How to Write an Evidence-Based Clinical Review Article

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Traditional clinical review articles, also known as updates, differ from systematic reviews and meta-analyses. Updates selectively review the medical literature while discussing a topic broadly. Non-quantitative systematic reviews comprehensively examine the medical literature, seeking to identify and synthesize all relevant information to formulate the best approach to diagnosis or treatment. Meta-analyses (quantitative systematic reviews) seek to answer a focused clinical question, using rigorous statistical analysis of pooled research studies. This article presents guidelines for writing an evidence-based clinical review article for *American Family Physician*. First, the topic should be of common interest and relevance to family practice. Include a table of the continuing medical education objectives of the review. State how the literature search was done and include several sources of evidence-based reviews, such as the Cochrane Collaboration, BMJ's *Clinical Evidence*, or the InfoRetriever Web site. Where possible, use evidence based on clinical outcomes relating to morbidity, mortality, or quality of life, and studies of primary care populations. In articles submitted to *American Family Physician*, rate the level of evidence for key recommendations according to the following scale: level A (randomized controlled trial [RCT], meta-analysis); level B (other evidence); level C (consensus/expert opinion). Finally, provide a table of key summary points. (Am Fam Physician 2002;65:251-8. Copyright© 2002 American Academy of Family Physicians.)

*A*merican Family Physician is particularly interested in receiving clinical review articles that follow an evidence-based format. Clinical review articles, also known as updates, differ from systematic reviews and meta-analyses in important ways.[1] Updates selectively review the medical literature while discussing a topic broadly. An example of such a topic is, "The diagnosis and treatment of myocardial ischemia." Systematic reviews comprehensively examine the medical literature, seeking to identify and synthesize all relevant information to formulate the best approach to diagnosis or treatment. Examples are many of the systematic reviews of the Cochrane Collaboration or BMJ's *Clinical Evidence* compendium. Meta-analyses are a special type of systematic review. They use quantitative methods to analyze the literature and seek to answer a focused clinical question, using rigorous statistical analysis of pooled research studies. An example is, "Do beta

blockers reduce mortality following myocardial infarction?"

The best clinical review articles base the discussion on existing systematic reviews and meta-analyses, and incorporate all relevant research findings about the management of a given disorder. Such evidence-based updates provide readers with powerful summaries and sound clinical guidance.

In this article, we present guidelines for writing an evidence-based clinical review article, especially one designed for continuing medical education (CME) and incorporating CME objectives into its format. This article may be read as a companion piece to a previous article and accompanying editorial about reading and evaluating clinical review articles.[1,2] Some articles may not be appropriate for an evidence-based format because of the nature of the topic, the slant of the article, a lack of sufficient supporting evidence, or other factors. We encourage authors to review the literature and, wherever possible, rate key points of evidence. This process will help emphasize the summary points of the article and strengthen its teaching value.

Topic Selection

Choose a common clinical problem and avoid topics that are rarities or unusual manifestations of disease or that have curiosity value only. Whenever possible, choose common problems for which there is new information about diagnosis or treatment. Emphasize new information that, if valid, should prompt a change in clinical practice, such as the recent evidence that spironolactone therapy improves survival in patients who have severe congestive heart failure.[3] Similarly, new evidence showing that a standard treatment is no longer helpful, but may be harmful, would also be important to report. For example, patching most traumatic corneal abrasions may actually cause more symptoms and delay healing compared with no patching.[4]

Searching the Literature

When searching the literature on your topic, please consult several sources of evidence-based reviews *(Table 1)*. Look for per-

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TABLE 1

Some Sources of Evidence-Based Medicine

Agency for Healthcare Research and Quality (AHRQ), formerly known as the Agency for Health Care Policy and Research (AHCPR): Clinical Guidelines and Evidence Reports*

http://www.ahrq.gov/clinic

The AHRQ Web site includes links to the National Guideline Clearinghouse, Evidence Reports from the AHRQ's 12 Evidence-based Practice Centers (EPC), and Preventive Services. The AHCPR released 19 Clinical Practice Guidelines between 1992 and 1996 that were not subsequently updated.

