American Urological Association

American Urological Association Clinical Practice Guidelines Development

[2015]

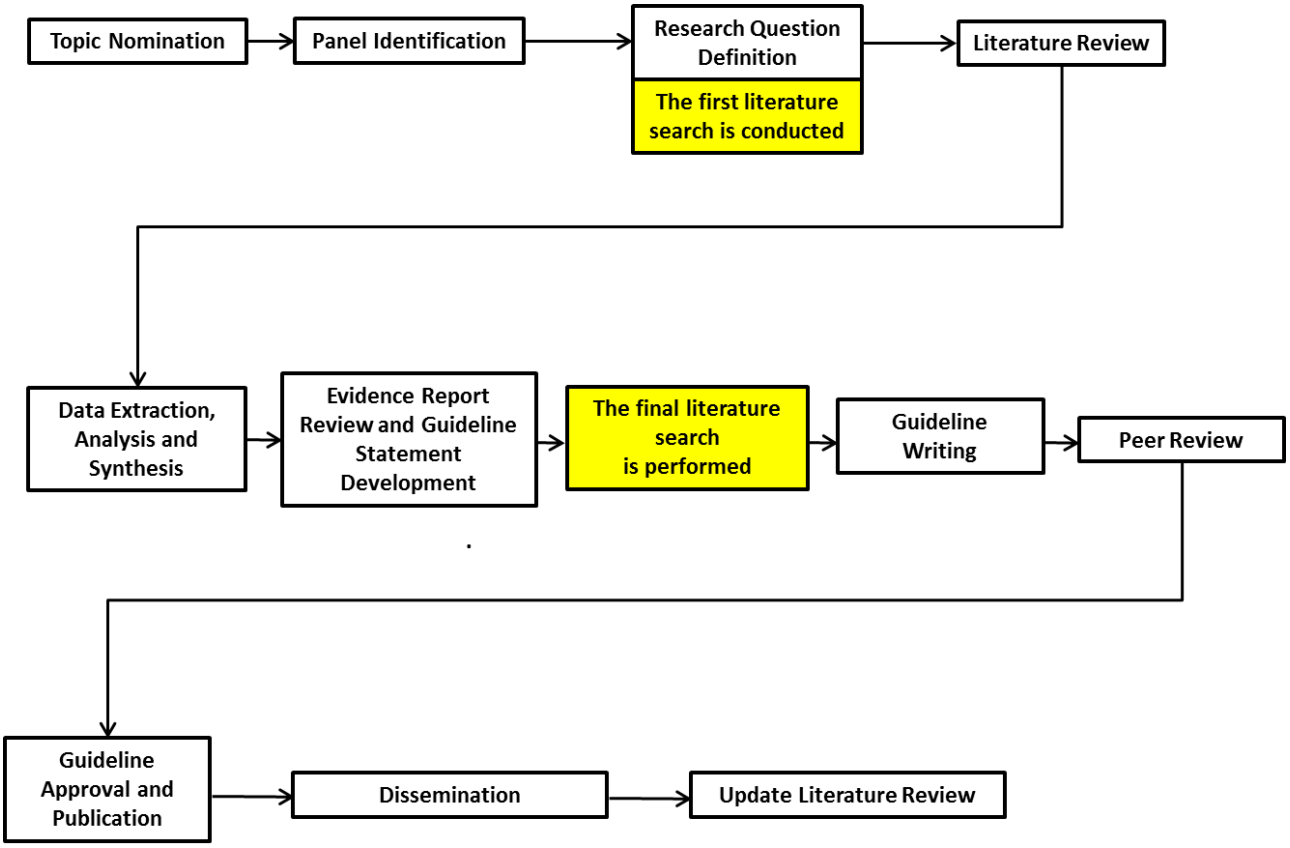
American Urological Association Guideline Development Process

The American Urological Association (AUA) is the premier professional association for the advancement of urologic patient care. The development of practice guidelines is a critical component of the organization's mission to promote the highest standards of urological clinical care through education and research. The American Urological Association Education and Research, Inc. (AUAER) is the arm of the AUA that is responsible for guideline development. For the purposes of this document, the term "AUAER" will be referred to as "AUA."

