



## ***Standard methods for preparation of evidence reports*** ***January 2022***

The University of Pennsylvania Health System (UPHS) Center for Evidence-based Practice (CEP) was established by the Chief Medical Officer in 2006 to promote the integration of evidence into practice and to provide decision support for administrators and clinicians (including physicians, nurses, and other health professionals) developing policy and practice for Penn Medicine. More information about the center can be found in references 3, 5, and 6.

CEP is committed to pragmatically following best practices in gathering and analyzing evidence. This document is intended to provide an overview of CEP products and methods in the interest of transparency. It is updated semiannually; previous versions are available on request.

### **CEP evidence products**

CEP offers a variety of evidence products to meet the varying needs of its stakeholders. Products are differentiated by the depth of searching and analysis. Evidence Reviews and Evidence Advisories make up a majority of CEP reports. CEP offers services for integrating evidence-based findings to into clinical practice (Penn Pathways); methods are presented in a separate document.

Evidence Review: A rapid systematic review of clinical evidence on a focused topic, carried out using streamlined methods to find and summarize the best available evidence. These reports include evidence tables, quality assessment of the evidence, meta-analysis where the quantity of combinable studies is sufficient, and GRADE analysis for reviews where patient-centered clinical outcomes are available.

Evidence Advisory: A report using systematic methods to review and analyze a limited range of information sources: usually secondary sources such as existing clinical practice guidelines or systematic reviews. Evidence tables are included, but *de novo* analysis of study results is beyond the scope of this type of report.

Evidence Inventory: A systematic search of the literature and tabulation of identified studies that describes available evidence on a topic, typically stratified by study design, population, or intervention (see reference 2). Articles are not critically appraised, so there are no conclusions about the results of clinical studies or the quality of the evidence. One of the primary goals of an Evidence Inventory is to help stakeholders determine whether a full Evidence Review on a topic would be likely to find sufficient data to support a decision.

Rapid Product Summary: A limited search for published health technology assessment reports on a drug, device, diagnostic, or procedure; and summary of the findings of those reports. Searches are limited to product name and other keywords and do not include general databases like Medline or Embase. This product was designed to meet the needs of hospital and systemwide committees that make decisions on acquisition of drugs, devices, and other technologies. A streamlined topic selection process is in place for participating committees so they can receive reports within one month of their request.

**Rapid Guidance Summary:** A limited search for published guidelines, systematic reviews, and medical center policies on a specific intervention. Primary databases such as MEDLINE and Embase may not be searched. This product has been designed to provide an ultra-rapid synopsis of current practices in prevention and treatment during the COVID-19 pandemic. It is a product in development and has not yet been used for other topics. Please see the separate [methods document](#) for full details of Rapid Guidance Summary methods.

**Annotated Bibliography:** A systematic but limited search of the literature and reference list of selected articles addressing a specific question. Articles are not critically appraised but they may be categorized by study design, patient population, or other characteristics that will help the reader find articles that are most relevant to his or her clinical question. The Annotated Bibliography usually is designed to give an overview of a topic, while the Evidence Inventory is focused on available clinical studies.

## **Acquisition and triage of topics**

CEP receives inquiries from Penn Medicine stakeholders including physicians and nurses, clinical department leaders, health system administrators, committees charged with purchasing and formulary decisions, and other health professionals. These inquiries are often made directly to the Director, but may also be made through Center analysts and liaisons, or through a form found on the CEP website. Reports may also be commissioned by outside partners such as The Children’s Hospital of Philadelphia. CEP faculty and staff communicate with requestors to clarify the specific issue or question to be addressed, the anticipated use of the evidence report, and desired time frame for the review, and then the inquiry is introduced at a weekly CEP meeting so CEP clinical and research staff can share their knowledge and suggestions.

