University of Wisconsin – Madison
School of Pharmacy

School of Pharmacy
UNIVERSITY OF WISCONSIN–MADISON

Tool for Writing and Evaluating a Clinical Inquiry

First developed by the School of Pharmacy 1992

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Introduction to Clinical Inquiry

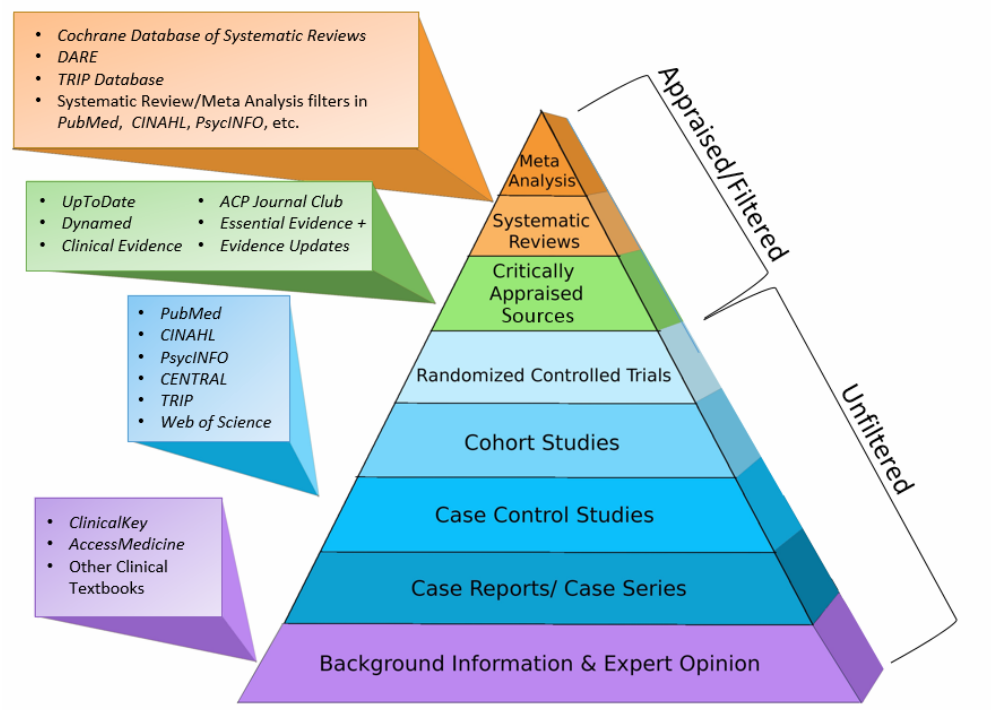
Introduction. The clinical inquiry assignment is structured such that students must demonstrate the ability to search for and use the highest quality evidence available to answer a question. All students are required to demonstrate that they know how to look for systematic reviews/meta-analyses and clinical trials/primary literature even if the search reveals no results. Students should refer to the information hierarchy pyramid regarding additional reference sources to answer the question if systematic reviews/meta-analyses and/or clinical trials/primary literature are not available. The assignment requires a brief written (1-2 pages evidence summary suggested) response with references and supporting materials.

The purposes of the assignment are:

1. to foster critical thinking skills related to evidence-based decision-making
2. to practice and refine written communication skills

The specific student objectives for this assignment are:

a. to develop competency in searching current medical literature
b. to interpret the literature with respect to the question to be answered
c. to create an answer to a question based on best evidence available



https://researchguides.library.wisc.edu/c.php?g=860707&p=6167866

1. ***PICO and Question Restatement***
   - The student should frame the question in a PICO construct using the following elements:
     - **P =** population and/or problem
     - **I =** Intervention
     - **C =** comparator (in some cases may be placebo or no comparison, n/a)
     - **O =** outcome/s (typically students choose one, there is a max of two outcomes)
   - In the DPh3 year, the clinical question is assigned by faculty. The clinical question should not be adjusted by the student.
   - In the APPE year, *students must discuss the PICO and question* with their clinical instructor to ensure the final draft is what the instructor intended.
     i. It is the ***student's responsibility*** to take initiative in creating the PICO construct.
   - The clinical question and PICO terms must match.

Example of clinical question and PICO format

Clinical question: How does gabapentin compare to hormone replacement therapy to decrease the severity and intensity of hot flushes in adults who have had a hysterectomy?

PICO format:
P: adults who have had a hysterectomy
I: hormone replacement therapy
C: gabapentin
O: decreased severity and intensity of hot flushes

**For APPE students, adjustments to the clinical question should only be made through discussion with the person who asked the question.

2. ***Formatting Requirements***
   a. Uploaded as a Word or PDF document
   b. One-inch margins
   c. Single-spaced
   d. Use an easy-to-read font in an appropriate size such as: 10 to 12 point Times New Roman, Arial, or Calibri.
   e. Block paragraph format (no indenting)
   f. Left-justified
   g. One blank line between paragraphs

3. ***Outline Requirements***
   a. Name & course in upper right corner of page 1 (APPEs also should include block)
   b. Final question
      - DPh3 students should use assigned clinical question as written when assigned
   c. PICO
   d. Evidence-based answer
   e. Strength of recommendation (SOR) & rationale
   f. Evidence summary
      - Presented in order of highest level of evidence to lowest level of evidence
   g. Recommendations from others
   h. References
   i. Search strategy screen shots

4. *Tips & Hints for Technical Writing*

a. ***Presentation of Clinical Data***

- Students should state the **actual data** related to the outcome measures used including the statistical analysis (whether it is statistically significant or not).
- Students should clearly indicate the directionality of the results in the context of the intervention and control. In other words, which agent had a higher rate or mean for the outcome of interest?
- Students MUST provide a p-value (as either an actual value [p=0.002] or a conditional value [p<0.05]) or a 95% confidence interval to describe the statistical significance of the findings.

    - **Example 1** The mean A1C reduction of metformin in combination with insulin (mean -1.43) compared to insulin monotherapy (mean -1.21) was non-statistically significantly different (MD: -0.22, 95% CI -0.74 to 0.10, p=0.72).
    - **Example 2** Proportion of subjects who achieved their serum uric acid goal was statistically significantly lower with allopurinol compared to febuxostat (36% versus 48%, p=0.002).
    - **Example 3** Among obese patients, there was a non-significant reduction in major bleeding with apixaban compared to warfarin (RR=0.90, 95%CI 0.81-1.01, p=0.08).

- If an author does not provide a p-value or a 95% confidence interval, students should question the significance of the difference (regardless of whether the author states it's significant or not) and should state “no p-value provided by authors”.
- When introducing scoring tools as the outcome of interest, students may choose to indicate if a higher or lower score is desired.