American College of Physicians Journal Club (ACPJC)

http://www.acponline.org/journals/acpjc/jcmenu.htm

ACP Journal Club evaluates evidence in individual articles. Commentary by ACP author offers clinical recommendations. Access to the online version of *ACPJC* is a benefit for members of the ACP-ASIM, but will be open to all until at least the end of 2001.

Bandolier*

http://www.jr2.ox.ac.uk/bandolier/

Features short evaluations/discussions of individual articles dealing with evidence-based clinical practice.

Centre for Evidence Based Medicine (CEBM)

http://cebm.jr2.ox.ac.uk/

The University of Oxford/Oxford Radcliffe Hospital Clinical School Web site includes links to CEBM within the Faculty of Medicine, a CATbank (Critically Appraised Topics), links to evidence-based journals, and EBM-related teaching materials.

Center for Research Support, TRIP Database

http://www.ceres.uwcm.ac.uk/frameset.cfm?section=trip

The AHRQ began the Translating Research into Practice (TRIP) initiative in 1990 to implement evidence-based tools and information. The TRIP Database features hyperlinks to the largest collection of EBM materials on the internet, including NGC, POEM, DARE, Cochrane Library, CATbank, and individual articles. A good starting place for an EBM literature search.

Clinical Evidence, **BMJ Publishing Group***

http:www.clinicalevidence.org

Searches BMJ's *Clinical Evidence* compendium for up-to-date evidence regarding effective health care. Lists available topics and describes the supporting body of evidence to date (e.g., number of relevant randomized controlled trials published to date). Concludes with interventions "likely to be beneficial" versus those with "unknown effectiveness." Individuals who have received a free copy of *Clinical Evidence* Issue 5 from the United Health Foundation are also entitled to free access to the full online content.

TABLE 1 *(Continued)*

Cochrane Database of Systematic Reviews*
  http://www.cochrane.org/
  Systematic evidence reviews that are updated periodically by the Cochrane Group. Reviewers discuss whether adequate data are available for the development of EBM guidelines for diagnosis or management.

Database of Abstracts of Reviews of Effectiveness (DARE)*
  http://agatha.york.ac.uk/darehp.htm
  Structured abstracts written by University of York CRD reviewers (see NHS CRD). Abstract summaries review articles on diagnostic or treatment interventions and discuss clinical implications.

Effective Health Care*
  http://www.york.ac.uk/inst/crd/ehcb.htm
  Bi-monthly, peer-reviewed bulletin for medical decision-makers. Based on systematic reviews and synthesis of research on the clinical effectiveness, cost-effectiveness and acceptability of health service interventions.

Evidence-Based Medicine*
  http://www.evidence-basedmedicine.com
  Bimonthly publication launched in 1995 by the BMJ Publishing Group. Article summaries include commentaries by clinical experts. Subscription is required.

Evidence-Based Practice* Newsletter (including *JFP* Patient-Oriented Evidence that Matters [POEM])
  http://www.ebponline.net
  This *JFP* newsletter features up-to-date POEM, Disease-Oriented Evidence (DOE), and tests approved for Category 1 CME credit. Subscription required.

InfoPOEMs
  http://www.infopoems.com
  Includes the InfoRetriever search system for the complete POEMs database and six additional evidence-based databases. Subscription is required.

Institute for Clinical Systems Improvement (ICSI)*
  http://www.ICSI.org
  ICSI is an independent, nonprofit collaboration of health care organizations, including the Mayo Clinic, Rochester, Minn. Web site includes the ICSI guidelines for preventive services and disease management.