Preliminary searches may be done to understand the feasibility and scope of a proposed review topic, and the Center Director (or the analyst) will communicate the results to the requestor to help the requestor refine the proposal. In some cases, a client inquiry can be satisfactorily addressed with information that is already available, such as an evidence-based guideline, a recent high-quality systematic review or a technology report from a reputable partner organization such as the ECRI Institute.

Once the preliminary scope of the investigation is decided, the Center Director formally adds the topic to the CEP work queue, assigns it to a lead analyst, and designates a project director/clinical director to oversee the project.

## **Report authorship**

The key personnel involved in the research and writing of CEP reports are the Lead Analyst and the Project Director. The Project Director is usually a member of CEP leadership or one of the physician liaisons. The Project Director is responsible for ensuring the quality and clinical validity of the report, and ensuring that the scope of the report addresses the question at hand. The Lead Analyst drafts the protocol, designs and carries out searches, selects references for inclusion, abstracts and analyzes data, and writes the bulk of the report. The Lead Analyst also manages internal review of reports under the supervision of the Project Director, who is responsible for ensuring that reviewer comments are satisfactorily addressed. At times, project staff may include a liaison librarian, a statistician, a pharmacoeconomist, and/or other CEP affiliates.

Authorship of reports and of manuscripts derived from reports will normally include the Lead Analyst as first author and the Project Director as last or senior author. Project requestors and other persons with significant participation in the development of the protocol and review of the draft report are recognized as co-authors. Additional persons who participate only in clinical and technical review of the draft report are acknowledged in the report for their contributions, but are not named as co-authors.

## **CEP Practicum**

CEP offers a practicum program where Penn Medicine clinical professionals and students learn to search for and review evidence under the tutelage of a full-time CEP Research Analyst. Student-produced evidence reports may be included in the regular CEP catalogue if they are prepared following the standard methods in this document. The student may be given Lead Analyst authorship; while the CEP staff member will be credited either as Lead Analyst or Practicum Preceptor.

## **Protocol development**

Once the topic is assigned, the lead analyst develops a draft review protocol that specifies the question to be answered. The protocol follows the PICOTS (population, intervention, comparison, outcomes, timing, setting) structure. The protocol specifies information sources to be searched, planned methods for evaluating the quality and quantity of evidence and methods for quantitative synthesis of study results where possible. Preliminary searches may be performed to approximate the amount and type of evidence that is available; this information helps the analyst and Project Director decide what type of report will be produced (Evidence Review/Evidence Advisory/Evidence Inventory).

The draft protocol is submitted to the Project Director for review and approval. Once preliminary approval is secured, the protocol is shared with the requestor for review and approval. Other clinical stakeholders may be included as reviewers at this stage.

## **Protocol adjustment**

In the interest of expediting reviews and ensuring they are responsive to client requests, the scope of reviews may need to be changed after approval of the review protocol. The need for such *post-hoc* revisions can be reduced with careful design of the initial scope, particularly by defining populations and study types to be prioritized, and pathways for broadening the review in the event that the evidence base is too small or weak to support any conclusions. Protocol changes made after initial approval that narrow the scope of the review should be disclosed in the final report.

## **Local information**

CEP Evidence Reviews and Evidence Advisories may start with a brief summary of existing Penn Medicine policies and/or guidelines that are relevant to the report topic. A summary of previous CEP reports on related topics is also included. The policy section allows Penn Medicine decision-makers to see whether current policy is in agreement with published guidelines and clinical evidence. Searches for Penn Medicine policies should include all affiliated hospitals including the Hospital of the University of Pennsylvania, Penn Presbyterian

Medical Center, Pennsylvania Hospital, Chester County Hospital, Lancaster General Hospital, and Penn Medicine Princeton Health, and also policies of Penn Medicine Medical Group (out-patient care) and Penn Home Care and Hospice Services where appropriate.

Sometimes UPHS financial and/or clinical information may be included in a report, so findings of the evidence review can be placed into local context. (See reference 4 for examples.) If a report contains confidential or sensitive information, that information may be redacted from copies of the report made available to outside requestors, or the report may not be made available to outside requestors.

