

ASTRO Clinical Practice Guideline Methodology Guide

Caroline Patton and Lisa Bradfield
on behalf of the Guideline Subcommittee

ASTRO

AMERICAN SOCIETY FOR RADIATION ONCOLOGY

Table of Contents

Introduction	3
Topic Selection	3
Guideline Initiation	4
Partnership or Collaboration with Other Societies	4
Task Force Selection and Topic Proposal	4
Disclosures and Conflict of Interest (COI)	4
Initiation and Key Question Development	5
Systematic Evidence Review	5
Development and Implementation of Search Protocol	5
Article Screening and Abstraction	5
Draft Development	6
Evidence Analysis and Recommendation Writing	6
Assigning Recommendation Strength and Quality of Evidence	6
Recommendation Supportive Text	8
Consensus Development and Voting	8
Review and Approval	9
Review Phase	9
Public Comment	9
Guideline Approval and Endorsements	9
Development of Executive Summary	9
Publication and Implementation	10
Post-Publication Monitoring and Initiation of Updates	10
Figure 1. Guideline Development Process	11
References	12

Introduction

As a recognized leader in bringing excellence to the field of radiation oncology within multidisciplinary cancer care, the American Society for Radiation Oncology (ASTRO) began producing evidence-based clinical practice guidelines (guidelines) in 2009 to translate the best available scientific evidence into recommendations. These documents provide guidance to radiation oncology professionals and the patients they serve to improve care, reduce practice variation and inappropriate resource utilization, identify gaps in the evidence base, and support quality measure development and national quality reporting requirements. While guidelines are based on interpretation of relevant evidence on a specific topic, individual physicians should make the ultimate judgment regarding therapy considering all the circumstances and utilizing a shared decision-making process with the patient.

Standards for developing guidelines have evolved over the years in part due to the publication of the National Academy of Medicine's (formerly U.S. Institute of Medicine) landmark report providing standards for systematic reviews and on developing trustworthy guidelines.^{1,2} It defined guidelines as "statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options."² The core standards were expanded upon by the Council of Medical Specialty Societies.^{3,4} They address the stages of the guideline development process summarized in Figure 1 and discussed in this article. Chief among these standards is a rigorous, transparent, reproducible, and unbiased review of the applicable evidence.

Topic Selection

Potential topics for guideline development come from multiple sources, including the Guidelines Subcommittee (GLSC), which oversees the policies, procedures, and content development for all guidelines; ASTRO leadership and other committees and resource panels; the ASTRO membership; and collaboration with other specialty societies. Potential new guideline topics are identified annually by the GLSC and priorities for the coming year are determined based on relevance to radiation oncology, prevalence of the disease/condition, degree of practice variation or controversy, potential impact on patient care and outcomes, strength of existing evidence, and availability of new data.

In addition to new guidelines, previously published guidelines are evaluated for currency beginning 2 years after publication by a work group with representations from the GLSC and the original guideline. If pivotal new evidence has been published that is likely to impact the recommendations, a review may be initiated earlier. Based on the assessment of the work group, the original document may be updated or replaced with a new guideline.

Before initiation of a new guideline or update, an environmental scan is conducted to identify and evaluate other guidelines on the same topic that are in progress or were published in the previous several years. This step is designed to minimize overlap between guideline documents and avoid providing discordant guidance.

Guideline Initiation

PARTNERSHIP OR COLLABORATION WITH OTHER SOCIETIES

ASTRO has approved a [framework](#) for developing guidelines with participation from other organizations to minimize duplication of effort and harmonize recommendations. Depending on the topic and scope, societies whose constituencies have a vested interest in the subject may be invited to participate at multiple levels. Joint partners receive representation on the task force, nominate official peer reviewers, and are offered the chance to approve the final document. Other societies collaborate by nominating a task force representative, providing peer review, and/or considering the final guideline for endorsement.

TASK FORCE SELECTION AND TOPIC PROPOSAL

After selection of a new topic, the GLSC develops a proposal which outlines the guideline's preliminary scope and key questions (KQs) and includes a list of task force nominees. Following multiple layers of review, a task force is selected if the proposal is approved by the ASTRO Board of Directors.