    - **Example** The difference in the patient health questionnaire (PHQ-9; decrease in score indicates improvement in symptoms of depression) indicated a lower score using citalopram versus placebo (mean decrease 2.1 versus 1.3, p=0.012).

b. ***Brand & Generic Medication Names*** Use of generic names is preferred. All generic medication names should begin with a lower-case letter (unless at the start of a sentence). Brand names of medications should begin with a capital letter, and should always be followed with a symbol (e.g. ®) reflecting the fact that brand names are registered trademarks of the manufacturer.

c. ***Abbreviations*** If an abbreviation is used, it must be spelled out the first time it is used. The following are School of Pharmacy-approved abbreviations adapted from *Evidence-Based Practice* and consistent with the Institute for Safe Medication Practices and The Joint Commission; these do not require definition at first use in an article:

- 95% CI
- A1C
- AIDS, HIV
- BID, TID
- COVID-19
- dL
- DNA, RNA
- DTaP, DTP, dT
- FDA
- GRADE
- FEV1
- HR (hazard ratio)
- mg/dL
- mmHg (no space)
- NSAID
- OR (odds ratio)
- RR (relative risk)
- SORT
- US

For scoring tools, organizations, and other acronyms, the full name should be listed with acronym in parentheses following the first time it is used.

- **Example** The evidence-driven American Diabetes Association (ADA) clinical practice recommendations use a grading system to assign an evidence grade of A through E

d. ***Numbers*** Use Arabic numbers (1, 2, etc.) for all numbers within the clinical inquiry assignment. This applies to numbers whether greater than OR less than 10. The exception is when a number is the first word in the sentence, then it should be spelled out.

e. ***Tone of Writing*** Conversational tone is not appropriate in technical writing. There are several conventions that must be followed:

(1) Avoid first person (never say "I have a concern regarding...").
(2) Avoid contractions (spell out "do not" rather than "don't").
(3) Avoid slang and other words and phrases that may be used commonly in spoken communication. For example, avoid "even with the *downsides* of this study design"
(4) Avoid labeling patients based on their diagnosis (i.e. state “a person with asthma” or “a person with diabetes” NOT “diabetic patient” or “asthmatic patient”).

f. ***Symbols*** Avoid the use of symbols (such as <, >, etc.) within sentences. While it is appropriate and necessary to use them within parentheses (e.g., p<0.05), do not use them within the non-parenthetic section of a sentence.

- **Example** spell out "All patients were less than 30 years of age" instead of "All patients were < 30 years of age."

g. ***Citation Formatting*** Students must follow the format published in the American Medical Association's Manual of Style. The AMA 11th Edition Manual of Style is available through Ebling:

(1) Access Ebling Library at: http://ebling.library.wisc.edu/
(2) Click on the “Pharmacy” topic guide
(3) Click “Citation Management” in the left hand menu
(4) Click " Link to the AMA Style Guide "; you may need to log in
(5) Scroll down to section 3 “References” and click the content of interest

The direct link is: https://www-amamanualofstyle-com.ezproxy.library.wisc.edu/
Please note you will have log in with your NetID to access.

h. ***Where in the Paragraph*** In the AMA Manual of Style, 11th edition, you’ll find those instructions in sections 3.6 Citation and 8.1.1.1 Placement.
(1) **Superscript** The superscript may be placed immediately after the author names OR at the end of the first sentence that refers to the citation; place superscript immediately after the period.
(2) **Citations** Cite the study at the end of the first sentence that describes that study in each new paragraph. Writers can continue to write about that particular study without citing every subsequent sentence. It is assumed you are referring to that study until the writer introduces another study and references it.

i. ***Appropriate Paraphrasing*** All text should be in a student’s own words. It is inappropriate to use another author’s text without appropriate documentation. If a direct

quote or direct definition from an original source is used, that text should be in quotations. For more guidance on appropriate paraphrasing please see the UW-Madison Writer's Handbook.

- University policy regarding paraphrasing:
- **Plagiarism:** Copying passages verbatim from another writer's work and representing them as one's own work constitute plagiarism. Yet, plagiarism involves much more. It is defined to include any use of another's work and submitting that work as one's own. This means not only copying passages of writing or direct quotations but also paraphrasing or using structures or ideas without citation.
- **Artificial Intelligence:** The use of artificial intelligence (AI) tools and applications (including, but not limited to, ChatGPT, DALL-E, and others) for clinical inquiries **is prohibited**. Using them in any way for this assignment is a violation of the course's expectations and will be addressed through UW– Madison's academic misconduct policy, specifically, UWS 14.03(1)b (b) Uses unauthorized materials or fabricated data in any academic exercise.

5. ***Evidence-Based Answer (EBA)***

a. ***Definitive*** The answer should be focused and respond directly to the question, committing to a definite answer. **Make sure to answer the question**—if it is a comparison, then state the comparison in the EBA.

- **Example** which medication is more effective? State which medication is more effective. If the two agents are similar, then state the two agents have similar efficacy.
  - Drug X may increase risk of outcome more than drug Y/placebo in population A.
  - In population A, drug X has a similar risk of outcome to drug Y.
  - Based on the best available evidence in population A, drug X may be increases outcome compared to drug Y in population B.
    - Use when extrapolating from a similar population
  - In population A, drug X increases outcome more than drug Y, except for in subpopulation B where drug X has similar impact on outcome to drug Y.
    - Use when a subpopulation has a different result (e.g., patients with low kidney function)

- Stating "the evidence is lacking, can't draw conclusions … etc." is UNACCEPTABLE
  - The SOR will help readers understand the certainty of the answer based on the quality of the information available.
  - Do NOT state "more research is needed".

b. ***Draw Conclusions from the Evidence Summary*** The EBA should:

(1) Answer the question based on the presented evidence explicitly contained in the Evidence Summary

(2) Do NOT include any background information or commentary

c. ***Original Response*** The answer should represent the student's response to the question based on what they have read & analyzed.

- Do not state, "the authors concluded….".
- If the question compares two medications for a condition, and the outcomes were safety and efficacy, the EBA might have two sentences—one about the relative efficacy of one agent versus another, and a second sentence summarizing the safety comparison.

d. ***Reference Citations*** The EBA should not use reference citations.

e. ***Strength of Recommendation (SOR)*** Provide an SOR using the American Academy of Family Physicians Strength of Recommendation Taxonomy (SORT) available at: https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html
   - Use **FIGURE 2** to determine the appropriate SOR.
   - Pay particular attention to whether the outcome is patient-oriented (e.g., morbidity, mortality, quality of life, and cost) or disease-oriented (e.g., biomarkers, FEV_1).
   - Strength of recommendation and rationale must be provided. Rationale should include highest level of evidence and outcome used to determine the SOR.

