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Literature Search

- Please review the HelpDesk Answers Search Sources and Tips document on the HDA Author Instructions webpage.
- Download the HDA Methods Section Worksheet from the HDA Author Instructions webpage and use it to record the results of your search. This information will be used in the Methods section of your manuscript so it is important to record the information as you do your literature search.
- Search all four databases and record results in the HDA Methods Section Worksheet even if no articles are found in a particular database.
- Refer to the Example of Completed Methods Section Worksheet to see how the results of an actual literature search are recorded in the worksheet.

Selecting the Best Available Evidence

- Direct your efforts at finding the best evidence:
  - Valid – as high on the evidence pyramid as possible.
  - Current – for most questions this means within the last five years.
  - Pertinent – PICO elements (patients, intervention, comparison, outcomes) match the question.
  - Practice guidelines are acceptable to contrast what the latest evidence is showing to what practice guidelines are recommending. They should not be the only references.
  - HDA style is to avoid referencing narrative reviews (review articles without a pre-specified search strategy and study inclusion/exclusion criteria).
- HDAs must have at least two references, but no more than five.
- The references must contain data that directly answers your question. Avoid using references that require extrapolation to answer your question.

What if you are unable to find references that contain data to directly answer your question?

- If you are unable to find references that contain data to directly answer your question, discuss with the HDA project manager.
  - Next steps are:
    1. Enlist the assistance of your medical librarian to help with your literature search. Sometimes the experts can find pertinent evidence.
    2. Change your question to something that can be answered with our current evidence base. We can leave your original question in waiting until evidence is available. Remember, any changes to questions must be discussed with the HDA manager prior to proceeding.
What if you are unable to find at least two references?

• HDAs are a synthesis of at least two evidence sources so must have at least two references.
  o If you are only finding one reference, here are your options (in order of preference):
    1. If you only have one meta-analysis/systematic review, include a study published subsequently.
    2. If you only have one meta-analysis/systematic review, include a study published before but not included because didn’t meet study inclusion criteria.
    4. If you only have one meta-analysis/systematic review, include an individual study from the review/meta-analysis if there is a reason to summarize separately such as the largest study that drove the results of the meta-analysis or a study reporting a different outcome or subgroup analysis than the review/meta-analysis.
    5. Broaden the question. You could include a broader population or intervention or an additional outcome in order to bring in another reference. Any changes to questions must be discussed with the HDA manager prior to proceeding.

What if you are finding more than five high-quality, current, and pertinent references?

• HDAs are also concise so the question must be narrow enough to be answered with five references or less.
  o If finding more than five references, you may need to narrow your question by narrowing the population, intervention, comparison, and/or outcomes. Again, any changes to questions must be discussed with the HDA manager prior to proceeding.
  o Critically review the references you found to see if there is a “top five” (or fewer)best references from the group.
    ➤ Is there a meta-analysis/systematic review that contains an RCT that you have listed separately such that you could forego using the RCT?
    ➤ Are there two or more meta-analyses/systematic reviews that have similar research questions and overlapping studies within them? For example, two meta-analyses may contain 80% of the same trials — does it make sense to include both or should just the more recent/higher quality one be included?
HDA Cover Page

HDA Question: [insert approved question here]

(ie, Does prescribing Naloxone for Chronic Opioid Users Decrease Opioid-related Deaths?)

Author Information:
authors named here will be published in the order they are listed- maximum of 5 authors allowed

[insert first authors first name, last name, credentials]
[insert additional authors first name, last name, credentials]
[insert program affiliation]
[insert city and state]

Example:
John Doe, MD, MPH
Jane Smith, PharmD
University of Texas-Austin Family Medicine Residency Program
Austin, TX

The corresponding author is John Doe; jdoe@gmail.com
HDA Template (Microsoft Word document; Times New Roman 12pt font, single space)

Title: [insert short title for HDA question here. E.g., Best Treatment for Cough]
Word Count: [insert word count of Evidence-Based Answer AND Evidence Summary]

HDA Question: [insert question verbatim here]

Evidence-Based Answer
The bottom-line conclusions from each of the references summarized in the Evidence Summary. Strength of recommendation indicators (SOR) based on the appropriate SORT grade are included in parenthesis after each statement with a different SOR. Each SOR is followed by a brief description of the type of study/studies the statement is based on [e.g. (SOR: B, meta-analysis of RCTs and cohort studies)].

Evidence Summary
Concise summary of each reference used to answer the question. Each reference should be summarized in a separate paragraph generally from highest level of evidence to lowest. Include enough information to allow readers to apply the results clinically:
1. A description of the study so readers know how strong or weak the evidence is,
2. Enough information on the patients and interventions so readers know who to generalize the results to and how to replicate the protocol or treatments,
3. Description of the outcome measures with numerical results and statistical analysis so readers know what to expect from the intervention and can counsel patients.
4. Important validity limitations.
Reference numbers are placed as superscripts after the first sentence summarizing the respective study, and must match the reference section.