Task force chairs and members are nominated by the GLSC, other ASTRO committees or resource panels, and for non-radiation oncology physicians, by their respective societies. All guidelines have a chair and vice-chair or two co-chairs who are selected by the GLSC, pending review of their disclosures. Potential members include radiation oncologists, radiation oncology residents, medical physics, and representatives of other relevant specialties, such as medical oncology or surgery. The radiation oncologists on the task force are drawn from academic, private or community, and/or government settings. A representative of the GLSC serves as a liaison between the task force and the subcommittee to provide methodological support, help monitor concordance with other guidelines and documents, provide status updates on the project to the GLSC, and assist with developing patient materials. A patient representative is also included on the task force to provide feedback related to quality of life, shared decision making, and treatment issues from a patient perspective. ASTRO strives to avoid bias by selecting a multidisciplinary task force of experts with variation in geographic region, gender, ethnicity, race, practice environment, and area of expertise.

DISCLOSURES AND CONFLICT OF INTEREST (COI)

ASTRO has detailed policies and procedures related to disclosure and management of industry relationships to avoid actual, potential, or perceived conflicts of interest. Based on the scope of the guideline, ASTRO staff initially identify categories of affected companies – commercial entities whose business and products may be influenced, positively or negatively, by the guideline recommendations. This list is reviewed during the proposal approval process and further refined by the selected task force chairs. All task force members are required to disclose industry relationships and personal interests that were active within the 12 months before initiation of the project. Disclosures go through a rigorous review process with final approval by ASTRO's Conflict of Interest Review Committee. A majority of task force members (>50%), including the chairs, do not have relationships with affected companies and certain types of relationships are not permitted at all. For the purposes of full transparency, task force members' comprehensive disclosure information is published in the guideline. See [ASTRO's comprehensive COI policy](#) for additional details.

INITIATION AND KEY QUESTION DEVELOPMENT

After confirmation of the task force, a kick-off call is held to review the disclosures, expectations and responsibilities of task force members and discuss the guideline development process and project timeline. The task force also assesses and refines the preliminary KQs using the **P**atients, **I**nterventions, **C**omparators, **O**utcomes, **T**iming, and **S**etting (PICOTS) framework, which guides a systematic approach to evidence review for guidelines.¹ Focused questions make the project more manageable and lead to specific recommendations and conclusions that support patient care. Once the KQs are finalized, writing assignments are determined, including leads for each KQ.

Systematic Evidence Review

DEVELOPMENT AND IMPLEMENTATION OF SEARCH PROTOCOL

Drawing on the PICOTS for the KQs, a search protocol is developed, which details the search strategies and inclusion and exclusion criteria. The literature is derived from research involving human subjects, published in English, and indexed in MEDLINE. Hand searches of other sources, particularly recent review articles and trial data, may confirm or supplement the electronic searches. Studies published after the end date of the literature search are not used to develop the recommendations but may be discussed in a future directions/emerging data section.

ARTICLE SCREENING AND ABSTRACTION

The literature search results go through a series of reviews to synthesize the evidence based on the pre-defined inclusion and exclusion criteria to determine their relevance to the identified KQs and scope of the guideline. An independent literature review team dual-screens first the titles and then the abstracts of the articles included from title screening. The studies included after the second round are reviewed and further refined by the task force. Study characteristics from the final group of selected articles is abstracted into detailed evidence tables, which summarize the primary evidence base for the guideline and are used to inform the recommendations. The evidence tables are published as a supplement to the document.

Draft Development

EVIDENCE ANALYSIS AND RECOMMENDATION WRITING

To ensure high standards in developing ASTRO's guidelines, a rigorous, transparent, reproducible, and unbiased review of the evidence is paramount. Through a series of conference calls, small work groups synthesize and summarize the evidence for each KQ to determine the quality of the evidence. These discussions inform the development of draft recommendations, which include assigning the recommendation strength and overall quality of evidence ratings, as defined in Table 1. It is important that guideline recommendations be clear and actionable statements that align with the PICOTS framework, denoting in most instances the patient group, intervention, comparator, and outcome. Implementation remarks are included sparingly to enhance the reader's interpretation and understanding of a recommendation or to append information like timing, setting, or dosing details to the recommendation.

Once the work groups have achieved consensus on their section recommendations, they present a summary of the evidence related to their respective KQs, including their analysis of the data and rationale for the draft recommendations. All task force members are encouraged to participate in the discussion to facilitate consensus. Once recommendations are agreed upon, work group members draft the supportive text for their KQ. Task force members are expected to meet the criteria of the International Committee of Medical Journal Editors in order to be included as authors.⁵

ASSIGNING RECOMMENDATION STRENGTH AND QUALITY OF EVIDENCE

ASTRO's recommendations are based on evaluation of multiple factors including the quality of evidence, *individual* study quality, and task force consensus, all of which inform the strength of recommendation. Strength of recommendation reflects the magnitude and certainty of benefit over risk or vice versa and is categorized as either strong or conditional. Quality of evidence is based on the body of evidence available for a particular KQ and includes consideration of number of studies, study design, adequacy of sample sizes, consistency of findings across studies, and generalizability of the populations, settings, and treatments in the studies. Quality of evidence denotes the confidence in or certainty offered by the body of evidence supporting the recommendation and is graded as high, moderate, low, or expert opinion. Recommendation strength and quality of evidence are complementary but distinct concepts; a strong recommendation can be made on low-quality evidence, or a conditional recommendation based on high-quality evidence. Table 1 includes more specific definitions to assist the task force when determining the appropriate strength and quality ratings.

