an appendix, cite it.

## Quality (Risk of Bias) Assessment of Individual Studies

- Describe the criteria and methods (decision rules) used for evaluating quality or risk of bias in individual studies; likely will need different explanations for different types of study designs.
- Give citations for any published tools or instruments used; cite the AHRQ Methods Guide if relevant.
- Give the terms and definitions of the final quality or risk of bias ratings; mention where the study-specific ratings are recorded (e.g., in evidence tables).
- Say whether a dual rating procedure was used and how disagreements were settled.
- Mention appendices, if any, where methods for quality/risk of bias rating are more completely described and/or forms for doing the assessments are given.

## Data Synthesis

- If the analyses are solely qualitative, just say so; explain the reasons; specify that, therefore, no quantitative synthesis was done.
- If specific patient-reported or clinician-reported outcome measures or quality-of-life assessment scales were used extensively in the articles in the report (especially if numerous different ones appear), consider using a table to name them, introduce their acronyms, and briefly describe their main properties (e.g., number of items, directionality) and interpretations of scores.
- If various quantitative analyses are done, then briefly cover the following steps as needed; refer readers to appendix if a long explanation or formulas are involved (*examples, and not a comprehensive list*):
  - Explain the purpose for pooling – is there an expectation that this will give greater power and precision, or is it being done to explore heterogeneity. If the latter, what hypotheses will be tested (date of study, quality, length of followup, etc.)?
  - Explain approaches to pooling. Be explicit about statistical details and numbers of studies needed before undertaking any meta-analysis, how data may have been obtained (e.g., taken from graphs; imputed in some fashion when necessary), and what kinds of information was not used in meta-analyses, etc.
  - Specify what dependent variable measures were calculated, what outcome measures (e.g., QOL instruments) were used
  - Describe any transformation of continuous variables
  - Describe or justify choices for presenting results (e.g., use of relative risk vs. odds ratios; baseline rates; random vs. fixed effects models)
  - Specify the assessments or tests used for heterogeneity, publication bias, etc.
  - Describe any decision rules for assessing subgroups, and specify which ones were identified a priori (e.g., in Key Questions).

**Note for structuring these subsections:**

Consider using second-level heads (Ariel 14 bold) to break up these kinds of descriptions in this section, especially if they differ by key question, study design, or other factors. *Examples appear below, but they are neither required nor comprehensive (others may be appropriate for a given CER).*

## Overall Approaches and Meta-Analyses for Direct Comparisons

## Indirect Comparisons with Mixed Treatment Comparisons Techniques

*And/or, for example*:

## Outcome Measures

## Statistical Analyses

## Event Rates

## Numbers Needed to Treat (or Harm)

# Strength of the Body of Evidence

- Describe briefly the elements of grading the strength of evidence—e.g., five main domains and the additional domains if used, and then overall score. Consider using a table to define domains and/or to define the four levels of the overall SOE grade.
- Cite the Methods Guide chapter on strength of evidence "Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update" and include the link to the AHRQ EHC website http://effectivehealthcare.ahrq.gov/ehc/products/457/1752/methods-guidance-grading-evidence-131118.pdf).
- Briefly describe how domains were assessed and scored—e.g., two independent graders; how conflict was resolved; etc. Describe any EPC-specific decision rules for how each domain was assessed.
  - Briefly describe how publication bias was assessed and whether searches for grey literature, FDA information, or additional information from authors were used to help mitigate the problem.
- Briefly describe how the overall SOE grades were reached—e.g., process, decision rules, etc.
- Specify where and how strength of evidence grades are reported in Results or Discussion chapters (or both). If Domain table is in appendix, say so.

# Applicability

- Define applicability briefly, using language to convey that it is assessed, not scored or rated.
- Cite Atkins et al. article in J Clin Epi* and say is also available from AHRQ EHC website at http://www.effectivehealthcare.ahrq.gov/ehc/products/272/603/Methods%20Guide--Atkins--01-03-2011KM.pdf.
- May want to indicate that
  - Applicability is evaluated in a PICOTS framework (or perhaps at least PICO), introduced above
  - Specific factors that may affect the applicability of the evidence for this particular CER.
- May want to say, *if true and relevant*, that
  - One (or more) of the KQs specify patient or population subgroups that pertain to applicability
  - Applicability is assessed with respect to specific (external) reference population(s) or specific subgroups, specific outcomes, specific settings, etc.
  - A distinction was made between efficacy and effectiveness studies (trials) (consider citing Gartlehner et al., article if used**).
- Describe briefly the process for assessing applicability for individual studies (if it was) and for the body of evidence (for each key question)—e.g., two independent evaluators; how conflict was resolved; etc.