     - **Example 1** SOR: B based on single randomized controlled trial with patient-oriented outcomes.
     - **Example 2** SOR: C based on several well done randomized controlled trials with consistent disease-oriented results.
     - **Example 3** SOR: A based on a single meta-analysis comprised of five well-done randomized controlled trials with consistent patient-oriented results.
     - **Example 4** SOR: B based on an indirect comparison of a patient-oriented outcome through a network meta-analysis including 13 well done randomized controlled trials.
     - **Example 5** SOR: B based on a systematic review with meta-analysis of a patient-oriented outcome with consistent results including 4 randomized controlled trials at a high risk for bias.

6. ***Evidence Summary***

a. ***Referenced*** The Evidence Summary should be referenced using superscripts. (See Tips and Hints for Technical Writing earlier in this manual.)

b. ***Evidence Only*** ONLY include evidence in this section. NO background information at the beginning of the section, and NO summary at the end of the section.

c. ***Descriptions of Data*** If more than one type of study design is included in a single clinical inquiry, the highest level of evidence should be presented first. Subsequent literature presented should follow the evidence-pyramid.
   1. Systematic reviews and meta-analyses
   2. Systematic reviews without meta-analysis
   3. RCTs
   4. Cohorts
   5. Case-controls
   6. Case reports/series

d. **Inclusion of Systematic Reviews** There may be times when it is more appropriate for a student to include the primary literature rather than secondary literature.
   - If the quality of a systematic review is suboptimal.
   - If only 1 piece of primary literature is included in the systematic review.
   - If only 2-3 pieces of primary literature are included in a systematic review without meta-analysis. When even a small of trials are pooled together in a meta-analysis, it may make sense to use either the primary or secondary literature, depending on the situation.
   - If a student chooses to use primary literature in place of secondary sources, it is suggested to explain the rationale for not using the systematic review in the search strategy section.

(1) ***Systematic Reviews & Meta-Analyses***

It is sometimes difficult to differentiate narrative/general reviews from systematic reviews. To determine if a publication may be a systematic review, please consider the following criteria:

1. a stated question to answer (like a clinical inquiry assignment!)
2. specific inclusion and exclusion criteria
3. an explicitly-stated search strategy (like a clinical inquiry assignment!)
4. an assessment of quality and/or risk for bias of the included studies
5. an evidence table

Please note:

- Some of these items may be in supplemental material.
- Meta-analyses are systematic reviews that ALSO have a statistical analysis of a pooled outcome.
- If there is NO methods section, or an article reviews many aspects of a medication or disease state, it is most likely a narrative review.

Descriptions of systematic reviews and meta-analyses MUST include the following items:

(a) Type of secondary publication (i.e. systematic review, meta-analysis, network meta-analysis)

(b) Total number of trials applicable to the clinical question

1. For network meta-analysis only: state the number of trials which are direct comparison and indirect studies
    - **Example** Of the 32 trials included, there were 13 RCTs (n=7,333) applicable to the clinical question with 2 (n=1,322) of those including a direct comparison.

(c) Total number of subjects applicable to the clinical question

(d) Brief description of trial inclusion criteria (e.g. the meta-analysis included double-blinded randomized controlled trials)

(e) Describe trial quality, not just the methods used to assess trial quality

- **Example** The Cochrane Collaboration tool for assessing risk of bias was used; 7 of the 10 included trials were determined to be at a low risk for bias and the remaining 3 were at high risk for bias due to lack of masking.

(f) Outcomes:

1. For meta-analyses only:
    - Outcomes in straightforward statistics (e.g. absolute difference, OR, RR, or HR with 95% CI)
        i. See tips and hints for technical writing section for guidance
2. For systematic reviews only:
    - Provide an **original** summary of the information. Statistical significance, directionality, and magnitude of the results need to be reported.
        - **Example 1** for systematic review which includes **direct comparisons:** All three of the trials which compared the two medications found drug X to statistically significantly decrease non-HDL cholesterol (ranging from -38% to -15%) compared to drug Y.

- **Example 2** for systematic review of **indirect primary literature**: The two trials comparing drug A to placebo were both statistically significant with a decrease in events ranging from 5% to 12%. The three trials comparing drug B to placebo were also all statistically significant with a decrease in events ranging from 9% to 23%.

(g) A brief mention, but not discussion, of analysis or publication bias
(h) A brief mention, but not discussion, of any major weaknesses/limitations in the context of your clinical question. (Remember topics from Drug Literature Evaluation course.)
- A limitation of manufacturer funding will NOT be accepted as a limitation as this is similar to accusing the investigators of fraud/mismanagement. Unless there is a press-release or other similar resource that is also cited related to study mismanagement, this limitation should not be used for this assignment.

(2) Original research descriptions MUST include the following items:
(a) Trial design (i.e. double-blind RCT, prospective cohort, etc.)
(b) Brief description of inclusion criteria (e.g. adults with diabetes)
(c) Number of subjects
(d) Intervention (e.g. 40 mg oral simvastatin once daily or placebo)
(e) For Non-inferiority (NI) studies only
- Typically, only the primary outcome will have an NI margin
- If the outcome of interest for the CI has an NI margin, the prespecified NI margin (or lack thereof) should be reported

(f) Outcome (e.g. absolute difference, OR, RR, or HR with 95% CI)
- See tips and hints for technical writing section for guidance

(g) A brief mention, but not discussion, of any major weaknesses/limitations in the context of your clinical question. (Remember topics from Drug Literature Evaluation course.)
- A limitation of manufacturer funding will NOT be accepted as a limitation as this is similar to accusing the investigators of fraud/mismanagement. Unless there is a press-release or other similar resource that is also cited related to study mismanagement, this limitation should not be used for this assignment

(3) Pharmacoeconomic research descriptions MUST include the following items:
(a) Study design (i.e. pharmacoeconomic evaluation)
(b) Analysis and type of model used (i.e. incremental, ratio, and/or Markov model)
(c) Perspective analysis was calculated from (i.e. patient, health system, payer, societal)
(d) Data source(s) used for efficacy (i.e. clinical trial(s) and/or database(s)) and comment on their quality (i.e. randomized controlled trials and/or retrospective population data)
(e) Data source or assumptions used for cost (i.e. source of cost and how valued such as what dollars/monetary units, was it appropriately discounted if using different years, etc.)
(f) Number of repetitions in model
(g) Outcome (e.g. The incremental cost-effectiveness ratios for dabigatran compared to warfarin was $45,372 per QALY)
(h) A brief mention, but not discussion, of any major weaknesses/limitations.

Please note: if any of the above items are missing from the above list, please state that the item was not included in the manuscript

For clinical inquiries where cost or cost effectiveness is an outcome, but no pharmacoeconomic literature is available, please use average wholesale cost (AWC) from UpToDate/Lexicomp as the cost component. Only this database will be accepted. Remember to consider the cost of the regimen or course of therapy and not just the cost of a tablet (or other dosage form). In some cases, it may be best to present the cost of the regimen in a table.