References:
HDAs must have at least two references but no more than five. Levels of Evidence (STEPs) must be assigned to each reference according to the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. References are listed in the order presented in the Evidence Summary. Format follows the AMA Style Guide.

Example:
1. Raux H, Coulon P, Lafay F, Flamand A. Monoclonal antibodies which recognize the acidic configuration of the rabies glycoprotein at the surface of the virion can be neutralizing. Virology 1995; 210(2):400–408. [STEP 3]
Methods (use the exact language below but fill the information between brackets)

The authors developed the clinical question, “[insert question here],” based on the clinical needs of their practice site. EBP editors approved the question based on its relevance and applicability to practicing primary care clinicians. EBP editors also verified the question does not duplicate other HelpDesk Answers written in the prior 3 years.

The table includes the databases and search terms the authors used to find studies matching the following study inclusion criteria: patients – [insert brief description of patients/population]; intervention – [insert brief descriptions of intervention/new test]; comparison – [insert brief description of the comparison/reference standard]; and outcome – [insert brief description of outcome here]. Authors selected the most relevant, highest evidence level studies published within the last [insert age of oldest reference here] years to prepare the HDA manuscript (Figure).

Table: HDA Search Strategy

<table>
<thead>
<tr>
<th>Search engine</th>
<th>Search term or combination of search terms</th>
<th>Total number of records identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>PubMed Clinical Queries</td>
<td>a) filter: [therapy, clinical prediction guides, diagnosis, etiology, or prognosis]</td>
<td>[insert number here]</td>
</tr>
<tr>
<td></td>
<td>b) scope: [broad or narrow]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c) filter: scope:</td>
<td></td>
</tr>
<tr>
<td>Trip Database</td>
<td>a)</td>
<td>[insert number here]</td>
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<tr>
<td>Cochrane Library</td>
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<td>[insert number here]</td>
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<tr>
<td>ECRI Guidelines Trust</td>
<td>a)</td>
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<td>c)</td>
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<tr>
<td>[Insert any other search engines used here. If none, delete this row.]</td>
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<td></td>
<td>c)</td>
<td></td>
</tr>
<tr>
<td>Hand search of reference lists of articles above [If none, delete this row.]</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>
To ensure your search is comprehensive and has the best chance of finding all the relevant studies, please search each of the 4 search engines and record the results in the Table. In the rare event you feel a search engine is not applicable to your question/search place an "NA" in the middle column for that search engine. Space is given to record the search terms or combination of search terms for up to three different searches for each search engine. You may use more or less depending on your question. Make note of the filter and scope you used in your PubMed Clinical Queries search.
Evidence Based Answer: (35 – 75 words)

- The bottom-line conclusions based upon the evidence presented in the Evidence Summary.
- The conclusions from each of the references are included and synthesized into 1 to 2 sentences.
- All the important outcomes in the Evidence Summary are represented in the EBA
- All the conclusions in the EBA are supported by evidence in the Evidence Summary
- The EBA directly answers the question
- The EBA is written in the present tense
- The EBA is presented in the same sequence as the data in the Evidence Summary
- The EBA includes some quantification of the magnitude of effect
  - eg “Achilles tendon ruptures treated non-operatively have a 5% higher risk of re-rupture than surgical treatment.” or “Acetaminophen moderately improves function in patients with osteoarthritis of the knee.”
- SOR indicators (using the SORT criteria) are placed after each conclusion of differing SOR
- Each SOR indicator is followed by a brief explanatory phrase (SOR: B, single RCT)
Evidence Summary: (250 – 825 words)

**Written in unique HDA style.** Consider the following:

- Rarely is an introductory paragraph needed; just jump into the evidence summary (occasionally allowable if the treatment/test is not very common and some additional explanation is needed).
- The Evidence Summary is written in the past tense.
- The style of HDAs is to answer a clinical question using the most relevant and highest quality original evidence. Use of narrative reviews is generally discouraged. Use of guidelines is acceptable but should not be the only references.
- There needs to be at least two references, but no more than five.
- HDAs must be a synthesis of at least two evidence sources so must have at least two references. See “Selecting the Best Available Evidence” section above.
- HDAs are also concise so the question must be narrow enough to be answered with five references or less. If finding more than five references, may need to narrow your question. See “Selecting the Best Available Evidence” section above. Discuss this with the HDA manager.
- Each reference should be summarized in a separate paragraph.
- Generally, the paragraphs should be sequenced with the highest quality of relevant evidence first OR according to the order in which the conclusions are sequenced in the Evidence Based Answer. If 2 or more studies are of the same relevance and quality, the most recent study should be summarized first.
- Studies are referred to by their design, not by lead author or catchy acronym; the latter do not give readers any information about the study.
  - Most studies can be categorized into one of the study designs listed below. Researchers may not abide by these categories so you may have to translate the researchers’ description to one of these types.
    - **Systematic review** – report on two or more studies, contain a methods sections with a pre-specified, comprehensive, literature search strategy and pre-specified study inclusion/exclusion criteria.
    - **Meta-analysis** – data from two or more studies is combined and pooled results reported, usually part of a systematic review.
    - **Randomized controlled trial** – patients randomly assigned to two or more groups, each receiving a different intervention/comparison.
    - **Randomized crossover trial** – all patients receiving all interventions/comparisons but in random order, usually separated by a washout period.
    - **Cohort study** – patients non-randomly assigned to two or more groups, each receiving a different intervention/comparison, can be prospective or retrospective.
Diagnostic cohort study – patients undergoing testing with a ‘new’ test and a reference test to determine the test characteristics of the ‘new’ test.