## **Literature searching: General**

Designing and conducting effective searches for evidence is a challenging task, which cannot be fully documented in this general methods summary. Literature searches for CEP reviews also must be tailored to the specific needs of the requestor, the timeframe in which the review needs to be completed, the nature of available evidence, and the quality of its indexing in the major bibliographic databases. Therefore, the following guidance is presented as a starting point and not as a strict protocol. Methods will necessarily differ, to a greater or lesser degree, in many CEP reports. When development of a search strategy is specifically challenging or additional sources of information are needed, the University of Pennsylvania Biomedical Library liaisons, who are part of the CEP team, are consulted.

For most report topics, searches will begin with a search for existing literature syntheses (guidelines and systematic reviews) and then be followed by a search for primary studies (randomized controlled trials, observational studies, etc.). Literature searches for Evidence Reviews, Evidence Advisories and Evidence Inventories will be systematic and comprehensive and designed to capture as many relevant studies as possible.

Literature searches for Annotated Bibliographies will be systematic, but not necessarily comprehensive, as the goal of this type of report is to present a selection of articles that address a particular issue for Penn Medicine stakeholders. These studies are informative and may provide important perspectives, but their validity and reliability are not evaluated or confirmed by the CEP analyst. Literature searches must include a minimum of two database sources, one of which should be MEDLINE or PubMed. The other large databases most commonly searched are Embase and CINAHL.

Literature searches for Rapid Product Summary reports are limited to a select list of sources of health technology assessment reports, such as the ECRI Institute, the Canadian Agency for Drugs and Technologies in Health, and the Health Technology Assessment subfile of NICE Evidence Search.

## **Literature searching: Guidelines**

A search for guidelines should include multiple sources. At minimum, a full search for guidelines will include MEDLINE, the ECRI Guidelines Trust, and NICE Evidence Search (Guidance subfile). Web sites of important US clinical specialty societies should also be searched. Professional societies in Canada, Europe, Australia, and Japan as well as global societies are often checked for guidelines, but this is not essential if American guidelines are available. If the topic is related to nursing, the Registered Nurses' Association of Ontario should

be searched. Searches for guidelines may be incorporated into the main searches of bibliographic databases such as MEDLINE, Embase and CINAHL when appropriate.

### **Literature searching: Reviews and health technology assessment reports**

Searches for systematic reviews are carried out in, at minimum, the Cochrane Library (which includes the Cochrane Database of Systematic Reviews (Cochrane), NICE Evidence Search (systematic review subfiles), INAHTA Health Technology Assessment Database, and MEDLINE. Reports from the ECRI Institute and the Canadian Agency for Drugs and Technologies in Health (CADTH) should be searched when the topic involves a drug, device, diagnostic test, or procedure. If the topic is related to nursing, CINAHL and the Joanna Briggs Institute database should also be searched. The Lead Analyst and Project Director will decide whether a search for reviews in other bibliographic databases should be conducted. Searches for reviews in MEDLINE and other bibliographic databases may be incorporated into the main searches of these databases when appropriate.

Searches will sometimes find proprietary reports made available only to the issuer's paying clients. These reports are normally excluded from our analyses.

### **Literature searching: Primary studies**

At minimum, searches for primary literature should encompass both the MEDLINE (Ovid interface preferred) and either the Embase or CINAHL databases. Embase includes numerous non-MEDLINE journals, particularly from Europe and other non-US sources. Embase also has greater coverage of conference proceedings. For CEP report topics related to nursing or the allied health sciences, CINAHL should be searched; for topics relating to mental health or psychology, PsycINFO should be searched. In addition, the Cochrane Central Register of Controlled Trials (CENTRAL: Wiley interface is preferred) should also be searched if comparative studies are expected to be found. When the scope of the report is to include economic factors, the economic evaluations subfile of NICE Evidence Search should also be searched. Specialty databases such as the NICE Evidence Libraries on transfusion and stem cell transplantation should be searched when relevant to the topic at hand.