This overview is intended to describe AUA's rigorous guideline development process and serve as a helpful resource for other guideline developers. For additional guideline information, please visit the AUA Web site at www.AUAnet.org.

The Guidelines Department is located within the AUA Science and Quality Division and provides staff support for the Practice Guidelines Committee (PGC), the body that provides physician oversight of the guidelines program. All guidelines are developed using an efficient nine-stage process through a partnership between Guidelines Department staff and guideline panel members.

Stages of Guidelines Development



Stage 1: Nominate the Topic

In selecting topics for guideline development, the AUA considers high-impact conditions, burden of disease, practice variability, available evidence, dearth of published guidelines on the topic and opportunity for collaboration with other specialties. The first step in the guideline development process is to nominate the topic. There are several sources for this:

1) Online topic nomination
2) Update Literature Review (ULR)
3) PGC chair nomination

Some additional avenues for topic nomination include the Agency for Healthcare Research and Quality (AHRQ) systematic reviews, the National Quality Forum, the Core Curriculum, the American Board of Urology (ABU) list of priority topics, Institute of Medicine resources as well as contacts from other specialties.

The AUA guidelines are not funded by industry in any way; the association underwrites all costs related to guideline development. If appropriate, the AUA may partner with other organizations to develop guidelines. This partnership can provide additional funding for guideline development and offer a potential vehicle for increased dissemination of the guideline.

For each topic, a preliminary literature search is conducted to verify the extent of the literature as well as to base budget projections. Prevalence articles are screened as well as review articles for current issues. A report of potential topics, including a literature analysis write-up, is then sent to the Director of Guidelines for approval. The Director of Guidelines also identifies an appropriate topic for submission to AHRQ for the development of an evidence report from this list. Potential guideline topics are reviewed, prioritized and approved/rejected by PGC. The PGC-approved topic(s) must then be submitted to the AUA Board of Directors (BOD) for final approval.

Note: Every topic nominated will include imaging where pertinent.

Stage 2: Identify the Panel

The PGC Chair and Vice Chair identify a panel chair nominee for the project based on leadership ability and topic expertise. A panel chair nominee must undergo extensive COI assessment in accordance with AUA policy before working on the project. The selected Panel Chair must be free of topic-related COI. Once this vetting is completed and approved, the Panel Chair selects a Vice Chair to assist in the activities of the panel. The Vice Chair must also be vetted through the AUA COI policy. The PGC Chair also appoints a PGC Representative to the panel. This individual reports project development progress to the PGC in addition to fulfilling all duties of a panel member.

The Panel Chair, Vice Chair, PGC Representative and Panel Manager are responsible for keeping the project within its initial scope, adhering to the project stages and timeline and developing the guideline in accordance with the system of aligning strength of evidence to guideline statements.

The Panel Chair nominates up to seven additional panel members based on expertise, ability to work as part of a team and willingness to participate. Factors that may influence panel composition include geographic diversity and representation of other clinical specialties, including nursing or pharmacy. To ensure the production of a well- balanced guideline, a variety of academic institutions are represented on the panel; the number of panel members from a single institution is limited to two participants. Additionally, a patient advocate is sought for all appropriate panels.

The AUA has a stringent conflict of interest policy and has adopted the *Council for Medical Specialty Society's* (*CMSS) Code for Interactions with Companies* (www.CMSS.org). Once nominated, panel members are asked to record their COI statements, providing specific details on the AUA interactive website. These details are first reviewed by the Guidelines Oversight Committee (GOC), a three-member sub-committee from the PGC consisting of the Vice Chair of the PGC and two other members. The GOC determines whether the individual has potential conflicts related to the guideline. If there are no conflicts, then the nominee's COI is reviewed and approved by the AUA Judicial and Ethics (J&E) Committee. A majority (51%) of panel members may not have relationships relevant to the guideline topic. This provision will have 100% panel compliance by 2016.