National Guideline Clearinghouse (NGC)
  http://www.guidelines.gov/index.asp
  Comprehensive database of evidence-based clinical practice guidelines from government agencies and health care organizations. Describes and compares guideline statements with respect to objectives, methods, outcomes, evidence rating scheme, and major recommendations.

National Health Service (NHS) Centre for Reviews and Dissemination (CRD)
  http://www.york.ac.uk/inst/crd/
  Searches CRD Databases (includes DARE, NHS Economic Evaluation Database, Health Technology Assessment Database) for EBM reviews. More limited than TRIP Database.

Primary Care Clinical Practice Guidelines
  http://medicine.ucsf.edu/resources/guidelines
  University of California, San Francisco, Web site that includes links to NGC, CEBM, AHRQ, individual articles, and organizations.

U.S. Preventive Services Task Force (USPSTF)*
  http://www.ahrq.gov/clinic/uspstfix.htm
  This Web site features updated recommendations for clinical preventive services based on systematic evidence reviews by the U.S. Preventive Services Task Force.

EBM = evidence-based medicine.

*—These Web sites are AAFP-approved sources of systematic evidence reviews. When these sources are used to prepare continuing medical education clinical content according to guidelines issued by the AAFP Commission of Continuing Medical Education, the content will qualify for the special designation of evidence-based CME. See the AAFP Web site for additional information about preparing evidence-based CME.

tinent guidelines on the diagnosis, treatment, or prevention of the disorder being discussed. Incorporate all high-quality recommendations that are relevant to the topic. When reviewing the first draft, look for all key recommendations about diagnosis and, especially, treatment. Try to ensure that all recommendations are based on the highest level of evidence available. If you are not sure about the source or strength of the recommendation, return to the literature, seeking out the basis for the recommendation.

In particular, try to find the answer in an authoritative compendium of evidence-based reviews, or at least try to find a meta-analysis or well-designed randomized controlled trial (RCT) to support it. If none appears to be available, try to cite an authoritative consensus statement or clinical guideline, such as a National Institutes of Health Consensus Development Conference statement or a clinical guideline published by a major medical organization. If no strong evidence exists to support the conventional approach to managing a given clinical situa-

tion, point this out in the text, especially for key recommendations. Keep in mind that much of traditional medical practice has not yet undergone rigorous scientific study, and high-quality evidence may not exist to support conventional knowledge or practice.

Patient-Oriented vs. Disease-Oriented Evidence

With regard to types of evidence, Shaughnessy and Slawson[5-7] developed the concept of Patient-Oriented Evidence that Matters (POEM), in distinction to Disease-Oriented Evidence (DOE). POEM deals with outcomes of importance to patients, such as changes in morbidity, mortality, or quality of life. DOE deals with surrogate end points, such as changes in laboratory values or other measures of response. Although the results of DOE sometimes parallel the results of POEM, they do not always correspond *(Table 2).*[2] When possible, use POEM-type evidence rather than DOE. When DOE is the only guidance available, indicate that key clinical recommendations lack the support of outcomes

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TABLE 2

Comparison of DOE and POEM

Intervention	DOE	POEM	Comment
Antiarrhythmic therapy	Antiarrhythmic drug X decreases the incidence of PVCs on ECGs	Antiarrhythmic drug X is associated with an increase in mortality	POEM results are contrary to DOE implications
Antihypertensive therapy	Antihypertensive drug treatment lowers blood pressure	Antihypertensive drug treatment is associated with a decrease in mortality	POEM results are in concordance with DOE implications
Screening for prostate cancer	PSA screening detects prostate cancer at an early stage	Whether PSA screening reduces mortality from prostate cancer is currently unknown	Although DOE exists, the important POEM is currently unknown

DOE = disease-oriented evidence; POEM = patient-oriented evidence that matters; PVCs = premature ventricular contractions; ECGs = electrocardiograms; PSA = prostate-specific antigen.