*Atkins D, Chang S, Gartlehner G, Buckley DI, Whitlock EP, Berliner E, Matchar D. (2011). Assessing applicability when comparing medical interventions: Agency for Healthcare Research and Quality and the Effective Health Care Program. J Clin Epidemiol. 2011 Apr 2. [Epub ahead of print]. *NOTE as of summer 2011: Check to see if the article has been published in print and use that citation.*

**Gartlehner, G., R.A. Hansen, D. Nissman, K.N. Lohr, T.S. Carey (2006). A Simple and Valid Tool Distinguished Efficacy from Effectiveness Studies. *J Clinical Epidemiol.* 59(10):1040-1048.

# Peer Review and Public Commentary

- Succinctly describe the process used for this systematic review
  Language along the following lines may be helpful (*example*):

  Experts in [X, Y, and Z] fields and individuals representing stakeholder and user communities were invited to provide external peer review of this systematic review; AHRQ and an associate editor also provided comments. The draft report was posted on the AHRQ website for 4 weeks to elicit public comment. We addressed all reviewer comments, revising the text as appropriate, and documented everything in a disposition of comments report‖ that will be made available 3 months after the Agency posts the final systematic review on the EHC website.

# 3. Results

## Introduction

- Consider whether it is necessary to give a brief roadmap for the results chapter – whatever might help readers to grasp what is in the chapter and how it is organized (assuming one chapter for all of results). Restrict this to no more than 200-300 words. Different systematic review topics may have quite different concerns about synthesis and presentation, and some may not need so much initial explanation, but others may.
- Cite the appendix for evidence tables.
- What follows are ideas for what might appear in the results chapter of systematic reviews on different topics, but this list is *only illustrative of what might be brought up in such a roadmap.*
  - Results of literature searches come first, followed by descriptions of included studies
  - Chapter is then organized by Key Question , first giving the key points of the findings and then a more detailed synthesis of the literature. When Key Questions are extremely long, complicated, or poorly worded, consider giving an abbreviated list of Key Questions or remind readers that they can look back to Chapter 1. Introduction and the Analytic Framework figure.
- If the results chapter is not organized by key question, or combines them in some unexpected fashion, or otherwise takes a different approach, alert readers to this organizational approach.
- If the systematic review presents results using several identified subsections (by subheadings) for one or more Key Questions, then they are organized in some specified way. *The following list is only illustrative*:
  - Certain kinds of interventions (and relevant comparisons) are considered first, followed by the interventions (and their comparisons)—e.g., psychotherapy before cognitive behavioral interventions; first-generation drugs before second generation; or x-ray before CT/MRI scanning.
  - Within interventions, by important population groups—e.g., those with no coexisting conditions before those with coexisting conditions; —pure patient populations before mixed patient populations—or by key outcomes (benefits for one key question; harms for another), or by whatever level of analysis is done next. Some of this may be dictated by the key questions themselves.
  - Within the above subsections, by types of comparisons—e.g., direct (head-to-head) comparisons, followed by indirect (e.g., placebo-controlled trial) comparisons, and/or data from trials before data from observational studies.
- Note whether meta-analyses (or similar pooling techniques) are presented (perhaps refer readers back to Chapter 2. Methods to remind them of methods used).
- Comment, if true, that only studies with low or moderate risk of bias, or good or fair quality ratings, are used or reported on in results; might say that if risk of bias or quality is, respectively, moderate or fair, then that is the rating for any study unless otherwise specified in text; consider noting where these ratings can be found (e.g., summary tables or in evidence tables [appendix]). The point is to reduce repetitive mention of information relating to these ratings.
- If something is especially important for readers to know about the overall approach (not explained in Methods chapter), then say so and indicate that additional information can be found in specifically identified appendices.
- Specify where readers might find a complete list of abbreviations and acronyms (not interchangeable concepts) and/or a glossary (alphabetical list of terms, but not necessarily a list of abbreviations and acronyms)—e.g., this chapter, an earlier chapter, or at end of report.