During the guideline development and for a 12-month period after publication, while individuals may be permitted to maintain current arms-length investments and current research, panel members cannot enter into wholly funded PhRMA-sponsored research; however, they may maintain private ownership in ancillary services either as an individual or part of a group, and they may serve as an officer or board member of an affiliated society. Panel members may *not* present themselves as spokespersons for the guideline when giving any guideline topic-related industry talks and must publicly disclaim when giving industry-sponsored talks that they are not an official spokesperson for the AUA guidelines panel.

The AUA also requires all participants, panel members and consultants to sign a non-disclosure agreement to keep all proprietary information pertaining to the guideline and its development from being released. The agreement restricts the release of any information prior to publication. The agreement provides penalties for disclosure depending on panel members' membership statuses with the AUA.

Once approved, the final list of panel members is provided to the PGC Chair and Panel Chair. When the Panel Manager notifies the panel members of their approval, he or she also gives them an overview of the task ahead, conveying the time commitment and cooperative effort necessary to ensure the project's success.

All panel members who participate in guideline development are volunteers. Their recompense is to advance the field of urology and to be involved with the AUA's rigorous and highly respected guidelines program. Another benefit is the ability to earn Continuing Medical Education (CME) credits for work on a guideline panel. Specifically, panel members can earn up to 11.5 *AMA PRA Category 1 Credits™* for structured panel meetings and meeting participation where the panel reviews the evidence report and develops guideline statements.

Stage 3: Define Research Questions and Review Schedule

Two key documents are produced that determine the scope of the guideline: the topic refinement document (TRD) and the methodology protocol. The TRD defines the participants, interventions, comparisons and outcomes (PICO) and provides background on the topic that may have evolved significantly from the time of initial nomination. The methodology protocol is a more detailed presentation of the information found within the TRD.

The TRD determines the general scope of the guideline by stating the core questions that the systematic review will address and the date range for the literature search. The Panel Chair develops the first draft of this document with support from the Panel Manager. It is shared with and reviewed by the Vice Chair. Next, the document is distributed to the full panel, both as an orientation tool and for their review. The TRD is a central point of discussion at the first face-to-face panel meeting.

The methodology protocol is the primary tool on which the systematic review is based. It includes a detailed statement of all pertinent research questions, far more comprehensive than in the TRD. The Medical Librarian uses the protocol to guide the literature search, and the Methodologist uses it to select studies for the systematic review and guide data extraction. The methodology protocol is under continuous development by the Methodologist after the initial face-to-face meeting until it is ready for review by the Panel Chair and Vice Chair. The protocol is then submitted to the entire panel for further review to ensure that every aspect of the topic is addressed; the final document is approved by the Panel Chair, the Vice Chair and the Director of Guidelines.

Scheduled several months in advance to ensure maximum attendance, the first face-to-face meeting is a chance for the panel to get acquainted with each other as well as with the project staff and consultants. The meeting begins with the Panel Chair disclosing the COIs for each panel member. The presentations that follow describe the process for awarding CME credits to panel members and include an outline of the AUA Guidelines Development Process, a discussion of the development and purpose of the TRD and the methodology protocol and a description of the methodology implemented for the systematic review. The panel discussions focus on making necessary revisions to the TRD. At this time, the Methodologist questions the panel extensively so he or she can develop the methodology protocol. The protocol may be refined subsequently through a series of conference calls as well. Minutes of the face-

to-face meeting are submitted to all attendees after its conclusion and subsequently approved by the panel at its next meeting.