Adapted with permission from Shaughnessy AF, Slawson DC. Getting the most from review articles: a guide for readers and writers. Am Fam Physician 1997;55:2155-60.

evidence. Here is an example of how the latter situation might appear in the text: "Although prostate-specific antigen (PSA) testing identifies prostate cancer at an early stage, it has not yet been proved that PSA screening improves patient survival." (Note: PSA testing is an example of DOE, a surrogate marker for the true outcomes of importance—improved survival, decreased morbidity, and improved quality of life.)

Evaluating the Literature

Evaluate the strength and validity of the literature that supports the discussion (see the following section, Levels of Evidence). Look for meta-analyses, high-quality, randomized clinical trials with important outcomes (POEM), or well-designed, nonrandomized clinical trials, clinical cohort studies, or case-controlled studies with consistent findings. In some cases, high-quality, historical, uncontrolled studies are appropriate (e.g., the evidence supporting the efficacy of Papanicolaou smear screening). Avoid anecdotal reports or repeating the hearsay of conventional wisdom, which may not stand up to the scrutiny of scientific study (e.g., prescribing prolonged bed rest for low back pain).

Look for studies that describe patient populations that are likely to be seen in primary care rather than subspecialty referral populations. Shaughnessy and Slawson's guide for writers of clinical review articles includes a section on information and validity traps to avoid.[2]

Levels of Evidence

Readers need to know the strength of the evidence supporting the key clinical recommendations on diagnosis and treatment. Many different rating systems of varying complexity and clinical relevance are described in the medical literature. Recently, the third U.S. Preventive Services Task Force (USPSTF) emphasized the importance of rating not only the study type (RCT, cohort study, case-control study, etc.), but also the study quality as

measured by internal validity and the quality of the entire body of evidence on a topic.[8]

While it is important to appreciate these evolving concepts, we find that a simplified grading system is more useful in *AFP*. We have adopted the following convention, using an ABC rating scale. Criteria for high-quality studies are discussed in several sources.[8,9] See the *AFP* Web site (www.aafp.org/afp/authors. html) for additional information about levels of evidence and see the accompanying editorial in this issue discussing the potential pitfalls and limitations of any rating system.

• Level A (randomized controlled trial/ meta-analysis): High-quality randomized controlled trial (RCT) that considers all important outcomes. High-quality meta-analysis (quantitative systematic review) using comprehensive search strategies.

• Level B (other evidence): A well-designed, nonrandomized clinical trial. A nonquantitative systematic review with appropriate search strategies and well-substantiated conclusions. Includes lower quality RCTs, clinical cohort studies, and case-controlled studies with non-biased selection of study participants and consistent findings. Other evidence, such as high-quality, historical, uncontrolled studies, or well-designed epidemiologic studies with compelling findings, is also included.

• Level C (consensus/expert opinion): Consensus viewpoint or expert opinion.

Each rating is applied to a single reference in the article, not to the entire body of evidence that exists on a topic. Each label should include the letter rating (A, B, C), followed by the specific type of study for that reference. For example, following a level B rating, include one of these descriptors: (1) nonrandomized clinical trial; (2) nonquantitative systematic review; (3) lower quality RCT; (4) clinical cohort study; (5) case-controlled study; (6) historical uncontrolled study; (7) epidemiologic study.

Here are some examples of the way evidence ratings should appear in the text:

• "To improve morbidity and mortality, most patients in congestive heart failure should

be treated with an angiotensin-converting enzyme inhibitor. [Evidence level A, RCT]"

• "The USPSTF recommends that clinicians routinely screen asymptomatic pregnant women 25 years and younger for chlamydial infection. [Evidence level B, nonrandomized clinical trial]"

• "The American Diabetes Association recommends screening for diabetes every three years in all patients at high risk of the disease, including all adults 45 years and older. [Evidence level C, expert opinion]"

When scientifically strong evidence does not exist to support a given clinical recommendation, you can point this out in the following way:

• "Physical therapy is traditionally prescribed for the treatment of adhesive capsulitis (frozen shoulder), although there are no randomized outcomes studies of this approach."