Example Cost comparison of regimen A versus regimen B

Medication	Cost/tablet	Tablets/day	Days of therapy	Total regimen cost
Drug A	$12.21	1	10	$122.10
Drug B	$3.26	2	14	$91.28

(4) Case reports/series The types of information to report for a case study are similar to original research. **Items that MUST be included for case reports/series:**

(a) Number of subjects and inclusion criteria (e.g. “a 76 yo woman with XXX” or “eight adults aged 37 to 59 years with XXX”)
(b) Trial structure (i.e. case report or case series)
(c) Intervention (e.g. “application of 0.1% vitamin K cream twice daily to the face and upper body”)
(d) Outcome (e.g. “postpone the development of the rash by XX days and reduce rash severity by XX%”)
(e) A brief mention of any major weaknesses/limitations of the report in the context of your clinical question.

7. Recommendations from Others

Recommendations from others are practice guidelines and/or consensus statements from authoritative, professional organizations.

- Clinical questions referring to a subset population within a disease state may need to extrapolate from the general disease state guideline. For example, a clinical question referring to patients with atrial fibrillation who are obese will need to use the general atrial fibrillation guidelines.
- Guidelines/consensus statements created by a United States national expert body or the United States government are preferred.
- Specific institutional policies are not appropriate for recommendations from others.
- Articles included in guidelines and/or consensus statements can still be included in the evidence summary. That is NOT considered duplicate presentation of the literature.

1. Topics with pertinent guidelines/consensus statements *that include the drug(s)/topic in clinical inquiry*:
    a. Items that **MUST be included**:
        i. A brief mention of how the guideline/consensus statement(s) were developed: expert panel versus evidence driven
        ii. A brief outline of any guideline/statement grading system that may have been used.
            - Can consider giving just the highest and lowest ratings as anchors to describe.
            - MUST be in student's own words.
        iii. A statement of how the recommendations pertain to the clinical question
        Example 1 Both agents are included in the guideline but one is not preferred to the other.
        Example 2 The guideline recommends agent A rather than agent B.
        Example 3 While agent A is recommended in the guideline, agent B is not mentioned.

2. Topics with pertinent guidelines/consensus statements but which *DO NOT include the specific drug(s)/topic from the clinical inquiry:*
    a. Items that **MUST be included**:
        i. A brief mention of how the guideline/consensus statement(s) were developed: expert panel versus evidence driven
        ii. A statement that the guidelines do not address the drug in the clinical inquiry

3. Topics (disease states or populations) *without pertinent guidelines/consensus statements:*
    a. **MUST include this language**:
        i. "There is not a guideline/consensus statement pertinent to this disease state or population."

8. Search Strategy

This section of the clinical inquiry demonstrates a student's ability to perform an "ideal" literature search using the appropriate terms from your PICO.

- The demonstrated search must include:
    - An attempt to identify pertinent secondary literature
    - A separate attempt to identify the highest level of primary clinical literature
    - Two screen shots are required
        - Guidance on the screen shots is available
- Students may need to perform multiple searches
    - Including screen shots of searches other than the "ideal" search are not required
    - However, students may elect to describe key pertinent searches (e.g. individual intervention and control searches for an indirect clinical inquiry)
- Students may choose to briefly describe why some articles were omitted from the clinical inquiry, but this is not required.

Criteria for Clinical Inquiry Evaluation

***Problem Analysis* (75%).**

Appropriate Literature.

1 - References are trivial, e.g., class notes.

2 - Provides bench research citations when clinical research was available OR too few literature sources to draw conclusions OR citations do not allow for answering the actual question OR **missed 1 or more references that could change the EBA**.

3 - Missing 2 or more pieces of pertinent literature (including guideline/s) or included 2 or more pieces of inappropriate literature that wouldn't change the EBA OR uses narrative/general review article or background source such as UpToDate.

4 - Missing 1 piece of pertinent recent literature (including guideline/s) that wouldn't change the EBA OR included 1 piece of inappropriate literature.

5 - All literature sources are appropriate for the question. Systematic reviews/meta-analyses, clinical trials/primary literature (as available), and guidelines are referenced (as available).

Depth and Insight of Supporting Information (Evidence Summary).

0 - Information presented is incorrect, inappropriately paraphrased (e.g., patchwork, word-for-word, or artificial intelligence is used), or no references provided. Adapting an existing table or copying figures from any source.

1 - Information presented contains much incorrect information that affects the evidence-based answer. A large amount of extraneous and/or irrelevant material. Omission of much key information.

2 - Information presented only addresses some issues of the question. Some incorrect information that affects evidence-based answer. Much extraneous and irrelevant material is included. May omit some key information. Reflects poor understanding.

3 - Information presented superficially addresses issues of the question. Some incorrect information that does not affect evidence-based answer. Some extraneous or irrelevant material or insufficient details, especially related to report of data/outcomes.

4 - Information presented discusses all issues concerning the question. Minor incorrect information that does not affect evidence-based answer. May include minor extraneous or irrelevant material. Minor omission of details.

5 - Information presented discusses and expands upon all issues concerning the question involved. All information given is accurate, necessary, and relevant and reflects a comprehensive understanding.

Evidence-Based Answer.

0 - No Evidence-Based Answer, or the question was not specifically answered.

1 - Evidence-Based Answer not supported by Evidence Summary. (i.e. no connection between answer given and material presented in evidence summary)

2 - Limited Evidence-Based Answer; incorrect conclusions reached for the question based upon Evidence Summary.

3 - Limited Evidence-Based Answer; incomplete (or partially-answered) Evidence-Based Answer.

4 - Limited Evidence-Based Answer; conclusions reached for the question are correct based upon the evidence summary but adds extraneous information not necessary for answering the question or omits a minor detail which could change the interpretation of the Evidence-Based Answer.

5 - Complete Evidence-Based Answer; all conclusions reached for the question are correct based upon Evidence Summary.

Style of Presented Material (25%).

Question Derived from PICO Format.

0 - Question does not follow PICO format.

3 - Question attempts to follow PICO format but is not correctly stated.

5 - Question completely follows correct PICO format.

N/A - Question cannot be stated in PICO format because it is not a clinical question.

Citation or Logical Support of all Statements.

0 - No statements are supported by accurate citation of the literature using superscripts.

3 - Some statements are supported by accurate citation of the literature using superscripts

5 - All statements in the Evidence Summary are supported by accurate citation of the literature using superscripts.

Literature Citation Format.

0 - More than 4 types* of citation format errors exist.

1 - 4 types* of citation format errors exist.

2 - 3 types* of citation format errors exist.

3 - 2 types* of citation format errors exist.