# Results of Literature Searches

- Document the searches and their yields.
- Present and call out the PRISMA figure (flow diagram). Diagram may indicate at the bottom the numbers of final included studies for each key question. *May be relegated to appendix for Condensed format.*
- Suggest citing at least the Moher et al. article,* if not both.**
- Specify the total number of *studies* finally used. Not every reader will look at the flow diagram and this may be the number needed for the executive summary.
- Note, if true, that the numbers of articles exceeded the numbers of studies (give the actual numbers), and describe how later text (or tables, or references) handles multiple articles on the same study. For some topics, the issue of multiple publications is a major complication, so be sure that readers are not confused between numbers of studies and numbers of articles.
- Note what appendix has the list of studies excluded at full-text review.
- Explain anything special about included or excluded articles if there is some important, or controversial, point about why articles were excluded (e.g., non-English language; small sample sizes) or some key point to make about special studies (e.g., indirect [network analysis] analyses). If multiple searches were done for, say, different key questions or perhaps some subquestion, consider covering the above points in the sections devoted to each specific key question, but this may then entail more than one PRISMA diagram to separate out numbers of studies. Multiple diagrams should probably go in the appendix.

*Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA statement. PLoS Medicine 6 (7), e10000097, July 2009;

**Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. PLoS Medicine 6 (7): e10000100, July 2009.

# Description of Included Studies

- Overview: Briefly describe all included studies. If the studies tend to be the same for most or all of the key questions, this can be done at the beginning of this section before getting into the individual key questions. Usually it is better to include this section under each Key Question section separately (see below) so that the reader can connect the characteristics of the studies with the specific question they apply to. In either case:
  - Give the citations for included studies.
  - Cite the appendix with the full evidence tables.
- Key properties of studies. Wherever this material appears, this description conveys some sense of the applicability, quality (or risk of bias), and strength of these studies. **Focus on only the key characteristics** of the evidence base that shape the findings and are important for readers to understand the analyses and results. *Examples* of what to note might include the following:
  - Numbers of studies by types of patient populations; types of interventions and comparators; range of outcomes measured; settings; geographic location; and/or study design factors such as sample size, single center vs. multicenter, or whatever particularly relevant study characteristics are important for this CER.
  - For systematic reviews focused on pharmaceuticals or invasive procedures, how many studies had active comparators or placebo/sham controls.
  - For systematic reviews about behavioral interventions, issues related to fidelity to protocol.
  - Number of studies (trials) that were efficacy trials or effectiveness trials.
- Study funding sources: Comment on funding sources of included studies (e.g., number and percentage with industry funding; number and percentage for which no funding source can be ascertained).

# Key Question 1. "Abbreviated Title"

or

# Key Question 1: "Abbreviated Title: Specific Diagnosis, Intervention, or Population"

or

# Key Question 1A: "Abbreviated Title: Topic of [this part of the key question]"

**Note for above first-level headings:**

For all **Key Question headings,** do *not* repeat whole key questions. Find a way (as suggested above with these alternatives) to make the headings succinct but clear. The aim is to make the structure of the results chapter as predictable as possible for readers; the more complex the systematic review, the more important is using an understandable way to organize this chapter.

## Description of Included Studies

**Note for Key Question-specific Descriptions of Included Studies:**

This section here may not be needed if covered earlier.

## Key Points

- This is the first of the two *required* parts of the results chapter of a systematic review. (The other required part is Detailed Synthesis [below].)
- The heading Key Points is a second-level heading, and it appears within *each* Key Question presentation (main section).
- Present *only* the critical analytic findings—no descriptions of the studies themselves. Do *not* give detailed, study-specific results (e.g., findings, statistical significance, etc.) here.
- If many outcomes have insufficient evidence and none are "pertinent negatives" that need to be called out for special attention, consider combining all the I outcomes into one bullet at the end "Evidence was insufficient for x,y,z" or even "Evidence was insufficient for all other outcomes and subgroups." However some outcomes with insufficient evidence may be considered "pertinent negatives" (i.e. the fact that there is insufficient evidence is important to decision makers) and should have their own key point.
- Findings can be done as bulleted points—e.g., complete sentence or two for each bullet.
- Include the direction and strength of evidence assessment pertaining to the finding in the bullet. Consider language such as (*examples, of which the second is more direct and easier for readers*):

—High strength of evidence for benefit of intervention X vs. intervention Y based on four good-quality RCTs with consistent results.