Stage 4: Review Literature

The literature review may begin as soon as the TRD is approved. This stage consists of two sub-stages: the literature search and the literature appraisal. While the search tries to identify all articles that might be relevant to the topic, the appraisal narrows the list down to studies that contain pertinent information.

To conduct the literature search, the Medical Librarian translates clinical research questions from the TRD into a search strategy that is consistent with the requirements of the National Library of Medicine's MEDLINE database. The searches are structured to be comprehensive. They consist of a broad search on the general topic, as well as a series of searches on the specific research questions. This strategy allows for the identification of nearly all relevant articles. Certain search parameters are standard across guidelines; for example, the policy to include English-language articles only, e-publications and those articles pertinent to domestic clinical practice; and to exclude abstracts only, the grey literature[1] or articles that have not yet been published.

In order to minimize the potential for error of judgment or bias, the Methodologist conducts the literature appraisal. He or she uses the methodology protocol to systematically apply the explicit inclusion and exclusion criteria to initially select articles for inclusion in the analysis and for background information. He or she does this by carefully reading the title and abstract of articles from the literature search results. The Methodologist then obtains and reviews the full text of the initially selected articles and further excludes those that appear to be relevant but, upon further review, are not. When the Methodologist is uncertain about the topic of an article, he or she consults the Panel Chair and Vice Chair and relies on their expertise to decide if the article meets the predefined criteria for inclusion. Both sub-stages of the literature appraisal are clearly documented with records of search strategies, results and reasons for study exclusion. The entire selection process is transparent and reproducible.

Stage 5: Extract, Synthesize and Analyze Data

Working from the methodology protocol, the Methodologist develops a data extraction template to capture pertinent data from the articles selected for the study. The data may include relevant patient characteristics, treatment alternatives, outcomes of interest, complications and adverse events. Then, under the supervision of the Methodologist, the data extractor(s) reviews the articles and extracts data into a spreadsheet. The data are quality checked by the Methodologist to ensure accuracy of the extraction.

[1] Grey literature is scientific literature that has not been indexed by a comprehensive tool or service that is widely available. Examples of grey literature are white papers, policy statements, drug inserts, technical reports, conference papers and pamphlets.

Next, the Methodologist assesses the design of each study for quality and assigns a rating (see table). Upon completion, the Methodologist analyzes and prepares the evidence in tabular and graphical format for panel review. The Methodologist works closely with the Panel Chair and Vice Chair to ensure that articles are interpreted accurately and the data is categorized correctly; their clinical expertise is critical. If the studies are sufficiently homogenous, the Methodologist may conduct a quantitative meta-analysis.

In addition, the Methodologist assesses the study design used in each article to determine a quality rating for it, employing a tool such as Higgins' 2007 article *Assessing risk of Bias in Included Studies*.[2]

The Methodologist then analyzes and qualitatively describes the data using charts, graphs, tables and figures. Next, the strength of the body of evidence for each question is rated using the grades as shown in the previous table.

Just before all the evidence is assembled into a report, the Medical Librarian conducts a second and final literature search to identify any published studies since the first literature search. This allows the panel to use a report that contains the very latest evidence when it makes decisions about the data and formulates guideline statements. It keeps the new guideline current longer and increases its usefulness for the clinician.

Strength of Evidence
Grade A *- high quality evidence: well-conducted randomized clinical trials (RCTs); exceptionally strong observational studies*
Grade B *- moderate quality evidence: RCTs with some weaknesses; generally strong observational studies*
Grade C *- low quality evidence: observational studies that provide conflicting information or design problems (such as very small sample size)*

Stage 6: Review Evidence Report and Develop Guideline Statements

The evidence report that the Methodologist has prepared is reviewed and discussed at the second face-to-face panel meeting. Typically, in advance of the panel meeting, the Panel Chair, Vice Chair, Methodologist and Panel Manager convene several conference calls to discuss the draft report, provide clinical input and revise accordingly. Again, the input of the Panel Chair and Vice Chair is important in ensuring that this second meeting runs smoothly. Prior to the meeting, the Panel Chair and Vice Chair

[2] Higgins, J.P. and Altman, D.G.: Assessing risk of bias in included studies. In: Cochrane Handbook for Systematic Reviews of Interventions. Edited by J.P. Higgins and S. Green. West Sussex, England: John Wiley & Sons, p.187-241, 2008.

assign subgroups of panel members to each treatment modality and to different research questions within the report. Working together, the panel members review the evidence for risk of benefits and harms and draft guideline statements. It is during this second meeting that the panel will refine each statement and begin to add in supporting text.