Case control study – two groups of patients (‘cases’ who have a condition and ‘controls’ who do not) who are evaluated retrospectively for some sort of previous exposure.

Case series – outcomes reported on a group of patients with the same condition who receive the same intervention.

Cross sectional study – population assessed at a point in time for a condition(s) and relevant exposures or risk factors.

Longitudinal study – population assessed serially for a condition(s) and relevant exposures or risk factors.

Case report – description of a single patient.

For more information, refer to the Centre of Evidence-Based Medicine website: https://www.cebm.net/2014/04/study-designs/

- Citation numbers go after the first sentence of the paragraph describing the reference

Each reference is summarized fully

Studies are described first and then results are presented so readers can put the results into context.

- For a single study include:
  - the study design (RCT, cohort study, case-control study, case series, etc.)
  - number of patients
  - the research question of the study

- For a systematic review or meta-analysis include:
  - the design of included studies
  - total number of included studies
  - total number of included patients
  - the research question of the systematic review/meta-analysis
  - if using data from a subgroup analysis, include these elements for the subgroup also

- For a practice guideline include:
  - the developing organization
  - a statement clarifying if it is evidence-based or consensus opinion-based
  - year of publication
  - any strength of recommendation or level/grade of evidence indicators for the recommendations, include a brief description of what the “strength” or “grade” means
  - guidelines are generally lowest level of evidence and summarized last
  - should be written in the past tense
• The PICO elements:
  o Summary of the patients so readers will know to whom the results generalize
    • demographics, criteria for diagnosis/inclusion, disease severity, recruitment
  o Description of the intervention(s) or test(s) so readers can replicate clinically
    • For medications - summarize dose, frequency, route, and duration of therapy
    • For other treatments/therapies – summarize treatment protocol with frequency and duration
    • For diagnostic tests – describe the test and summarize the testing protocol
  o Description of the comparison(s)
    • For medications and other treatments/therapies – similar to above
    • For diagnostic studies:
      • describe the reference standard and if all patients received the new test and the reference standard
      • include the prevalence of disease in the study population
  o Summary of the outcome measures so readers will know what to expect
    • When outcomes are given according to a scale or scoring system:
      • describe the parameters the scale is measuring or assessing
      • provide the range of scores (for continuous data) or summarize the categories (for categorical data) so the readers can see the magnitude of effect (is it a 1–10 or 1–100 scale?)
      • make sure it is clear if higher or lower numbers indicate improvement
  • Duration of trial or follow-up period
  • Any pertinent limitations

References are summarized concisely
• Remember that HDAs are concise. Avoid the following practices that increase the word count without adding value.
  o Summarizing patient subgroups, interventions, or outcomes that are not pertinent to the question.
    ▪ If question asks ONLY about oral NSAIDs for knee osteoarthritis:
      ▪ **NO**: A 2017 systematic review and meta-analysis of 22 RCTs (N=1243) evaluated oral NSAIDs, topical NSAIDs, acetaminophen, opiates, anticonvulsants, and antidepressants for the treatment of knee osteoarthritis.
      ▪ **YES**: A 2017 systematic review and meta-analysis of 22 RCTs (N=1243) evaluated pharmacologic treatments, including oral NSAIDs (8 RCTs, N=873), for the treatment of knee osteoarthritis.
  o Long lists of exclusion criteria. Pick only the most relevant or lump them into groups with single descriptors.
    ▪ **NO**: Exclusion criteria were renal dysfunction; seizure history; allergy or intolerance to quinolones, cephalosporins, or penicillins; antibiotic therapy within 48 hours of enrollment; or confirmed or suspected pregnancy.
YES: Exclusion criteria included renal dysfunction or antibiotic use in the previous 48 hours.

- Including long lists of interventions that are pooled when it is clear that only one or two drove the results.
- NO: Patients in the included studies received ibuprofen 800mg TID (10 trials, N=4578), ibuprofen 600mg QID (2 trials, N=230), naproxen 500mg BID (9 trials, N=4367), diclofenac 50mg BID (1 trial, N=34), diclofenac 75mg BID (1 trial, N=25), piroxicam 20mg daily (1 trial, N=36), or celecoxib (1 trial, N=56).
- YES: Patients in the included studies received various NSAIDs, most commonly ibuprofen 800mg TID (10 trials, N=4578) or naproxen 500mg BID (9 trials, N=4367).

- Describing multiple secondary outcome scales in detail when results are negative.
- NO: Secondary outcomes were scores on the Repetitive Behavior Scale–Revised (RBS), Spence Children’s Anxiety Scale, Aberrant Behavior Checklist–Community Version (ABC), and the CGI-I. There were no significant differences between the two groups in secondary outcomes.
- YES: There were no significant differences in scores between the two groups on four secondary outcomes scales.