### **Search development**

After drafting a tentative search strategy, the person tasked with developing the literature search should submit the draft strategy to the project director for comment and approval. The search strategy is not normally submitted to the requestor for approval.

Ovid MEDLINE searches should include both the main MEDLINE file (1946-present) and e-publication ahead of print, in-process, and other non-indexed references. Searchers should be aware that searches that rely on index terms (i.e. one or more dimensions of the search is based entirely on index terms without an OR statement joining to a keyword search) will miss references from the latter groups.

MEDLINE searches should include both index terms and keywords for relevant concepts, unless a preliminary search determines that index terms are lacking or unreliable, or the keyword components pick up all articles under the relevant index terms. It is our experience that searches based only on index terms have inadequate sensitivity because NLM bibliographers may not

capture all of the most relevant concepts when indexing articles. Ovid qualifiers .mp (multi-purpose) or .ti,ab,kw (title, abstract, keyword) are both acceptable in keyword searching.

Embase search strategies should be developed with specific reference to the Emtree indexing structure, as it differs in some important aspects from the MeSH indexing used in MEDLINE and PubMed. Embase indexing is more reliable, but inclusion of keywords for free-text searching in Embase searches is still suggested.

When adapting MEDLINE or Embase search strategies for use in CENTRAL, search elements relating to study design should be left out, as the CENTRAL database is pre-screened for controlled studies. This can allow for a broader search on other axes such as population or intervention.

CEP uses a variety of standard filters for identifying specific types of literature such as guidelines, randomized trials, and clinical pathways. They are based on filters published by the Cochrane Collaboration, CADTH, Health Technology Assessment International, and other experts in information retrieval. These filters are documented in a separate [Methods Appendix](#).

CEP does not have a minimum or maximum number of database hits to screen.

## **Date restrictions**

Literature searches may be restricted to specified periods of time so that evidence considered in the review does not reflect obsolete versions of a technology or outdated practices of care, or if a previous CEP report is being updated. Date restrictions may also be necessary if the search returns an excessive number of hits and there are no other reasonable approaches to narrow it. Such restrictions should be documented *a priori* in the review protocol.

## **Language restrictions**

CEP reviews are typically limited to articles published in the English language. Multiple studies suggest that the reliability of systematic review conclusions is often not adversely affected by limiting searches to English-language literature (see reference 1).

In order to broaden the evidence base, the analyst may include non-English literature at his or her discretion, so long as he or she is able to sufficiently translate the article (with or without automated translation software) so as to understand the population, methods, and results, and adequately assess threats to the validity of the results and conclusions. If so, the languages of articles that will be included or excluded should be documented in the report.

## **Full versus abstract publications**

CEP data analyses and evidence tables exclude evidence from studies published only in abstract form, even if their abstracts are published in a peer-reviewed journal. Abstracts rarely provide sufficient information about study methods and outcomes to allow us to adequately assess the reliability of the results.

However, if the evidence from studies published in full form is weak or insufficient, results from studies published in abstract form may be reported in the text of the review for purposes of corroborating findings from the published studies. In this case, the weakness of evidence from abstract-only publications should be called to the reader's attention. Abstract publications may

also be included in Evidence Inventories and Annotated Bibliographies, which are focused mostly on identifying the amount and nature of available evidence.

## **Preprints and non-peer-reviewed manuscripts**

If there is an absence of evidence from published primary studies, and the need for information is urgent enough that the benefits of considering emerging and non-peer-reviewed studies outweigh the risks, searches may include the medRxiv database of manuscripts and preprints. Instances where data from these sources are cited in a report should be called out as such and the lack of peer-review should be noted.