In 2018, ASTRO's guideline methodology was modified to incorporate an expert opinion strength of recommendation category and to quantify the number and type of studies that determine the quality of evidence. Expert opinion recommendations are used where guidance is considered essential due to factors such as high prevalence, mortality, or morbidity but either relevant data do not exist, the available evidence does not reflect current technology/practice, or there is substantial variation in practice or controversy.

TABLE 1. ASTRO RECOMMENDATION GRADING CLASSIFICATION SYSTEM

ASTRO's recommendations are based on evaluation of multiple factors including the quality of evidence (QoE), individual study quality, and panel consensus, all of which inform the strength of recommendation. QoE is based on the body of evidence available for a particular key question and includes consideration of number of studies, study design, adequacy of sample sizes, consistency of findings across studies, and generalizability of samples, settings, and treatments.

Strength of Recommendation	Definition	Overall QoE Grade	Recommendation Wording
Strong	<ul style="list-style-type: none"> Benefits clearly outweigh risks and burden, or risks and burden clearly outweigh benefits. All or almost all informed people would make the recommended choice. 	Any (usually high, moderate, or expert opinion)	"Recommend/Should"
Conditional	<ul style="list-style-type: none"> Benefits are finely balanced with risks and burden or appreciable uncertainty exists about the magnitude of benefits and risks. Most informed people would choose the recommended course of action, but a substantial number would not. A shared decision-making approach regarding patient values and preferences is particularly important. 	Any (usually moderate, low, or expert opinion)	"Conditionally Recommend"

Overall QoE Grade	Type/Quality of Study	Evidence Interpretation
High	<ul style="list-style-type: none"> 2 or more well-conducted and highly-generalizable RCTs or meta-analyses of such trials. 	The true effect is very likely to lie close to the estimate of the effect based on the body of evidence.
Moderate	<ul style="list-style-type: none"> 1 well-conducted and highly-generalizable RCT or a meta-analysis of such trials OR 2 or more RCTs with some weaknesses of procedure or generalizability OR 2 or more strong observational studies with consistent findings. 	The true effect is likely to be close to the estimate of the effect based on the body of evidence, but it is possible that it is substantially different.
Low	<ul style="list-style-type: none"> 1 RCT with some weaknesses of procedure or generalizability OR 1 or more RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes OR 2 or more observational studies with inconsistent findings, small sample sizes, or other problems that potentially confound interpretation of data. 	The true effect may be substantially different from the estimate of the effect. There is a risk that future research may significantly alter the estimate of the effect size or the interpretation of the results.
Expert Opinion*	<ul style="list-style-type: none"> Consensus of the panel based on clinical judgement and experience, due to absence of evidence or limitations in evidence. 	Strong consensus (≥90%) of the panel guides the recommendation despite insufficient evidence to discern the true magnitude and direction of the net effect. Further research may better inform the topic.

QoE = quality of evidence; RCTs = randomized controlled trials.

*A lower quality of evidence, including expert opinion, does not imply that the recommendation is conditional. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials but there still may be consensus that the benefits of a treatment or test clearly outweigh its risks and burden.

RECOMMENDATION SUPPORTIVE TEXT

In light of changing standards from the National Academy of Medicine and the Council of Medical Specialty Societies, as well as member feedback, ASTRO evaluated its guideline methodology with the goal of implementing a more streamlined process and producing a more user-friendly guideline. The GLSC decided to focus on standardization across guidelines, limiting the text length, and incorporating more tables and figures where appropriate. To this end, guideline text will focus mainly on providing a high-level summary of the body of evidence that supports the recommendation and the authors' interpretation of those data. Important information about the key studies that may help the reader understand the guidance is also included when needed. The recommendations from each KQ include a hyperlink to evidence tables so the reader can see the specific study characteristics easily, alleviating the necessity of detailing each study in the text. In addition, the benefits and harms of the intervention may be discussed, as well as nuances or details about the recommendation that may be important to the reader.