- Describing outcome scale ranges in detail when percent change might be easier to follow.
- NO: Function was evaluated on the physical function subset of the Western Ontario and McMaster Universities Arthritis Index (WOMAC) consisting of 17 items rated on a scale from 0 (no functional impairment) to 4 (extreme impairment); total range of scores of 0 to 68. Mean WOMAC physical function scores were 8 points lower with intervention than placebo (mean difference 8.0; 95% CI, 6.0–10).
- YES: Function was evaluated on the physical function subset of the Western Ontario and McMaster Universities Arthritis Index (WOMAC). The intervention improved function scores 12% more than placebo (mean difference 8.0 points; 95% CI, 6.0–10).

- Describing multiple outcome scales in detail when results are pooled and reported as standardized mean differences (or effect size, Cohen’s d, Hedge’s g). Since the scores for each individual scale are not reported, can simply state, “…multiple validated scales…”
- Listing study weaknesses in a separate sentence that are already apparent from previous information in the Evidence Summary.
  - If it is already stated the study only had 12 patients, there is no need to include a separate sentence to say that it may have suffered from small study bias.
  - If study is already described as a cohort study, there is no need to mention lack of control group as a weakness.

Results are presented transparently

- Need to show the actual numerical data so the readers can see the magnitude of effect, ie “How much better?”
  - Definitely for outcomes that are positive (significant difference)
  - For outcomes that are negative (no significant difference), showing the numerical data is not mandatory. Decision can be based on:
importance of the negative outcome
is it a primary or secondary outcome?
is the negative outcome definitive or marginal?
is it expected or a surprise?

manuscript length

manuscript readability (ie ‘number clutter’)

• Avoid “floating P values”, ie P values that are not associated with numerical data
  o may show statistical significance, but do not show magnitude of effect, always provide the actual numerical data that the P value compares (remove the P value if numerical results are not reported).
• For pooled outcomes of a meta-analysis, authors should provide the number of trials and patients that were pooled: (6 trials, N=567; OR 8.7; 95% CI, 7.0–9.8) or the number of trials/patients should be included in the text
• Make sure the description of the outcome measure (continuous/discrete vs. dichotomous outcome) matches the numerical result (continuous/discrete vs. dichotomous variable)
  o Continuous variable
    ➔ Measured along a continuum
    ➔ Measured not counted
    ➔ Example is weight loss
  o Discrete variable
    ➔ Only integer values
    ➔ Counted not measured
    ➔ Example is number of recurrent UTIs
  o Dichotomous variable
    ➔ Only 2 categories
    ➔ Response or no response, cured or not cured, dead or alive
    o Risk ratio, odds ratio, number needed to treat – used to report dichotomous outcomes
    o Mean difference, standardized mean difference – used to report continuous/discrete outcomes

Review for common pitfalls:
• Studies that are included in a systematic review/meta-analysis should not be summarized separately unless there is a good reason such as the single study presents a different outcome or subgroup analysis
  o If summarized separately, you must explicitly state in the text why the study is being singled out and presented separately
  o If a study was published within the search dates of the systematic review/meta-analysis but was not included in the review, you should clarify why the study was not included
• When 2 or more systematic reviews/meta-analyses with similar research questions are summarized, it is important to look at how much overlap exists among included studies.
  o If there is considerable overlap, you should briefly explain what unique information the older systematic review/meta-analysis provides and why it should be included
  o It may not make sense to include the older systematic review/meta-analysis if it provides no unique information (such as different outcome measures, different subgroup analyses, etc.)
If there is very little overlap and this is unexpected, you should briefly explain why. A comparison of the study inclusion criteria may reveal reasons why this occurred and this should be briefly summarized. If no reason can be found, it should be stated.

- For diagnostic studies:
  - The reference standard used to determine which patients actually have the condition must be clearly identified
  - In discussing clinical tests, include likelihood ratios (LR+/LR–) with any sensitivity/specificity data. You may need to calculate them.
  - Predictive values (PPV/NPV) are not as useful as likelihood ratios for diagnostic tests and are discouraged
  - Predictive values are appropriate for population-based screening tests (mammography, Pap smear)

- Limit use of the passive voice – the subject of the sentence is not performing the verb
  - Avoid starting a paragraph with passive voice
  - Avoid excessive use elsewhere but occasional use is acceptable

- Numbers with decimals are rounded to 2 significant digits
  - 0.324 becomes 0.32
  - 2.45 becomes 2.5
  - 12.7 becomes 13
  - 136 remains 136
Template for an Evidence Summary paragraph for an individual RCT:

Evidence summary:

Sentence 1: Set up the study design/study aim/research question
For example: “A multicenter RCT (N=X) examined the effectiveness of Y intervention for x disease compared to control.”