The evidence report forms the basis for development of guideline statements. As statements are developed, they are categorized according to three statement type: Strong Recommendation, Moderate Recommendation and Conditional Recommendation.

Strong Recommendation: If the benefits of taking a decisive action outweigh the risks/burdens OR the risks/burdens outweigh the benefits for a substantial net benefit or harm, then the statement is categorized as a Strong Recommendation. The panel is making a directive statement to take or to *not* take a specific action. This applies to most patients in most circumstances and future research is unlikely to change confidence. This can be supported by Evidence Strength A, B, or C; however, Evidence Strength C is rarely used to support a Strong Recommendation. In the case of Evidence Strength A, future research is unlikely to change confidence. In the case of Evidence Strength B, better evidence could change confidence. In the case of Evidence Strength C, better evidence is likely to change confidence.

Moderate Recommendation: If the benefits outweigh the risks/burdens OR the risks/burdens outweigh the benefits for a moderate net benefit or harm, the statement is categorized as a Moderate Recommendation. The panel is making a directive statement to take or to *not* take a specific action. This applies to most patients in most circumstances and future research is unlikely to change confidence. This can be supported by Evidence Strength A, B or C. In the case of Evidence Strength A, future research is unlikely to change confidence. In the case of Evidence Strength B, better evidence could change confidence. In the case of Evidence Strength C, better evidence is likely to change confidence.

Conditional Recommendation: If the benefits and the risks/burdens are either evenly balanced or unclear, the statement is categorized as a Conditional Recommendation. In this case, the decision to take or to *not* take a specific action is dependent upon individual patient circumstances, and alternative strategists may be equally reasonable. This can be supported by Evidence Strength A, B or C. In the case of Evidence Strength A, future research is unlikely to change confidence. In the case of Evidence Strength B, better evidence could change confidence. In the case of Evidence Strength C, better evidence is likely to change confidence.

In the guidelines, the strength of the body of evidence for each research question can support any guideline statement. See the chart that follows**.**

Guidelines Statement Classification			
	Evidence Strength A (High Certainty)	**Evidence Strength B (Moderate Certainty)**	**Evidence Strength C (Low Certainty)**
Strong Recommendation (Net benefit or harm substantial)	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances but better evidence could change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) appears substantial Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances but better evidence could change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) appears moderate Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (No apparent net benefit or harm)	Benefits = Risks/Burdens Best action depends on individual patient circumstances Future research unlikely to change confidence	Benefits = Risks/Burdens Best action appears to depend on individual patient circumstances Better evidence could change confidence	Balance between Benefits & Risks/Burdens unclear Alternative strategies may be equally reasonable Better evidence likely to change confidence

At the face-to-face meeting, the panel member subgroups present their proposed statements. The panel discusses them in detail making any necessary revisions in the language. During the discussion, the panel members' clinical expertise enriches the evidence review by providing a background for interpretation of the findings.

Next, the members categorize each statement and discuss strength of the body of evidence for the research question as assigned by the Methodologist. Ultimately it is the responsibility of the Panel Chair and the PGC Representative to ensure that statements are accurately categorized. The Vice Chair, Panel Manager and Methodologist provide strong support in accomplishing this charge.

When evidence is lacking and the panel wants to make a statement about the research question, it can select from two other statement types, Expert Opinion or Clinical Principle.