## **Study size**

By default, the minimum sample size for comparative studies to be included in a CEP review is 10 patients per group. Smaller studies are at increased risk of having non-representative samples of patients. The study size threshold may be increased if the evidence base is particularly large, or reduced if the evidence base is very small. This is managed as a protocol revision.

## **Study design (primary studies)**

The study designs eligible for inclusion in CEP reports depend on the type of CEP report (Annotated Bibliography, Evidence Inventory, Evidence Advisory, or Evidence Review) as well as the topic/question of the report. For reports that aim to summarize the literature on efficacy or effectiveness, the randomized controlled trial (RCT) design will be prioritized. Non-randomized controlled trials with comparison groups will be sought as a second-line priority and analyzed if there is not sufficient RCT data to answer the research question. Hedges are often used to filter searches by study design (see reference 8 and the [CEP Methods Appendix](#)).

## **Study design (reviews)**

Inclusion of review articles may be limited to systematic reviews (review articles that document a systematic process for identifying and/or quantitatively analyzing primary studies), and further limited to systematic reviews that include quantitative data synthesis. These restrictions may be added to the protocol after searches are completed, if a large number of reviews are found or if there is a substantial difference in quality among reviews.

## **Setting**

Because CEP reports are primarily used by physicians, nurses, and other staff of Penn Medicine entities, study inclusion criteria may include a limit to hospital inpatient units or other specific care settings. For some topics, evidence applicable to health systems in low- and moderate-income countries may not be applicable to care in the United States. For those topics, location may be an additional inclusion/exclusion criterion. Member countries of the Organization for Economic Cooperation and Development (OECD) may be used as a working definition of countries with advanced health care systems.

## **Reference database and search documentation**

CEP presently uses RefWorks software to manage references and prepare bibliographies for each report. The full results of each primary literature search (a listing of all hits in the final search)

should be retained in one form or another: either as a downloaded reference list (RIS format) or in the bibliographic database (RefWorks).

Final search strategies and a count of hits from each database are included in each report, along with counts of how many articles were marked for retrieval and how many articles were ultimately included in the evidence tables. A full PRISMA diagram describing the disposition of references is not included in CEP reports, in the interest of expediting completion.

### **Duplicate detection**

RefWorks has a duplicate detection function with good sensitivity and specificity, but all marked duplicates are verified by the analyst before deletion. Records of deleted duplicates are retained either in the database or on paper.

### **Title/abstract screening**

Title/abstract screening is done by a single analyst rather than by two independent analysts, in order to expedite review. Records of which references were excluded at this stage are maintained, but providing the specific reason for each exclusion is not necessary.

### **Full-text retrieval**

It is expected that with available online resources and interlibrary loan, all articles marked for retrieval will be retrieved and screened. If any articles are unable to be retrieved, this should be documented in the report. Copies of all full-text articles (in electronic or paper form) are maintained with project files.

### **Full-text screening**

Full-text screening is also done by a single analyst rather than by two independent analysts, in order to expedite review. Reasons for each exclusion at this stage should be recorded on paper or in the database, but do not need to be included in the report.

### **Data abstraction**

Data abstraction is done by a single analyst rather than by two independent analysts, in order to expedite review. Data may be abstracted directly into the evidence tables, into a spreadsheet or computer database, or on paper. In all cases, the abstraction forms should be maintained with project files.

### **Preferred methods for meta-analysis**

Most CEP meta-analyses involve datasets from clinical trials comparing the results of two groups in terms of whether or not patients had a specific clinical outcome or adverse event. Our standard tool for meta-analyzing this data is RevMan version 5.4.1 (Cochrane Collaboration), though other validated tools including Comprehensive Meta Analysis and Open Meta-Analyst are also acceptable. Selection is at the analyst's discretion, considering the differences in analysis and graphing capabilities and ease of use of those different tools.