*or*

—Intervention X had better patient-centered outcomes than intervention Y based on three RCTs and five prospective cohort studies (moderate strength of evidence).

- Other considerations:
  - Consider giving the KQ verbatim as the very first element of the section if it is very long or very complicated (or if the EPC is dealing with poorly worded or very complex KQs); this may help clarify how the remainder of the KQ section is organized.
  - Depending on the number of separate key questions or the complexity of any given KQ, the Key Points section part may have subdivisions—e.g., for safety and tolerability, by drugs, and then for adverse events, by drugs. Such subdivisions would be identified by third- and possibly fourth-level heads.

## Detailed Synthesis

- The goal of the detailed synthesis is to show the reader how the evidence leads to the conclusion.
- This is the second *required* part of each key question section in the results chapter of a systematic review.
- Use a second-level head; then use third- and four-level heads to subdivide the detailed synthesis section as needed; do not go beyond that number of heads.
- Each section should conclude with a statement about the direction and strength of evidence and what it is based on that summarizes the preceding section.
- If methods used for any Key Question section have details that are meaningfully different than those for other Key Question sections, consider giving a very brief recap of the methods used for that section.
- Focus on "synthesis" of the results; do *not* simply give extensive, study-by-study data in text.
  - Present only information critical to readers' understanding of the EPC's analysis; make this section as easy as possible for users to read.
  - Focus on information necessary to document evidence for the bulleted Key Points, above.
- Provide text and figures/plots of any meta-analyses or similar analyses. If the systematic review has many such analyses, consider presenting only key ones graphically and refer readers to an appendix for the remaining figures/plots.
- Consider reporting briefly in these sections on important points relating to the applicability of the findings (e.g., note what populations may not be covered, what outcomes were not measured, what

settings were not covered).

- Rely on summary tables or possibly graphics that summarize key findings; explain them as succinctly as possible.
- When details about studies (design; main findings; quality or risk of bias rating) are needed in this chapter (or just for specific key questions), consider presenting such information only in tables in this chapter:
  - Consider using pairs of tables for critical studies and information: one presenting study characteristics and the quality or risk of bias rating, and one presenting study findings.
  - Keep such summary tables to a minimum – if study data can be found easily in evidence tables, that may be sufficient, but be sure to cite where the evidence tables can be found.
- Do *not* repeat detailed study-specific data in text if they appear in tables.
- Consider including a SOE table for each Key Question, which includes the domains, summary grade, and conclusion for all major comparisons and outcomes graded.
  - Use or adapt as a template the final table in the Methods Guide chapter,

**Note for remaining structure of results:**

REPEAT this organizational structure—Key Question as a main division; Key Points with subsections if needed; Detailed Synthesis with subsections if needed—for as many Key Questions (or split Key Questions) as the systematic review covers.

# 4. Discussion

The subheaders below indicate the essential elements that need to be covered in the discussion. They are not, however, intended to be a straightjacket or require mindless repetition. If there is a clearer and more succinct way to organize the discussion, talk to your TOO.

## Key Findings and Strength of Evidence

- Summarize and synthesize the main results for all key questions using narrative text to **answer** the key questions., Do *not* simply reiterate or repeat the bulleted Key Points from Chapter 3 (Results).
  - Give the bottom line of the results of the analysis, referring to the SOE table from the results section.
  - Interpret the findings for the audiences that are expected to read and use the report and place them in clinical context.
- Strength of Evidence if not presented in the results section
  - Include (at least) one summary table, or several tables if that works better for presenting these data. Use or adapt as a template the final table in the Methods Guide chapter, which presents principal findings and gives the overall strength of evidence grade for all *major* comparisons and outcomes graded:
    - Use the current definitions of the SOE grades.
    - Presumably this table or set of tables are the same as those to be included in the Executive Summary.
  - Consider presenting or discussing interpretations of the strength of evidence domain scores, if other potential domains (for observational studies, such as dose-response relationship) were used.
  - Consider commenting on issues of publication bias or outcome reporting bias if either or both problems are of particular concern.
  - Consider commenting on issues relating to the overall SOE grades, especially problems of interpreting—low vs.—insufficient grades.
  - Introduce key issues or reasons that authors could not reach important conclusions and whether these reasons relate to specific key questions, the overall topic of the systematic review, or the field in general.
  - Note that problems with the evidence base per se (e.g., methodologic deficiencies of included studies) are discussed below.