1) Expert Opinion: A statement achieved by panel consensus that is based on members' clinical training, experience, knowledge and judgment and for which there is no published evidence.

2) Clinical Principle: A statement about a component of clinical care that is very widely agreed upon by urologists or other clinicians and for which there may or may not be evidence in the medical literature.

As the final drafting of statements nears its end, the panels follow a modified Delphi technique to document input and achieve consensus. The Panel Manager circulates ballots and questionnaires to elicit anonymous input from the panel and to determine the level of consensus on a particular issue. The anonymous nature of the process allows panel members to speak their minds freely without concern for others' reactions. All comments are carefully reviewed, and, if needed, a second questionnaire is circulated. In this way, consensus is reached through a process of identifying similar viewpoints rather than through a face-to-face discussion in which the loudest voice may sway others' opinions.

Stage 7: Write Guideline

Following the second meeting, each of the earlier-assigned subgroups of panel members is responsible for drafting text to support the guideline statements. The Panel Manager and Guidelines Medical Writer/Editor provide writing instructions that include an outline of the document, a reference style to be used and a sample of an AUA guideline. While the panel begins drafting supporting text for each statement, a second literature review is conducted to identify any literature that may have been released just prior to guideline publication. Once potential literature is evaluated using the same criteria as the initial literature review, any relevant literature is forwarded to the panel. This ensures that a guideline is as up-to-date as possible when it is released to the public.

The Medical Editor combines all text submissions into one logical, organized document so that it reads as if written by one author. At this time, panel members identify key data tables and graphs/charts to be included in the document or as an appendix. Staff checks and formats all references to ensure content and citation accuracy. Panel members may review and discuss several iterations of the document as it is prepared for peer review. The Panel Manager coordinates the final panel vote to approve the document before it is circulated for peer review.

Stage 8: Undergo Review

The Guidelines Validation Committee provides an initial strategic review. This three-person committee is comprised of 1) the PGC Vice Chair, 2) a second PGC member with extensive methodological expertise,

and 3) a content expert that has specialized knowledge on the guideline topic. The Committee is charged with reviewing the document from an overview perspective, providing insight into the clarity of the document, identifying the clinical questions defined by the panel, providing definitions of the levels of evidence and ensuring the document's adherence to the overall AUA mission. If there are concerns, the panel will revise the document before circulating it for peer review.

It is the goal of the guideline panels to identify and confirm at least 30 peer reviewers (in addition to the PGC, S&Q and BOD members) for each guideline. COI disclosure is sought from all peer reviewers, and each reviewer is required to sign a non-disclosure agreement form to ensure that the confidentiality of the guideline is protected until final publication.

In addition to peer review, the document is also made available for public comment. Approximately six to eight weeks prior to a document entering the review period, a notice is placed on the AUA Guidelines website announcing the availability of a draft guideline document. All interested parties are invited to apply to review the document. All respondents are sent COI and NDA forms as with invited peer reviewers. All forms must be completed and returned to Guidelines staff before a draft guideline will be sent for review. The public comment period will occur simultaneously with peer review.

During the review period, AUA legal counsel reviews the document to update the legal disclaimer, if needed, and raise any issues of concern. An editor from *The Journal of Urology®* is assigned to review the document and provide feedback to the *Journal*. The panel, in turn, provides a prompt response to the Editor's comments following peer review so that the *Journal* receives timely feedback. This facilitates submission of a summary of the guideline to *The Journal of Urology®*, which is discussed below under Dissemination of Guidelines. When a guideline contains imaging recommendations, an imaging expert (such as a member of the AUA Urologic Treatment and Diagnosis Imaging Committee) participates in peer review.