Sentence 2: Describe population and disease of interest. Include any important patient characteristics, disease type, duration, severity so readers can get a sense of whether the population reflects their own patient populations. List any important exclusions.
For example: “Patients were immunocompetent, non-pregnant, adult women recruited from US inner city, STD clinics presenting for XXX. The mean age was X and all participants had disease Z (define the disease). Patients requiring hospitalization were excluded.”

Sentence 3: Describe the interventions and comparisons. Provide enough information so readers could replicate the intervention in their clinical practice if appropriate and know if the control is the relevant comparison or appropriate alternate treatment.
For example: “The intervention group received X (list treatment protocol or drug, dose, route, frequency) for X weeks while the control group received Y (placebo, usual care, etc).”

Sentence 4: Describe primary/secondary outcomes (including how the outcomes were measured/assessed)
For example: “The primary outcome was X and secondary outcomes were Y, Z measured at X time follow-up.”
You should also explain scales here. Define the scale and the minimum and maximum score so readers can interpret if statistically significant findings are clinically meaningful. For example: “Researchers assessed outcomes using a 0 to 100 visual analog pain scale and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) which assess pain, stiffness, and function. Scores range from 0 to 96 with higher scores indicating greater symptoms and disability; a change of X is considered clinically relevant.”

Sentence 5: Give the results in one to three sentences. Include the numerical results and statistical information for all primary outcomes and statistically significant secondary outcomes. If a secondary outcomes is not statistically significant, numerical results and statistical information are not mandatory and the numbers can be omitted to reduce “number clutter”. For pooled results from a meta-analysis, report the number of studies and patients that were pooled for each outcome.
For example: “Drug X reduced myocardial infarctions by 50% compared to placebo (RR 0.50; 95% CI, 0.30–0.63; NNT= 10). Drug X did not reduce cardiovascular mortality (RR 0.99; 95% CI, 0.93–1.1) or all-cause mortality (RR 0.80; 95% CI, 0.77–1.3).” Pooled example: (X trials, N=X; RR 0.XX; 95% CI, 0.XX–0.XX; NNT X)

Sentence 6: Harms of the intervention
For example: “Side effects were minimal and included throat irritation and mild cough (give % of participants in each group reporting side effects).”

Sentence 7: Limitations of the study that are not already apparent from the preceding PICO description of the study (no need to mention that a study is limited by small sample size when “N=7” is included in the first sentence of the paragraph. For a meta-analysis this should typically include an assessment of the quality of the included studies and may include information such as heterogeneity and publication bias.
For example: “This RCT was limited by the lack of blinding and allocation concealment and was underpowered to detect the primary outcome so conclusions about Y should be cautiously interpreted.”
Template for an Evidence Summary Paragraph for a Systematic Review/Meta-Analysis:

Evidence summary:

First: Give the overall study design (systematic review or systematic review and meta-analysis), the design of the included studies, and the research question. To inform readers of the size of the review and included studies, include the number of studies and overall number of patients.

For example: “In 2017, a meta-analysis of seven RCTs (N=810) compared the efficacy of long term BiPAP with usual care for the treatment of adults with stable COPD and chronic hypercapnia.”

Second: Describe the study inclusion criteria and any important characteristics of the patients who were ultimately included such as demographics, disease type, disease duration, and disease severity so readers can get a sense of whether the population reflects their own patient populations. List any important exclusions. There may be only a subgroup of studies that are most pertinent to your question. If so state that here.

For example: “The review only included trials of at least 3 months duration with patients who at baseline had a PaO2 less than 60 mmHg, PaCO2 greater than 50 mmHg, and FEV1 less than 50% predicted.”

Third: Summarize the interventions and comparisons in the included studies. Provide enough information so readers could replicate the intervention in their clinical practice if appropriate and know if the control is the relevant comparison or appropriate alternate treatment.

For example: “Patients assigned to BiPAP received inspiratory pressures ranging from 10 to 21.6 cm of H2O and expiratory pressures from 2 to 5.1 cm H2O for at least five hours/day over three to six months while those assigned to usual care received X.”

Fourth: Describe any outcome measures that are not obvious to the readers such as scales or scores. Outcome measures that are clear such as mortality, do not require further explanation.

For example: “In addition to mortality some studies evaluated hospitalization rates and exercise capacity with the six-minute walk distance.”

You should also explain scales here. Define the scale and the minimum and maximum score so readers can interpret if statistically significant findings are clinically meaningful. For example: “Researchers assessed outcomes using a 0 to 100 visual analog pain scale and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) which assess pain, stiffness, and function. Scores range from 0 to 96 with higher scores indicating greater symptoms and disability; a change of X is considered clinically relevant.”

Fifth: Give the results in one to three sentences. Include the numerical results and statistical information for all primary outcomes and statistically significant secondary outcomes. If a secondary outcomes is not statistically significant, numerical results and statistical information are not mandatory and the numbers can be omitted to reduce “number clutter”. For pooled results from a meta-analysis, report the number of studies and patients that were pooled for each outcome.