4 - 1 type* of citation format errors exist.

5 - No citation format errors

Search Strategy Provided.

0 - No search strategy is provided.

3 - Only some search strategy is provided.

5 - Provides search terms & shows specific search strategies to find systematic reviews/meta-analyses + original/primary literature. (Includes PubMed Clinical Queries search showing *narrow* scope clinical studies & a search of systematic reviews.)

Answer Organized Logically, Expressed in a Clear, Concise Manner.

1 - Answer unorganized, skips around. Wordy discussion.

2 - Answer unorganized at times, skips around. Wordy discussion.

3 - Answer consistently organized, logically flows from statement to statement. Frequently wordy discussion.

4 - Answer organized, logically flows from statement to statement. Occasionally wordy discussion.

5 - Answer organized, logically flows from statement to statement. Concise discussion.

Appropriate Medical Terminology Used. **Instance = Same error appearing more than once*

0 - More than 4 instances* of inappropriate medical terminology and/or abbreviations used.

1 - 4 instances* of inappropriate medical terminology and/or abbreviations used.

2 - 3 instances* of inappropriate medical terminology and/or abbreviations used.

3 - 2 instances* of inappropriate medical terminology and/or abbreviations used.

4 - 1 instance* of inappropriate medical terminology and/or abbreviations used.

5 - Fully appropriate medical terminology and abbreviations used.

Grammar, Spelling, and Punctuation Correct (Including Required Document Formatting and stylistic requirements from the tips and hints for technical writing). ** Type = Same error appearing more than once*

0 - More than 4 types* of errors are present.

1 - 4 types* of errors are present.

2 - 3 types* of errors are present.

3 - 2 types* of errors are present.

4 - 1 type* of error is present.

5 - No errors are present.

Recommendations from Others

0 - No strength of recommendation provided

1 - One or more required items are missing or incomplete AND there are errors.

3 - One or more required items are missing or incomplete.

5 - All required items are included and accurate.

Strength of Recommendation

0 - No strength of recommendation provided.

2 - Strength of recommendation provided but no rationale provided.

3 - Strength of recommendation AND rationale is incorrect or incomplete.

4 - Strength of recommendation or rationale is incorrect or incomplete.

5 - Strength of recommendation AND rationale provided. (Rationale should include highest level of evidence upon which SOR was determined and whether outcome is patient- or disease-oriented.)

Example Clinical Inquiry

Student Name
Course number, block number

Clinical Question: How does the addition of a sodium glucose cotransporter 2 inhibitor to insulin therapy compare to insulin monotherapy regarding fasting plasma glucose reduction in adults with type 1 diabetes mellitus?

P: adults with type 1 diabetes mellitus
I: addition of sodium glucose cotransporter 2 (SGLT2) inhibitor to insulin therapy
C: insulin monotherapy
O: fasting plasma glucose reduction

Evidence-Based Answer:
The addition of an SGLT2 inhibitor to insulin therapy reduces fasting plasma glucose in adults with type 1 diabetes more than insulin monotherapy. (Strength of recommendation = C based on 2 well-done meta-analyses with consistent disease-oriented results)

Evidence Summary:
A 2021 meta-analysis of double-blind randomized controlled trials (RCTs) compared the absolute reduction in fasting plasma glucose (FPG) from baseline with use of SGLT2 inhibitors versus placebo among adults 18 years and older with type 1 diabetes not controlled on insulin alone.[1] Out of the 15 RCTs (7109 total subjects) included in the meta-analysis, 14 trials of 6630 subjects reported changes in FPG. The Cochrane Collaboration Tool was used to assess the quality of included trials. Included trials were determined to have a low risk of bias, though 2 trials did not have sufficient data to assess risk of bias. Use of SGLT2 inhibitors as an adjunct to insulin therapy showed a statistically significant decrease in FPG levels compared to insulin alone (absolute difference= -1.15 mmol/L, 95%CI -1.37 to -0.93 mmol/L, $p<0.0001$). Analysis of publication bias was not included by the authors. The heterogeneity of the trials was low ($I^2=0\%$). A limitation of this study is that the included trials may not have been adequately powered to assess the impact of SGLT2 inhibitor use on FPG, as the outcome of FPG reduction was not a primary outcome for any of the RCTs.

In a 2020 meta-analysis of 18 RCTs (7396 total subjects), Musso et al.[2] investigated the weighted mean difference in FPG from baseline in adults using SGLT2 inhibitors versus placebo or active comparator as an add-on to insulin therapy in type 1 diabetes. All 18 RCTs (7396 subjects) were included in FPG data analysis. Investigators used the Cochrane Collaboration Tool to evaluate the quality of included trials, and all except 2 trials were found to have a low risk of bias in all categories assessed. The weighted mean difference in FPG from baseline was -19.20 mg/dL for SGLT2 inhibitor adjunct therapy compared to placebo or active comparator adjunct therapy, which was statistically significant (95%CI -22.28 to -16.12 mg/dL, $p<0.001$). Publication bias was not assessed for the FPG outcome, though an Egger's test was completed for 14 other outcomes which found no statistically significant bias ($p>0.59$ for all assessments). The heterogeneity for the FPG data was low ($I^2=0\%$). A limitation of this study is that 1 included trial compared the efficacy of SGLT2 inhibitor versus placebo as an adjunct to patients on both insulin and liraglutide therapy. This limits generalizability of the results with respect to the specific patient population targeted in the clinical question on insulin monotherapy.

Recommendations from Others:
The American Diabetes Association published a clinical guideline for the treatment of diabetes mellitus with evidence-driven recommendations from a consensus panel in 2023.[3] Quality of evidence for

recommendations is evaluated using a scale ranging from A indicating high quality evidence (i.e. well-done meta-analyses or multicenter RCTs) to E indicating no evidence (i.e. expert opinion). The guideline recommends that individuals with type 1 diabetes be treated with both basal and prandial insulin (Grade A).[4] Evidence of SGLT2 inhibitor therapy improving glycemic outcomes in type 1 diabetes is mentioned; however, no recommendation is given for use of SGLT2 inhibitors in combination with insulin therapy.

An expert panel developed a consensus statement on the use of SGLT2 inhibitors in type 1 diabetes after the Advanced Technologies & Treatment for Diabetes Congress in 2019.[5] No rating system was used to grade recommendations, and the consensus statement mainly focuses on the management of diabetic ketoacidosis resulting from use of SGLT2 inhibitors in type 1 diabetes. The statement recommends insulin therapy as a foundational therapy for type 1 diabetes but endorses a glycemic control benefit for use of SGLT2 inhibitors as an adjunct to insulin in certain populations with type 1 diabetes. The panel recommends SGLT2 inhibitors may be appropriate in patients with blood ketone levels less than 0.6 mmol/L who are willing to perform ketone testing as needed.