As comments are received, the Guidelines Operations Manager captures all comments, organizing them for efficient review. The Panel Manager convenes a series of conference calls with the panel to discuss the comments. Working with the Panel Chair and Vice Chair, the Panel Manager identifies areas of controversy and comments to be discussed in depth with the entire panel. Other comments of lesser significance, with the agreement of the panel, are addressed by the Panel Chair and Vice Chair. All revisions are noted in the database to facilitate tracking of actions. After all peer review comments are addressed, Panel Chairs should begin work with the Guidelines Medical Writer on the executive summary for submission to the *Journal of Urology®.*

Stage 9: Obtain Approval and Publish

Once approved by the panel, the document is distributed to the PGC for the next level of approval. If approved by the PGC, the document is sent to the BOD for final approval. If the document is distributed via e-mail or fax, unanimous approval is required. During this time period, Panel Chairs should complete work with the Guidelines Medical Writer on the executive summary for submission to the *Journal of Urology®.*

Update Literature Reviews (ULRs)

In an effort to ensure AUA guidelines are current, Guidelines staff periodically assess whether an existing guideline remains current through the ULR process. This is a systematic review of the literature published since the initial release of the guideline.

The ULR panel consists of the Panel Chair from the existing guideline, a member of the guideline panel and a third member not previously involved in the development of the guideline but considered an expert in the subject. To conduct the review, a Medical Librarian performs a search of literature published since the cutoff date in the existing guideline. This search should include a review of all published guidelines or appropriate use criteria related to the guideline under review. Next, the Methodologist conducts a systematic review of the search results and presents the findings to the panel. The panel then determines whether a limited update is required or if a full revision of the guideline is warranted.

The ULR is conducted in four stages:

- Stage 1: Identify the panel
- Stage 2: Develop the TRD
- Stage 3: Conduct the literature review
- Stage 4: Develop the recommendation to revise or delay

The Panel Manager notifies the Guidelines Operations Manager to initiate a modification to the AUA website and the NGC website to show that the Guideline has been verified as accurate or recommended for revision or amendment and notifies the Panel Manager when these tasks are completed.

Guidelines Amendment Process

The Guidelines Amendment Process ensures that targeted yet substantive changes to guidelines, such as changes to one or a few guideline statements or lines of treatment, are based on a rigorous systematic review and analysis of newly available peer-reviewed literature. This amendment process is a substitute for developing a full revision of the guideline when only a few guideline statements are in need of amending.

A subset of three members from the original guideline serves as the amendment panel along with a senior methodologist who develops the updated systematic review. This panel is held to the same COI requirements as the original panel with a requirement that 51% of the panel must be free of topic-related COI. The amendment panel reviews the systematic review, which includes publications released since the last publication of the guideline. A guideline amendment occurs when the methodologist and amendment panel members agree that new evidence is sufficient to require an evidence-based statement change or addition or that patients and clinicians would be better-served with the provision of a new Clinical Principle or Expert Opinion statement. Following a series of conference calls when potential changes to the guideline are discussed, the Guidelines Medical Writer works with the panel to incorporate all changes. The final amended document is then sent out for review and approval (via email) first by the amendment panel, followed by the full guideline panel, the PGC, S&Q council members and finally the BOD. Once the amendment has received approval, it is published to the AUA Guidelines website with a note indicating that the original guideline has been amended to incorporate newly published information. The Guidelines Operations Manager is responsible for sending a copy of the newly amended guideline to ABU, NGC and GIN.

Sunsetting of Guidelines

Following the periodic review through the ULR program, a guideline can remain on the AUA website as long as it is deemed current. Guidelines that are not revised or amended following 10 years of publication are to be archived.

DISCLAIMER: While AUA guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technology advances, the guidelines will change. Today, these evidence-based guideline statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases.

Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Conformance with any clinical guideline does not guarantee a successful outcome. The guideline text may include information or recommendations about certain drug uses ('off label') that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These guidelines are not intended to provide legal advice about use and misuse of these substances.

Although guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data as of close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices. For this reason, the AUA does not regard technologies or management which are too new to be addressed by these guidelines as necessarily experimental or investigational.