For example: “BiPAP did not decrease overall mortality compared to usual care (6 studies, N=401; risk ratio [RR] 0.78; 95% CI, 0.54-1.1). However, when including only the 310 patients from 2 trials in whom BiPAP use was driven by the goal of normalizing PaCO2 with an average inspiratory pressure of 20 cm H2O, BiPAP did decrease mortality compared to control (RR 0.35; 95% CI, 0.19-0.64).” Format for reporting pooled results: (X trials, N=X; RR 0.XX; 95% CI, 0.XX–0.XX; NNT X)

If results are not pooled, summarize the results of the individual studies. For example: “Although meta-analysis was not possible, four of five trials evaluating hospitalization rates and three of four trials evaluating exercise capacity with the six-minute walk distance showed no significant difference between patients on BiPAP versus usual care.”
Sixth: Harms of the intervention

For example: “Side effects of BiPAP were reported in only two studies and included throat irritation (9% of patients) and soreness on the bridge of the nose (12% of patients).”

Seventh: Limitations of the review that are not already apparent from the preceding PICO description of the review (no need to mention that a systematic review is limited by small size of included studies when “N=20” is included in the first sentence of the paragraph). For a meta-analysis this should typically include an assessment of the quality of the included studies and may include information such as heterogeneity and publication bias.

For example: “Two of the trials were rated as low risk of bias (including one of the trials with goal of normalizing PaCO2) but the other five trials had unclear concealment of allocation and unclear blinding of outcome assessors.”

Template for an Evidence Summary Paragraph for a Guideline:

Evidence summary:

First: Summarize who developed the guideline, the purpose of the guideline, and methods for formulating the recommendations (evidence-based or consensus opinion-based). The year of publication is especially pertinent when summarizing guidelines.

For example: “The 2010 American Psychiatric Association practice guidelines for the treatment of major depression discussed the use of stimulants as adjunct therapy for major depression based on a few clinical trials and case reports.”

Second: Summarize the pertinent recommendations. Include an strength of recommendation or level of evidence indicators with a short explanation of what these indicators mean.

For example: “The guideline stated that stimulants may help ameliorate otherwise suboptimal response to therapy (Level of clinical confidence III, may be recommended on the basis of individual circumstances).”

Third: Comment on the quality of the guideline.

For example: “Several practice guideline panel members reported consulting, research, or speaking for multiple pharmaceutical companies. This guideline was reviewed by an independent review panel without conflicts of interest.”
Tables

- Tables should be used when they communicate the numerical results significantly more clearly than a textual description of the results. As a general guideline, paragraphs which contain more than 3 or 4 statistical outcomes may be clearer when the results are moved to a table.
- The evidence summary provides information regarding the validity and generalizability of the data in the table, but readers should generally understand the take home point of a table without relying on the information in the evidence summary.
- In your draft manuscript, tables should be placed at the end of the manuscript after the reference section.
- The title should be complete enough to orient the reader to the table independently of the rest of the manuscript.
- Citation numbers should be in the title or the left-most column.
- Column headings are typically number of trials (for meta-analyses), number of patients, and outcome measures (RR, OR, MD, SMD, LR+, LR-, etc.).
- The left-most column and the top-most row should contain the text.
- Put only numbers in the other boxes.
- Put only 1 or 2 numbers in each box.
- Rows to be compared should be next to each other.
- Consider shading or bold type to draw the eye (eg statistically significant outcomes).
- Abbreviations and other clarifications should be placed in footnotes below the table.
- In the text of the paragraph, refer readers to a table using “(TABLE)”.
- A single table does not need to be numbered so “(TABLE 1)” is only used when there is also a “(TABLE 2)”.
- Generally, numerical data provided in the table should not be repeated in the text of the paragraph. Rather, the results sentence in the evidence summary should summarize the results and/or provide more details about the studies (especially weaknesses). Example: “The intervention improved all outcomes versus the control except for the secondary outcome of X (TABLE).”

Example of Table:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of trials</th>
<th>No. of subjects</th>
<th>Relative risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic antidepressant</td>
<td>9</td>
<td>829</td>
<td>0.73</td>
<td>0.63–0.86</td>
</tr>
<tr>
<td>SSRI</td>
<td>21</td>
<td>4,000</td>
<td>0.75</td>
<td>0.67–0.84</td>
</tr>
<tr>
<td>Monoamine oxidase inhibitors</td>
<td>1</td>
<td>29</td>
<td>0.55</td>
<td>0.34–0.88</td>
</tr>
<tr>
<td>Selective norepinephrine reuptake inhibitor</td>
<td>4</td>
<td>1,531</td>
<td>0.61</td>
<td>0.41–0.91</td>
</tr>
<tr>
<td>Reboxitine</td>
<td>1</td>
<td>82</td>
<td>0.71</td>
<td>0.51–0.97</td>
</tr>
</tbody>
</table>
References

- Each study in the Evidence Summary is cited in the reference section
- References are numbered in order of appearance
- The references are formatted according to the AMA Style Guide (list first three authors, then et al.)
  - AuthorLastName, FirstInitialMiddleInitial. Title in sentence case. Abbreviated Journal Title in Title Case. Year Month Day; volume(Issue#): PP-PP. [STEP #]
  - AMA Formatting Tips:
    ➤ Search article in PubMed and click the cite button.
    ➤ Use the Mick Schroeder Citation Generator and insert the Pubmed ID or DOI name.
    ➤ Insert reference in Microsoft Word.
- Each reference is followed by the level of evidence indicator (based on the CEBM table) in the STEP format “(STEP 1).”
- Please do not use “End Notes” or similar apps to insert references
**Text standards**