Format of the Review

INTRODUCTION

The introduction should define the topic and purpose of the review and describe its relevance to family practice. The traditional way of doing this is to discuss the epidemiology of the condition, stating how many people have it at one point in time (prevalence) or what percentage of the population is expected to develop it over a given period of time (incidence). A more engaging way of doing this is to indicate how often a typical family physician is likely to encounter this problem during a week, month, year, or career. Emphasize the key CME objectives of the review and summarize them in a separate table entitled "CME Objectives."

METHODS

The methods section should briefly indicate how the literature search was conducted and what major sources of evidence were used. Ideally, indicate what predetermined criteria were used to include or exclude studies (e.g., studies had to be independently rated as being high quality by an established evaluation process, such as the Cochrane Collaboration). Be comprehensive in trying to identify all major relevant research. Critically evaluate the quality of research reviewed. Avoid selective referencing of only information that supports your conclusions. If there is controversy on a topic, address the full scope of the controversy.

DISCUSSION

The discussion can then follow the typical format of a clinical review article. It should touch on one or more of the following subtopics: etiology, pathophysiology, clinical presentation (signs and symptoms), diagnostic evaluation (history, physical examination, laboratory evaluation, and diagnostic imaging), differential diagnosis, treatment (goals, medical/surgical therapy, laboratory testing, patient education, and follow-up), prognosis, prevention, and future directions.

The review will be comprehensive and balanced if it acknowledges controversies, unresolved questions, recent developments, other viewpoints, and any apparent conflicts of interest or instances of bias that might affect the strength of the evidence presented.

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Emphasize an evidence-supported approach or, where little evidence exists, a consensus viewpoint. In the absence of a consensus viewpoint, you may describe generally accepted practices or discuss one or more reasoned approaches, but acknowledge that solid support for these recommendations is lacking.

In some cases, cost-effectiveness analyses may be important in deciding how to implement health care services, especially preventive services.[10] When relevant, mention high-quality cost-effectiveness analyses to help clarify the costs and health benefits associated with alternative interventions to achieve a given health outcome. Highlight key points about diagnosis and treatment in the discussion and include a summary table of the key take-home points. These points are not necessarily the same as the key recommendations, whose level of evidence is rated, although some of them will be.

Use tables, figures, and illustrations to highlight key points, and present a step-wise, algorithmic approach to diagnosis or treatment when possible.

Rate the evidence for key statements, especially treatment recommendations. We expect that most articles will have at most two to four key statements; some will have none. Rate only those statements that have corresponding references and base the rating on the quality and level of evidence presented in the supporting citations. Use primary sources (original research, RCTs, meta-analyses, and systematic reviews) as the basis for determining the level of evidence. In other words, the supporting citation should be a primary research source of the information, not a secondary source (such as a nonsystematic review article or a textbook) that simply cites the original source. Systematic reviews that analyze multiple RCTs are good sources for determining ratings of evidence.

REFERENCES

The references should include the most current and important sources of support for key statements (i.e., studies referred to, new information, controversial material, specific quantitative data, and information that would not usually be found in most general reference textbooks). Generally, these references will be key evidence-based recommendations, meta-analyses, or landmark articles. Although some journals publish exhaustive lists of reference citations, *AFP* prefers to include a succinct list of key references. (We will make more extensive reference lists available on our Web site or provide links to your personal reference list.)

You may use the following checklist to ensure the completeness of your evidence-based review article; use the source list of reviews to identify important sources of evidence-based medicine materials.

Checklist for an Evidence-Based Clinical Review Article

• The topic is common in family practice, especially topics in which there is new, important information about diagnosis or treatment.

• The introduction defines the topic and the purpose of the review, and describes its relevance to family practice.

• A table of CME objectives for the review is included.