Binary data should be analyzed using a random-effects model. Results should be reported in full, including summary effect size and 95% confidence interval, and heterogeneity as measured

with the  $I^2$  statistic (considered significant at 30-50% or more). A forest plot including results of individual studies and the summary results should be included in the report.

Continuous data are also analyzed using a random effects model. Where possible, results are combined in their original metric, but if results are reported in different ways, standardized mean differences are meta-analyzed. Results should be reported in full, including forest plot, summary effect size and 95% confidence interval, and heterogeneity as measured with the  $I^2$  statistic (considered significant at 30-50% or more).

Diagnostic data are analyzed using a two-dimensional model: either the bivariate approach (Reitsma) or logistic regression (Littenberg-Moses). Results are reported as summary ROC curves and selected points from the curve in the clinically-relevant range of thresholds. Area under the ROC is not an appropriate metric for diagnostic test effectiveness.

### **Quality assessment of published guidelines**

CEP has developed a guideline appraisal instrument based on the IOM publication “Clinical Practice Guidelines We Can Trust.” (see reference 7). The current version of this instrument is found on the [CEP Methods page](#).

### **Quality assessment of published systematic reviews**

CEP uses a modified AMSTAR scale to assess the quality of systematic reviews. This streamlined scale was developed in-house in 2016 and reviewed by external methodological experts. A copy of the scale is found on the [CEP Methods page](#).

### **Quality assessment of randomized controlled trials**

CEP uses a modified Jadad scale to assess the quality of randomized controlled trials. This scale was developed in-house in 2006 and updated in July 2019. A copy of the scale is found on the [CEP Methods page](#).

### **Quality assessment of non-randomized studies**

CEP uses a modified Newcastle-Ottawa scale to assess the quality of non-randomized studies including pre-post, cohort, and other study designs. This scale was adapted by CEP in 2016. A copy of the scale is found on the [CEP Methods page](#).

### **Quality assessment of studies of diagnostic tests**

CEP uses a modified QUADAS scale to assess the quality of studies measuring the performance of a diagnostic or prognostic test. This scale was adapted by CEP in 2017. A copy of the scale is found on the [CEP Methods page](#).

### **Quality assessment of clinical pathways and algorithms**

CEP is developing its own scale to assess the quality of published clinical pathways and algorithms. The instrument is expected to be finalized in 2022. A copy of the current draft scale is available on request.

## **GRADE summary**

When appropriate, the evidence for each outcome is graded by the analyst for overall quality and given a rating of high, moderate, low, or very low based on the system proposed by the [GRADE Working Group](#). Quality assessments are based on the nature of the evidence as well as its validity, directness, consistency, precision and other factors. Summaries of GRADE methods for evaluating evidence on interventions and for evaluating evidence on diagnostic tests are included with the supplemental documents.

## **Bibliography**

When possible, clickable web links to sources should be included with each reference in the bibliography. These should be direct general links such as a Digital Object Identifier (DOI) rather than proxy access links or links to resolvers such as PennText. Citations to non-journal online sources such as guidelines on professional organization sites should include the original URL.

## **Internal review**

The first draft of the report is reviewed by the Project Director, who is responsible for ensuring that the review methods are sound, conclusions are supported by evidence, and the content of the report is accurate. The Lead Analyst revises the report in response to the reviewer comments, and the review loop continues until the Project Director is satisfied with the draft.

Then the report is circulated to the requestors for review and comment. Additional internal reviewers, specifically Penn Medicine clinicians, may also be invited to review the report at this time. The Project Director determines whether or not revisions to the report are sufficiently responsive to reviewer comments and, if necessary, decides whether reviewers have been given sufficient time to review and comment on reports when no response has been received. The Project Director then gives approval for the report to be finalized. Final reports are converted to PDF files before dissemination, to maintain the integrity of the contents.

There normally is no external (non-UPHS) review of draft reports because this adds substantially to the time needed to complete a report. Also, the local reviewers are more responsive to questions about their comments and more willing to participate in additional review loops as necessary to improve the report.