## Findings in Relationship to What is Already Known

- This section is specifically about what this review adds to previous reviews and guidelines and to discuss any conflicting findings. It is not about what the findings mean or how they fit into the general context.
- Comment on how findings relate to or compare with other published findings important for the topic (or specific key questions):
  - Published findings might come from seminal review articles (systematic reviews) on the same topic; authoritative clinical or community practice guidelines; policy documents, etc.
  - Note whether the systematic review‘s findings support or contradict such previous published findings (e.g., from the sources noted above).
- Consider discussing major disagreements or departures between the systematic review findings and other groups‘ reviews and the reasons for accepting the systematic review ‘s findings (or methodologic and analytic approaches).

## Applicability

- Discuss the applicability of bodies of evidence in terms of PICOTS—populations, interventions, comparisons, outcomes, timeframes (in context of trajectory of the condition or disease in question), and settings of care.

- Describe the presumed context of usual care and how the evidence reviewed in the report may be limited in applicability to usual practice or may be limited to a subset of populations, comparisons or practices.
- Cite the Atkins et al. article* and indicate it is also available in the Methods Guide at http://www.effectivehealthcare.ahrq.gov/ehc/products/272/603/Methods%20Guide--Atkins--01-03-2011KM.pdf.
- If useful, adapt a table like Table 2 in the Atkins et al. article to present key findings about applicability of bodies of evidence.
- If not already covered, discuss findings (or lack of them) for any specific subgroup analyses. Indicate whether the analyses were specified in key questions (i.e., a priori subgroup analyses) or
- post hoc. If post hoc, explain what prompted the analysis.
- Comment if any issues of trials or observational studies may have constrained applicability to different or broader populations. *Examples* include (*not a comprehensive list*): sample bias and/or volunteer bias; practitioner bias (e.g., expertise); reality of the interventions tested and compared; issues of interventions being single components vs. combinations or clusters of interventions.
- Comment if there is a danger in relying on means for this body of evidence, especially for subgroups.
- Comment if other methods issues if they are likely to be constraints on applicability, such as measurement instruments used, breadth of independent variables included in studies.
- Discuss any other issues of heterogeneity (clinical heterogeneity; heterogeneity of treatment effects, statistical heterogeneity; methodologic heterogeneity, etc.), if not already covered.

*Atkins D, Chang S, Gartlehner G, Buckley DI, Whitlock EP, Berliner E, Matchar D. (2011). Assessing applicability when comparing medical interventions: Agency for Healthcare Research and Quality and the Effective Health Care Program. J Clin Epidemiol. 2011 Nov;64(11):1198-207.

# Implications for Clinical and Policy Decisionmaking

- Discuss specific clinical and broad implications for decisionmaking, picking up on issues raised in Chapter 1 (Introduction) in the context of whatever audiences were the target for this systematic review. (As a reminder: EPCs are cautioned not to say "should" or make definitive decisions or recommendations about clinical or policy decisionmaking.)
- Consider including informal decision analysis that provides a context for clinical or policy decisionmaking.
- *For example,* consider the issues or implications listed below. This list includes topics raised by the EHC Stakeholder group, but it *is neither required nor comprehensive.*
  - Implications if the conditions are life-threatening, severe or progressively debilitating, or rare, or, alternatively, if they are not serious but are quite prevalent.
  - Implications with respect to alternative interventions, particularly if those have not been part of the comparator set.
  - Implications if the interventions must be provided in specialized settings or by specially trained clinicians or if other constraints on access might exist.
  - Implications if the interventions may not (yet) be covered by public or private insurance programs.
  - Implications if findings suggest continued (or additional) constraints on access (e.g., need specialized settings) or, alternatively improvements in access to care.
  - Implications of particular areas of uncertainty and the clinical or policy considerations that decisionmakers may still need to deal with e.g., areas of low or insufficient strength of evidence that may have an impact on decisionmaking. Perhaps discuss implications of making a decision‖ in the face of this uncertainty vs. waiting to make a decision.
  - Issues relating to benefits and harms, net benefits, and considerations that might be used in weighing or balancing them.
  - For diagnostic tests, relationship to decisionmaking about therapy.
  - For screening tests and preventive interventions, relationship to access to diagnostic or therapeutic followup or decisionmaking about next steps.
  - For invasive interventions (diagnostic; therapeutic), tradeoffs with less invasive (or more invasive) alternatives.