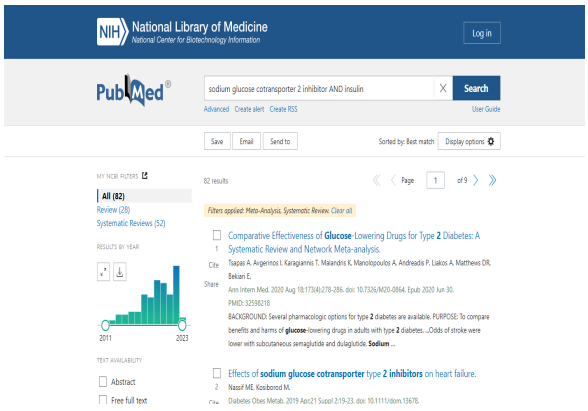
References:

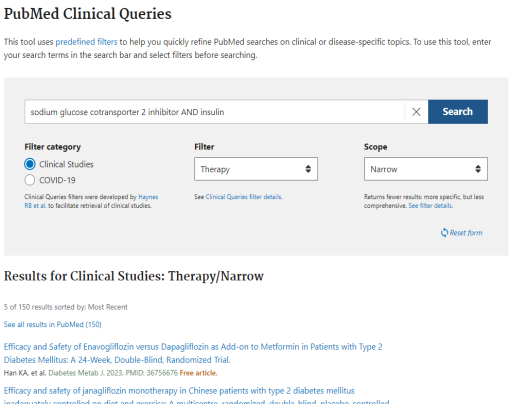
1. Rao L, Ren C, Luo S, Huang C, Li X. Sodium-glucose cotransporter 2 inhibitors as an add-on therapy to insulin for type 1 diabetes mellitus: meta-analysis of randomized controlled trials. *Acta Diabetol*. 2021;58(7):869-880. doi:10.1007/s00592-021-01686-x
2. Musso G, Sircana A, Saba F, Cassader M, Gambino R. Assessing the risk of ketoacidosis due to sodium-glucose cotransporter (SGLT)-2 inhibitors in patients with type 1 diabetes: a meta-analysis and meta-regression. *PLoS Med*. 2020;17(12):e1003461. doi:10.1371/journal.pmed.1003461
3. ElSayed NA, Aleppo G, Aroda VR, et al; American Diabetes Association. Introduction and methodology: standards of care in diabetes—2023. *Diabetes Care*. 2023;46(suppl 1):S1-S4. doi:10.2337/dc23-Sint
4. ElSayed NA, Aleppo G, Aroda VR, et al; American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: standards of care in diabetes—2023. *Diabetes Care*. 2023;46(suppl 1):S140-S157. doi:10.2337/dc23-S009
5. Danne T, Garg S, Peters AL, et al. International consensus on risk management of diabetic ketoacidosis in patients with type 1 diabetes treated with sodium-glucose cotransporter (SGLT) inhibitors. *Diabetes Care*. 2019;42(6):1147-1154. doi:10.2337/dc18-2316

Search Strategy:

Of note, multiple outdated systematic reviews and meta-analyses were excluded (Zou et al. 2021, Lu et al. 2019, Li et al. 2019, Musso et al. 2019, Yamada et al. 2018, Yang et al. 2017, and Chen et al. 2017).

PubMed:





How to Create an Evidence Summary Section in Table Format

1. May be used instead of multiple paragraphs in place of evidence summary section if many **primary/clinical studies** in order to present information concisely.
2. **PLEASE NOTE**: It is **NOT** appropriate to re-create a table that was presented in a systematic review or meta-analysis.
3. Note all of the following elements must be present in order to use this type of evidence summary format:
    a. Evidence summary section heading
    b. Introduction prior to table
    c. Table is labeled
    d. Table includes each element of the required descriptions of data for evidence summary section
    e. Abbreviation explanations immediately below table
    f. Limitations paragraph follows the abbreviations

Example:

Evidence Summary:

The information in the table below (**TABLE 1**) describes three trials which compare canagliflozin to placebo as add-on therapy to metformin for treatment of type 2 diabetes.

TABLE 1: Effect of Canagliflozin Compared to Placebo as Add-On Therapy to Lower A1C in Patients with Type 2 Diabetes

Reference	Design	Inclusion Criteria	Number of Participants	Intervention	Results
Rosenstock et al (2012)[1]	Multicentered, randomized, double- blind, placebo-controlled, dose range study with 7 parallel treatment groups, 12 weeks	-T2DM -metformin monotherapy	N=451 (placebo= 65, CANA 50mg = 64, CANA 100mg = 64, CANA 200mg = 65, CANA 300mg = 64, SITA 100mg = 65; twice daily CANA 300mg = 64)	CANA vs SITA or placebo as add-on therapy to metformin	Change in A1C from baseline to 12 weeks: -CANA 50mg, - 0.79% -CANA 100mg -0.76% -CANA 200mg, -0.70% -CANA 300mg, -0.92% -SITA, -0.74% -CANA 300mg twice daily, -0.95% -placebo, -0.22% (all $p < 0.001$ vs. placebo)
Fulcher et al (2013)[2]	Multicenter, randomized, double- blind, placebo-controlled, 18 weeks	-T2DM - sulfonylurea monotherapy	N=119 CANA 100mg= 42, CANA 300mg= 40, placebo= 45	CANA vs. placebo as add-on therapy to sulfonylureas	Change in A1C from baseline to 18 weeks: -CANA 100mg,-0.74% -CANA 300 mg, 0.83% compared to placebo, (all $p < 0.001$ vs. placebo)
Forst et al (2013)[3]	Randomized, double- blind, 52 weeks	-T2DM - metformin and PIO	N=342 (CANA 100mg= 113, CANA 300mg= 114, placebo= 115)	CANA vs placebo as add-on therapy to metformin plus PIO	Change in A1C from baseline to 52 weeks: CANA 100mg -0.98% (95% CI: -1.12, -0.85) CANA 300mg -1.07% (95% CI: -1.21, -0.93) Both compared to placebo

Abbreviations: T2DM= type 2 diabetes mellitus, CANA= canagliflozin, SITA= sitagliptan, PIO= pioglitazone, A1C= hemoglobin A1C, BMI= body mass index, SCr= serum creatinine, CI= confidence interval, vs= versus

Despite the data presented in the evidence summary table above, there are weaknesses associated with each trial. One inclusion criterion used by Rosenstock et al. was hemoglobin A1C of 7% to 10.5% at baseline, however actual A1C of study participants was 7.6% to 8% which suggests that study

participants were already better controlled than the inclusion criteria demonstrate, and this potentially limits the generalizability of the study results to patients with higher hemoglobin A1C values.[1] In addition, the trial period for comparison was 12 weeks which is sufficient to reflect initial changes in A1C but limits the long term generalizability of the study results.[1] Fulcher et al. had a small sample size creates a sampling bias that may not accurately represent the patient population that would benefit from the study drug.[2] In Forst et al., while baseline characteristics are balanced between study arms, the trial included significantly more males and Caucasian participants, which limits generalizability of study results to females and other races.[3]

Frequently Asked Questions

1. **HOW DO I FIND A JOURNAL ARTICLE IF IT IS NOT AVAILABLE ELECTRONICALLY IN EBLING'S COLLECTION?**
   1. Access PubMed from the Ebling website and search for the article of interest.
   2. Click on the "find it @UW" button in the upper right hand corner.
      - Often this will give several ways to access the article.
   3. If the article is not available online, click the "request a copy" link on the right side of the next screen and it will bring up the interlibrary loan request box.
      - Review the form information and submit.