## **Report dissemination and implementation**

Once final, CEP reports are disseminated by email to key stakeholders across Penn Medicine as identified by the clinical liaisons and posted to the [CEP web site](#) (direct download of reports is limited to Penn Medicine staff). Select reports are also presented by either directors or analysts at in-person meetings to decision makers, and integrated into clinical decision support tools, clinical pathways, or quality improvement initiatives.

CEP reports are prepared primarily for the purpose of informing clinical and policy decisions at Penn Medicine entities. However, many of the topics of CEP reviews are of interest to a much broader audience. In the interest of improving the quality and safety of healthcare everywhere, full text of most CEP reports will be made available (in PDF form) on request to persons outside

Penn Medicine. Exceptions will be made, at the discretion of the Director, for reports containing confidential or proprietary information such as cost and operational data.

Bibliographic information and summaries of CEP reports are submitted quarterly for indexing in the [INAHTA Health Technology Assessment database](#), and a listing of newly-completed reports is published on the [CEP public internet site](#). Selected reports are submitted for publication in the peer-reviewed literature, especially reports that address topics of general interest, have sufficient evidence to synthesize, and have no recent published systematic reviews in the peer-reviewed literature.

## **Version control**

Revisions to a CEP report may become necessary if errors are discovered in the report as published, if important new evidence comes to light, or if evidence relied on for the conclusions of the report is retracted or corrected.

In the event that revisions to a CEP report become necessary after the report is published to the CEP web site, the following procedures should be followed. The lead analyst will report the situation to the center director, who will determine how to proceed.

If the changes are minor, and purely typographical or grammatical in nature, and results or data in tables are not changed, no notice of revision is necessary. If changes affect data, results, or conclusions, or if there is a substantive revision to the text, the reason for and nature of the change should be stated in a note to readers on the first interior page of the report with the heading “Correction” or “Update” as appropriate.

In all cases, a bullet symbol (•) will be inserted after the project number (e.g. R236•) in the cover page footer to denote a revised version of the report. A copy of the revised report shall be sent to all persons who received the original report.

## **Conflict of interest disclosures**

CEP analysts and staff (including the Lead Analyst and Project Director of every report) are not permitted to work on any project where they or an immediate family member have a financial or employment relationship with a manufacturer, supplier or other party that would present the appearance of a conflict of interest. All CEP personnel are [required](#) to disclose any such relationships when they occur. Conflict of interest disclosures for all CEP faculty and staff are updated annually. Additional disclosures are filed as required when CEP reports are submitted for publication in the peer-reviewed literature.

Project requestors and other co-authors of CEP reports are required to disclose any financial relationships that are potentially relevant to the topic of the review. Those disclosures (if any) will be included in the report. Persons whose only contributions to a report are minor technical or clinical review comments are acknowledged but not listed as co-authors, and not required to complete disclosure forms. If there is a potential conflict of interest, the Center Director (or his/her designate) will decide whether the conflicted individual may serve as a report co-author. Individuals with such conflicts may submit review comments on a draft report.

Physicians on faculty of the University of Pennsylvania Perelman School of Medicine are required to file financial disclosures annually with School of Medicine administration. Faculty disclosures can be searched at <http://www.med.upenn.edu/fapd/conflict-of-interest.html>.

## CEP funding

The Center for Evidence-based Practice is supported by institutional funds administered through the Office of the UPHS Chief Medical Officer. All CEP reports are funded internally, with the exception of reports done for partners such as the Children's Hospital of Philadelphia.

CEP holds or has held contracts and subcontracts from federal government agencies including the Centers for Disease Control and Prevention and the Agency for Healthcare Research and Quality. These contracts support specific projects which are separate from CEP's regular production of evidence reports. Funding of such extramural reports is disclosed in the report.

CEP does not accept funds from drug or device manufacturers.

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