**Number usage:**
- Generally, spell out integers from one to nine; numerical form for integers 10 and higher
  - spell out all numbers at the beginning of a sentence
  - use numerical form for all numbers when reporting results
  - use numerical form for all non-integers (eg 1.1)
- Hyphens between numbers and descriptors, eg ‘5-year risk’, ‘3-fold’
- No spaces between symbols and digits, space between numbers and labels (>3 cm)
- 1 to 4 days in text (1–4 days in parentheses). Note use of ‘en-dash’ instead of hyphen for ranges
- Use commas for numbers 1,000 and higher
- “greater than 40 mg” in text (“>40 mg” in parentheses)
- Fractions in text are generally spelled out, eg ‘one-third’
- For reporting pooled results in a meta-analysis - (3 trials, N=26,244; ...)
- Use en-dashes for minus signs (–2.5, LR–) (Note: the en-dash is created by pressing Ctrl and (-) key on the number key pad, not the dash key on the keyboard)
- Round numerical results with decimals to 2 significant digits (4.56 should be 4.6)

**Presentation of results and statistical analysis:**
- (relative risk [RR] 0.67; 95% CI, 0.46–0.84; number needed to treat [NNT] 43)
- (absolute risk reduction [ARR] 3.8%;...)
- (odds ratio [OR] 0.54;...)
- (hazard ratio [HR] 0.09;...)
- For subsequent use of same outcome, can use abbreviations (RR 0.67; 95% CI, 0.46–0.84; NNT 43)
- The treatment group had 15 less hospitalizations than the control group (P<.0001). Note the lack of leading zero when reporting P values
- For complex meta-analysis: outcome A (7 trials, N=7,500; odds ratio [OR] 2.5; 95% CI, 1.5–3.1) and outcome B (5 trials, N=6,300; OR 5.9; 95% CI, 3.2–7.2)
- Use the en-dash for CI ranges (95% CI, 3.5–27), unless there's a negative number, in which case use "to" for denoting the range (95% CI, –23 to 120)
- If a confidence interval is presented, no need to provide a P value.
- Level of evidence in references
  - [STEP 2]
  - [STEP 3]
- LR+ for positive likelihood ratio; LR– for negative likelihood ratio
- “We found that 13% (3 of 23) of patients”. ... rather than “We found that 13% (3/23) of patients ...”
• For reporting P values, use $P=.02$ (upper case italic P, no space between symbols and letter/digits, no leading zero)
• "greater than or equal to" in text ($\geq$ in parentheses & tables)

Abbreviations
• Define abbreviations the first time they are used (except from the approved list below)
  - …standardized mean difference (SMD)…
• Minimize use of idiosyncratic abbreviations
  - Occasional use is okay—especially for long, complex phrases that are used repeatedly (like WOMAC or USPSTF)
  - avoid for 1 or 2-word phrases or phrases that only appear 2 or 3 times
  - avoid more than 2 or 3 abbreviations in a paragraph

Approved abbreviations: (do not need to be defined the first time)

<table>
<thead>
<tr>
<th>Approved abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-1</td>
<td>Angiotensin-converting enzyme inhibitor</td>
</tr>
<tr>
<td>ACL</td>
<td>Anterior cruciate ligament</td>
</tr>
<tr>
<td>ADHD</td>
<td>Attention deficit hyperactivity disorder</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired immune deficiency syndrome and</td>
</tr>
<tr>
<td>ALT</td>
<td>Alanine aminotransferase</td>
</tr>
<tr>
<td>AST</td>
<td>Aspartate aminotransferase</td>
</tr>
<tr>
<td>BID, TID, QID, PO, IV, IM</td>
<td>Dosing frequencies and routes of administration</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>dL, mL, mm, cm, mmHg, etc.</td>
<td>Units of measure</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>DTaP</td>
<td>Diphtheria, tetanus, and acellular pertussis vaccine</td>
</tr>
<tr>
<td>DTP</td>
<td>Diphtheria, tetanus, whole-cell pertussis</td>
</tr>
<tr>
<td>eg, ie (no periods)</td>
<td>For example, in other words</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Glycosylated hemoglobin</td>
</tr>
<tr>
<td>HDL</td>
<td>High-density lipoprotein</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>LDL</td>
<td>Low-density lipoprotein</td>
</tr>
<tr>
<td>MMR</td>
<td>Measles, mumps, rubella</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>NSAID</td>
<td>Nonsteroidal anti-inflammatory drug</td>
</tr>
<tr>
<td>Q4H, Q6H, etc.</td>
<td>Dosing frequencies</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized controlled trial</td>
</tr>
<tr>
<td>RNA</td>
<td>Ribonucleic acid</td>
</tr>
<tr>
<td>SSRI</td>
<td>Selective serotonin reuptake inhibitor</td>
</tr>
<tr>
<td>Definition</td>
<td>Abbreviation</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Absolute risk reduction</td>
<td>ARR</td>
</tr>
<tr>
<td>Diabetes mellitus type 2</td>
<td>DM-2</td>
</tr>
<tr>
<td>Food and Drug Administration</td>
<td>FDA</td>
</tr>
<tr>
<td>Forced expiratory flow</td>
<td>FEF</td>
</tr>
<tr>
<td>Forced expiratory volume in 1 second</td>
<td>FEV1</td>
</tr>
<tr>
<td>Forced vital capacity</td>
<td>FVC</td>
</tr>
<tr>
<td>genus and species: <em>Escherichia coli</em></td>
<td><em>E coli</em> (no period)</td>
</tr>
<tr>
<td>Negative predictive value; positive predictive value</td>
<td>NPV, PPV</td>
</tr>
<tr>
<td>Number needed to treat; number needed to harm</td>
<td>NNT, NNH</td>
</tr>
<tr>
<td>Positive likelihood ratio; negative likelihood ratio</td>
<td>LR+, LR–</td>
</tr>
<tr>
<td>Relative risk reduction</td>
<td>RRR</td>
</tr>
<tr>
<td>Risk ratio; hazard ratio; odds ratio; mean difference; adjusted mean difference</td>
<td>RR, HR, OR, MD, aMD</td>
</tr>
<tr>
<td>Standardized mean difference</td>
<td>SMD</td>
</tr>
<tr>
<td>United States</td>
<td>U.S.</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>US</td>
</tr>
</tbody>
</table>