      The article will be located in another library and emailed to the requestor. Ebling states items will be available within 1-9 days. In the course coordinators' experience, items are generally received within 1-2 days.

2. **WHAT IF THERE ARE NO DIRECT (HEAD TO HEAD) COMPARISONS?**
   Seek indirect comparisons: drug A vs drug C and drug B vs drug C. Drug C may either be another drug or placebo as long as the comparator and outcomes are the same.

3. **WHAT IF THERE ARE MULTIPLE SYSTEMATIC REVIEWS AND/OR META-ANALYSES AVAILABLE? DO I HAVE TO INCLUDE THEM ALL?**
   1. If more than one recent systematic review (with or without meta-analysis) is available, more than one should be included. Different investigators may use different methods and resources; therefore, results can differ even among recently completed similar systematic reviews. There is value in having more than one reference both if the results are consistent or conflicting.
      - It is expected that there will be overlap of the included trials within the systematic reviews included in a clinical inquiry.

   2. Not all systematic reviews (with or without meta-analysis) need to be included.
      - If there is an outdated systematic review and more recent literature exits, the outdated article may not need to be included.
      - Systematic reviews WITH meta-analysis may be prioritized over systematic reviews without meta-analysis.
      - If an article is omitted, please briefly state in the search strategy section why the manuscript was excluded.

4. **CAN CASE REPORTS BE USED?**
   If well-designed, adequately sized clinical trials or cohort studies are available, case reports are not needed. If no other evidence exists then case reports are acceptable.

5. **CAN ABSTRACTS FROM MEETINGS BE USED?**
   Abstracts from relevant professional meetings (e.g. American Diabetes Association meeting abstracts) may be used. See The AMA Manual of Style for formatting of citations for meeting abstracts in section 3.

6. **CAN ARTICLES IN A LANGUAGE OTHER THAN ENGLISH BE USED?**
   It depends:
   1. If the student is truly fluent in that language the article may be used.
   2. If an abstract is available in English, the abstract may be used with appropriate AMA citation format for only the abstract. See The AMA Manual of Style for formatting of citations for meeting abstracts in section 3.
   3. If the article and abstract are in a language other than English that the student is not fluent in, then it should not be included. However, it is recommended to state why it was not included in the search strategy.

7. **SHOULD I INCLUDE BACKGROUND MATERIAL?**
   No, do not include background material. Students should assume the requester of the clinical inquiry is familiar with the background.

8. **CAN STUDY SPECIFIC INFORMATION FROM A SYSTEMATIC REVIEW OR META-ANALYSIS BE INCLUDED IN AN EVIDENCE SUMMARY PARAGRAPH?**
   No, if individual study-specific information is relevant to the evidence based answer, the original article should be included in its own summary paragraph with appropriate citation. A secondary source should only be used for aggregate information.

9. **HOW SHOULD I SELECT SOURCES FOR RECOMMENDATIONS FROM OTHERS?**
   This section is meant for guidelines and consensus statements/papers from professional groups. The original source should be used rather than a summary of the guideline. For students on domestic rotations, U.S. guidelines are preferred. If there is no U.S. guideline or consensus statement for the topic/population of interest, then the most applicable international source may be used. Students on international rotations may use guidelines specific to that country. A maximum of 2 sources should be included for recommendations from others.

10. **CAN I INCLUDE EXACT DEFINITIONS OF STRENGTH OF RECOMMENDATIONS FROM GUIDELINES?**
    No, like the rest of the clinical inquiry assignment, descriptions of strength of recommendation and level of evidence should either be paraphrased or in quotations. See the example clinical inquiry and UW-Madison Writing Center website for suggestions on successful paraphrasing: https://writing.wisc.edu/Handbook/QuotingSources.html

    > **Example 1** The evidence-driven American Diabetes Association (ADA) clinical practice recommendations use a grading system to assign an evidence grade of A through E.[4] An A level is based on high-quality evidence such as meta-analysis and an E is based on expert consensus.
    > **Example 2** The level of evidence (LOE) was determined using a scale ranging from Level A (high-quality evidence from a meta-analysis or RCT) to Level C-EO (consensus of expert opinion).

11. **WHAT IF A CLINICAL INSTRUCTOR REQUIRES A DIFFERENT FORMAT?**
    Provide the clinical instructor with the format as they request, as that would be an appropriate requirement for that site. Do not submit the clinical instructor's preferred format document to the School. Use the document/assignment format as specified in the clinical inquiry manual for the version that is submitted.

Citing Sources using the (J)AMA Style

University of Wisconsin-Madison | 608.262.2020 | http://ebling.library.wisc.edu | askebling@library.wisc.edu

- This handout provides quick reference to using the *American Medical Association* style for citing common information sources. For more detailed information, please see the *AMA Manual of Style 11th Edition* available at https://www-amamanualofstyle-com.ezproxy.library.wisc.edu/view/10.1093/jama/9780190246556.001.0001/med-9780190246556
- Use NLM title abbreviations for journal names available at: https://www.ncbi.nlm.nih.gov/nlmcatalog/journals/

Books (NOT appropriate for clinical inquiry assignment)	
Single author	Sacks O. *Uncle Tungsten*. Alfred A Knopf; 2001.
2-6 authors	Goldberg L, Elliot DL. *Exercise for Prevention and Treatment of Illness*. FA Davis Co; 1994.
>6 authors	Simon LS, Lipman AG, Jacox AK, et al. *Pain in Osteoarthritis, Rheumatoid Arthritis, and Juvenile Chronic Arthritis*. 2nd ed. American Pain Society; 2002.
Edited book	Armitage JO, Antman KH, eds. *High Dose Cancer Therapy: Pharmacology, Hematopoietins, Stem Cells*. Williams & Wilkins; 1995:24-37.
Book chapter	Solensky R. Drug allergy: desensitization and treatment of reactions to antibiotics and aspirin. In: Lockey P, ed. *Allergens and Allergen Immunotherapy*. 3rd ed. Marcel Dekker; 2004:585-606.
Online book	Lunney JR, Foley KM, Smith TJ, Gelband H, eds. *Describing Death in America: What We Need to Know*. National Cancer Policy Board, Institute of Medicine; 2003. Accessed December 6, 2005.http://www.nap.edu/books/0309087252/html