• The review states how you did your literature search and indicates what sources you checked to ensure a comprehensive assessment of relevant studies (e.g., MEDLINE, the Cochrane Collaboration Database, the Center for Research Support, TRIP Database).

• Several sources of evidence-based reviews on the topic are evaluated *(Table 1)*.

• Where possible, POEM (dealing with changes in morbidity, mortality, or quality of life) rather than DOE (dealing with mechanistic explanations or surrogate end points, such as changes in laboratory tests) is used to support key clinical recommendations *(Table 2)*.

• Studies of patients likely to be representative of those in primary care practices, rather than subspecialty referral centers, are emphasized.

TABLE 3

Essential Steps in Writing an Evidence-Based Clinical Review Article

Choose a common, important topic in family practice.

Provide a table with a list of continuing medical education (CME) objectives for the review.

State how the literature search and reference selection were done.

Use several sources of evidence-based reviews on the topic.

Rate the level of evidence for key recommendations in the text.

Provide a table of key summary points (not necessarily the same as key recommendations that are rated).

• Studies that are not only statistically significant but also clinically significant are emphasized; e.g., interventions with meaningful changes in absolute risk reduction and low numbers needed to treat. (See http://cebm.jr2.ox.ac.uk/docs/glossary.html.)[11]

• The level of evidence for key clinical recommendations is labeled using the following rating scale: level A (RCT/meta-analysis), level B (other evidence), and level C (consensus/expert opinion).

• Acknowledge controversies, recent developments, other viewpoints, and any apparent conflicts of interest or instances of bias that might affect the strength of the evidence presented.

• Highlight key points about diagnosis and treatment in the discussion and include a summary table of key take-home points.

• Use tables, figures, and illustrations to highlight key points and present a step-wise, algorithmic approach to diagnosis or treatment when possible.

• Emphasize evidence-based guidelines and primary research studies, rather than other review articles, unless they are systematic reviews.

The essential elements of this checklist are summarized in *Table 3*.

REFERENCES

1. Siwek J. Reading and evaluating clinical review articles. Am Fam Physician 1997;55:2064,2069-70,2072.
2. Shaughnessy AF, Slawson DC. Getting the most from review articles: a guide for readers and writers. Am Fam Physician 1997;55:2155-60.
3. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al., for the Randomized Aldactone Evaluation Study Investigators. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. N Engl J Med 1999;341:709-17.
4. Flynn CA, D'Amico F, Smith G. Should we patch corneal abrasions? A meta-analysis. J Fam Pract 1998;47:264-70.
5. Slawson DC, Shaughnessy AF, Bennett JH. Becoming a medical information master: feeling good about not knowing everything. J Fam Pract 1994;38:505-13.
6. Shaughnessy AF, Slawson DC, Bennett JH. Becoming an information master: a guidebook to the medical information jungle. J Fam Pract 1994;39:489-99.
7. Slawson DC, Shaughnessy AF. Becoming an information master: using POEMs to change practice with confidence. Patient-oriented evidence that matters. J Fam Pract 2000;49:63-7.
8. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al., Methods Work Group, Third U.S. Preventive Services Task Force. Current methods of the U.S. Preventive Services Task Force. A review of the process. Am J Prev Med 2001;20(3 suppl):21-35.
9. CATbank topics: levels of evidence and grades of recommendations. Retrieved November 2001, from: http://cebm.jr2.ox.ac.uk/docs/levels.html.
10. Saha S, Hoerger TJ, Pignone MP, Teutsch SM, Helfand M, Mandelblatt JS, for the Cost Work Group of the Third U.S. Preventive Services Task Force. The art and science of incorporating cost effectiveness into evidence-based recommendations for clinical preventive services. Am J Prev Med 2001;20(3 suppl):36-43.
11. Evidence-based medicine glossary. Retrieved November 2001, from: http://cebm.jr2.ox.ac.uk/docs/glossary.html.