**Military Disclaimers**

Air Force:
*The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Air Force Medical Department, the Air Force at large, or the Department of Defense.*

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Author Checklist (see also MET Review Checklist)

Evidence Based Answer:
☐ All the important conclusions in the Evidence Summary are represented in the EBA
☐ All the conclusions in the EBA are supported by evidence in the Evidence Summary
☐ The EBA directly answers the question
☐ The answer is presented in the same sequence as the data in the Evidence Summary
☐ As appropriate, the answer includes some quantification of the magnitude of effect
☐ SOR indicators placed after each conclusion of differing SOR
☐ SOR indicator followed by a brief explanation explanatory phrase

Methods:
☐ The methods section matches the format of the template, text is verbatim from the template except the inserted information
☐ The HDA question is inserted verbatim into the methods section
☐ The PICO elements listed in the methods section are appropriate for the question
☐ The age of the oldest reference in years is inserted into the methods section
☐ The search terms used and number of ‘hits’ or records found with each search term are included in the Table
☐ The Literature Search Flow Diagram is completed

Evidence Based Summary:
☐ No introductory paragraph unless needed to explain an uncommon treatment/test
☐ At least 2 references and no more than 5
☐ Each reference summarized in a separate paragraph
☐ Paragraphs sequenced with the highest level of evidence first or according to the order in which the conclusions are sequenced in the Evidence Based Answer
☐ Studies are referred to by their design, not by lead author or acronym
☐ Citation numbers placed after the first sentence of the paragraph describing the reference
☐ Studies are described first and then results are presented
☐ For a single study, the following are present:
  ☐ the study design
  ☐ number of patients
  ☐ the research question of the study
☐ For a systematic review or meta-analysis, the following are present:
  ☐ the design of included studies
  ☐ total number of included studies
  ☐ total number of included patients
  ☐ the research question of the systematic review/meta-analysis
For a practice guideline include:

- the developing organization
- evidence-based or consensus opinion-based
- strength of recommendation or level/grade of evidence indicators including a brief description

The PICO elements are present:

- Summary of the patients
- Description of the intervention(s) or test(s)
  - For medications - dose, frequency, route, and duration of therapy
  - For other treatments/therapies – treatment protocol with frequency and duration
  - For diagnostic tests – description of the test and the testing protocol
- Description of the comparison(s)
  - For medications and other treatments/therapies – similar to above
  - For diagnostic studies, description of the reference standard and the prevalence of disease in the study population
- Summary of the outcome measures and description of any scales or questionnaires
- Duration of trial or follow-up period
- Numerical data given for all positive outcomes
- For studies on diagnostic tests, LR+ and LR– are reported as appropriate
- For meta-analyses, the number of trials and patients that were pooled are reported
- Description of the outcome measure matches the numerical result
- Pertinent limitations
- Use of passive voice is limited
- Numbers with decimals are rounded to 2 significant digits
- Word Count (EBA & EBS) does NOT exceed 900 words

Tables:

- Descriptive title
- Abbreviations and other clarifications are defined in footnotes below the table
- Citation numbers present
- Table stands alone (understood without reading the text)
- In the text of the paragraph, readers are referred to the table

References:

- Each study in the Evidence Summary is cited in the reference section
- Citations numbered in order of appearance
- References in AMA style
- Each reference has a level of evidence in the STEP format

Title Page:

- Author names, credentials, program name, and location included as per the template