- Informed decisionmaking (consumers and clinicians) or shared decisionmaking (patients and clinicians), including considerations of patient preferences.
- Any pertinent ethical, legal, or social issues.
- Findings in the context of costs of the interventions and likely alternatives (assuming costs can be discussed at all).

# Limitations of the Systematic Review Process

- Discuss any problems encountered in conducting the SR, how they were addressed, and how they may have influenced the review. *Examples* may include:
  - Inadequate scoping problems, such as problems with key questions, study designs included or excluded, etc.
  - Difficulties with conducting searches, retrieving articles, getting information to supplement data missing from articles.
  - Other issues as encountered for this specific SR.
- Note any substantive points raised in peer review or public comment that did not lead to major revisions to the systematic review and, if necessary, discuss the implications of such decisions for, for instance, research gaps or clinical or policy decisionmaking, *Examples* may include: Decisions to include or exclude certain types of studies (for example, non-English language studies), to use or not use certain types of outcome measures, or to constrain comparisons in some way that may have upset reviewers or commentators.

# Limitations of the Evidence Base

- Summarize the *main gaps in the evidence* for the systematic review, both for key questions and specific PICOS.
- Be clear as to what pertains to a study level (perhaps unlikely), a specific key question, the topic of the systematic review itself, and/or the entire field; perhaps use a table to present gaps by key question.
- Refer as appropriate or helpful to the strength of evidence table in the Discussion chapter (or possibly those in the Results chapter), particularly the topics for which strength of evidence was graded low or insufficient. Describe why evidence was considered low or insufficient. What domains were lacking? Was there high risk of bias because of study designs or conduct? Was there a lack of precision, directness, consistency? Was there evidence of publication or outcome reporting bias?
- Summarize the *principal methodologic problems* with the bodies of evidence amassed for this CER.
- Use (sparingly) examples of specific studies that illustrate particular problems that may have contributed to strength of evidence ratings of low or insufficient (e.g., quality ratings of poor or risk of bias ratings of high).
- Consider commenting on the seriousness of these limitations in the evidence base and on whether any are so severe that they point to high priority issues for future research.
- Consider commenting on any challenges in conducting research on this particular topic and how these might contribute to gaps in the evidence.
- Consider commenting on whether any *strengths* of the evidence base - e.g., outcomes or comparisons with strength of evidence ratings of high (or perhaps even moderate) - suggest that no further research is (likely to be) warranted.

# Research Recommendations

- Provide specific recommendations for topics for future research that correspond to gaps and limitations identified above:
  - Be as detailed as possible in describing what a next round or generation of research should do so that a funder could use the recommendation to shape a funding announcement or

assess proposals and a researcher could use it to guide research design.
  - Consider using PICOTS or the original key questions as an organizing principle.
  - Comment on whether any important studies are ongoing or expected to be published in the near term.
  - Comment on feasibility of proposed research.
- Consider providing specific recommendations for reporting on studies in the future, especially if lack of information was a major deficiency of articles included in the systematic review.
- Provide specific recommendations for improving or expanding methods of future research. *Examples* include:
  - study designs
  - selection of outcome measures, including use of ultimate health outcome measures instead of or supplementary to surrogate measures
  - whether there is a need to standardize or harmonize outcome measurement
  - standardization of cutpoints or thresholds for laboratory tests
  - statistical tests
  - modeling exercises.

# Conclusions

Give a very short general statement (maybe 50 words) that interprets the results in context of all the factors noted above—e.g., essentially what might appear in the structured abstract.