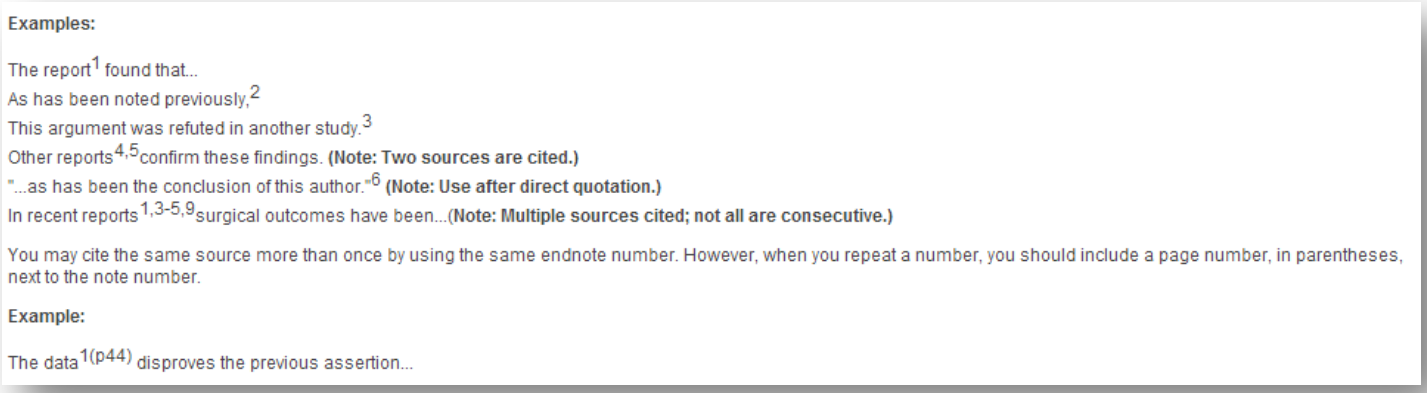
Journal Articles/Newspapers	
Single author	Rainier S. Myofibrillogenesis regulator 1 gene mutations cause paroxysmal dystonic choreoathetosis. *Arch Neurol*. 2004;61(7):1025-1029. doi:10.1001/archneur.61.7.1025
2-6 authors	Sofowora A, Ogunbodede E, Onayade A. The role and place of medicinal plants in the strategies for disease prevention. *Afr J Tradit Complement Altern Med*. 2013;10(5):210-229. doi:10.4314/ajtcam.v10i5.2
>6 authors	Siris ES, Miller PD, Barrett-Connor E, et al. Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the National Osteoporosis Risk Assessment. *JAMA*. 2001;286(22):2815-2822. doi:10.1001/jama.286.22.2815
Group author	Eye Diseases Prevalence Research Group. Prevalence of age-related macular degeneration in the United States. *Arch Ophthalmol*. 2004;122(4):564-572. doi:10.1001/archopht.122.4.564
From a supplement	Nasser R, Kosty JA, Shah, S, Wang J, Cheng J. Risk factors and prevention of surgical site infections following spinal procedures. *Global Spine J*. 2018;8(suppl 4):44s-48s. doi:10.1002/aorn.12710
Without volume or issue *(eg. Prepub)*	Tamburini S, Shen N, Chih Wu H, Clemente JC. The microbiome in early life: implications for health outcomes. *Nat Med*. Published online July 7, 2016. doi:10.1038/nm4142
Online Newspaper	Weiss R. The promise of precision prescriptions. *Washington Post*. June 24, 2000. Accessed April 29, 2020. https://www.washingtonpost.com/archive/politics/2000/06/24/the-promise-of-precision-prescriptions/013a8541-3ed3-4e81-91e6-a8cda958f124/

Online Databases (NOT appropriate for clinical inquiry assignment)	
Author(s). Title of the database. Publisher or database owner or host; year of publication and/or version number. Updated [date]. Accessed [date]. URL	
UpToDate *(suggested by publisher)*	Marion DW. Diaphragmatic pacing. Basow DS, ed. UpToDate. Waltham, MA:UpToDate Inc.URL (Accessed on April 29, 2020.)
ClinicalTrials.gov	Evaluation of phage therapy for the treatment of *Escherichia coli* and *Pseudomonas aeruginosa* wound infections in burned patients (PHAGOBURN). ClinicalTrials.gov identifier: NCT02116010. Updated July 23, 2015. Accessed October 13, 2016. https://www.clinicaltrials.gov/ct2/show/NCT02116010

Other Media	
Author(s), if given Title of the specific item cited (if none is given, use the name of the organization responsible for the site). Name of the website. [Date published]. Updated [date]. Accessed [date]. URL [provide URL and verify that the link still works as close as possible to publication]	
Websites	Charlton G. Internal linking for SEO: examples and best practices. SearchEngineWatch. Accessed February 10, 2016. https://searchenginewatch.com/sew/how-to/2428041/internal-linking-for-seo-examples-and-best-practices Zika travel information. Centers for Disease Control and Prevention. January 26, 2016. Updated August 11, 2016. Accessed June 18, 2019. https://wwwnc.cdc.gov/travel/page/zika-travel-information
Government Reports	World Health Organization. *Equitable access to essential medicines: a framework for collective action*. March 2004. Accessed December 6, 2005. http://whqlibdoc.who.int/hq/2004/WHO_EDM_2004.4.pdf

Citing Sources Within the Text

- Cited works are numbered in order of initial appearance in the text, and appear in the bibliography in numerical order.
- Use Arabic superscript numerals outside periods and commas, and inside colons and semicolons.
- Use commas to separate multiple citation numbers in text. Use hyphens for multiple consecutive citation numbers in text.
- Unpublished works and personal communications should be cited parenthetically (and not placed in the bibliography).
- When citing the same source more than once, give the number of the original reference, and then include the page number (in parentheses) where the information was found.



Examples:

The report[1] found that...
As has been noted previously,[2]
This argument was refuted in another study.[3]
Other reports[4,5] confirm these findings. **(Note: Two sources are cited.)**
"...as has been the conclusion of this author."[6] **(Note: Use after direct quotation.)**
In recent reports[1,3-5,9] surgical outcomes have been...**(Note: Multiple sources cited; not all are consecutive.)**

You may cite the same source more than once by using the same endnote number. However, when you repeat a number, you should include a page number, in parentheses, next to the note number.

Example:

The data[1(p44)] disproves the previous assertion...