CONSENSUS DEVELOPMENT AND VOTING

General agreement on the recommendations is achieved during task force discussions throughout the writing process. Formal consensus is then evaluated using a modified Delphi approach. In an online survey, task force members anonymously indicate their level of agreement on each recommendation based on a 5-point Likert scale, from "strongly agree" to "strongly disagree". Members may abstain from rating recommendations that they feel are outside of their expertise. A pre-specified threshold of $\geq 75\%$ ($\geq 90\%$ for expert opinion recommendations) of raters that select "strongly agree" or "agree" indicates consensus is achieved. Recommendation(s) that do not meet this threshold are removed or revised. Recommendations edited in response to task force or reviewer comments are re-surveyed prior to submission of the document for approval.

Review and Approval

REVIEW PHASE

While the guideline is undergoing consensus voting, peer reviewers are identified who have an active clinical and/or research interest in the topic of the guideline. They are drawn from multiple sources, including the ASTRO membership and partner or collaborating organizations, and are selected to provide a variety of perspectives and areas of expertise. The task force chair(s), GLSC, and, where applicable, other committees and panels propose official ASTRO reviewers. Partner, collaborating, and potential endorsing societies are also encouraged to nominate reviewers on their behalf since this is their primary opportunity to recommend changes to the guideline. Like task force members, reviewers must disclose all industry relationships and personal interests and their disclosures are evaluated using a stringent COI review process.

Once consensus on the draft guideline is achieved by the task force, the document undergoes review simultaneously by the invited peer reviewers, the GLSC (including in-depth review by 2-3 members for content, process and consistency with other ASTRO clinical documents), and ASTRO staff and legal counsel. The resulting comments are adjudicated by the task force and the guideline revised as appropriate.

PUBLIC COMMENT

Following peer review, guidelines are posted on ASTRO's website for 4-6 weeks for public comment. Announcements are made via emails and postings on the ASTRO website inviting comments from ASTRO members and committees; patient support and advocacy groups; and other potential stakeholders. Partner, collaborating, and potential endorsing societies are also encouraged to share the link with their membership so additional reviewers can be involved in the review process. This is the last opportunity for societies to suggest changes, since substantive revisions cannot be made later during the endorsement process after the final guideline is approved. Comments are addressed using the same process as peer review. Any recommendations that are changed as a result of the reviews or public comments are voted on again by the task force to ensure consensus agreement is maintained.

GUIDELINE APPROVAL AND ENDORSEMENTS

The completed guideline undergoes a multi-level review and is ultimately approved by the ASTRO Board of Directors. For guidelines developed in partnership with other societies, the document is submitted for approval to the respective organizations' leadership, based on their standard processes. The approved version of the guideline is sent to potential endorsing societies, along with the responses to their representatives' peer review and/or public comments, and a final decision on endorsement requested.

DEVELOPMENT OF EXECUTIVE SUMMARY

An Executive Summary is developed during the approval process, adhering to the journal word count requirement. It contains abbreviated Introduction and Methods sections, the recommendations with implementation remarks where applicable, and potentially a short Conclusion and/or Future Directions section. It does not include the full supporting text for the recommendations. The Executive Summary appears in print, with the full-text guideline and evidence table supplements available online.

Publication and Implementation

All approved ASTRO guidelines are submitted to *Practical Radiation Oncology (PRO)*, which conducts a separate peer review and approval process. If accepted, *PRO* publishes the guideline online followed by print publication. When ASTRO partners with other societies, they may simultaneously publish a summary of the guideline in their respective journal or link to the ASTRO publication.

Guideline publications are available on ASTRO's website, publicized to its membership through weekly news emails and meeting presentations, and ultimately incorporated into measures, educational products, and other programs. It is broadly disseminated through a press release, developed in conjunction with partner societies as appropriate. Additional products, including slides, webinars, podcasts, and patient materials may also be developed. Lastly, guidelines are submitted to the Guidelines International Network Library and ECRI Guidelines Trust.

Post-Publication Monitoring and Initiation of Updates

Another aspect of the GLSC's oversight role includes monitoring publication of new clinical research that might support an update or replacement of published guidelines. A request to modify a guideline may also be made by an ASTRO member or participating society. Guidelines more than 2 years post publication are evaluated for currency and revised or reaffirmed approximately every 5 years. As part of this topic identification and prioritization process, ASTRO staff contact the original guideline task force annually to ask if practice-changing data has been published that may lead to changes to the key questions and/or recommendations.

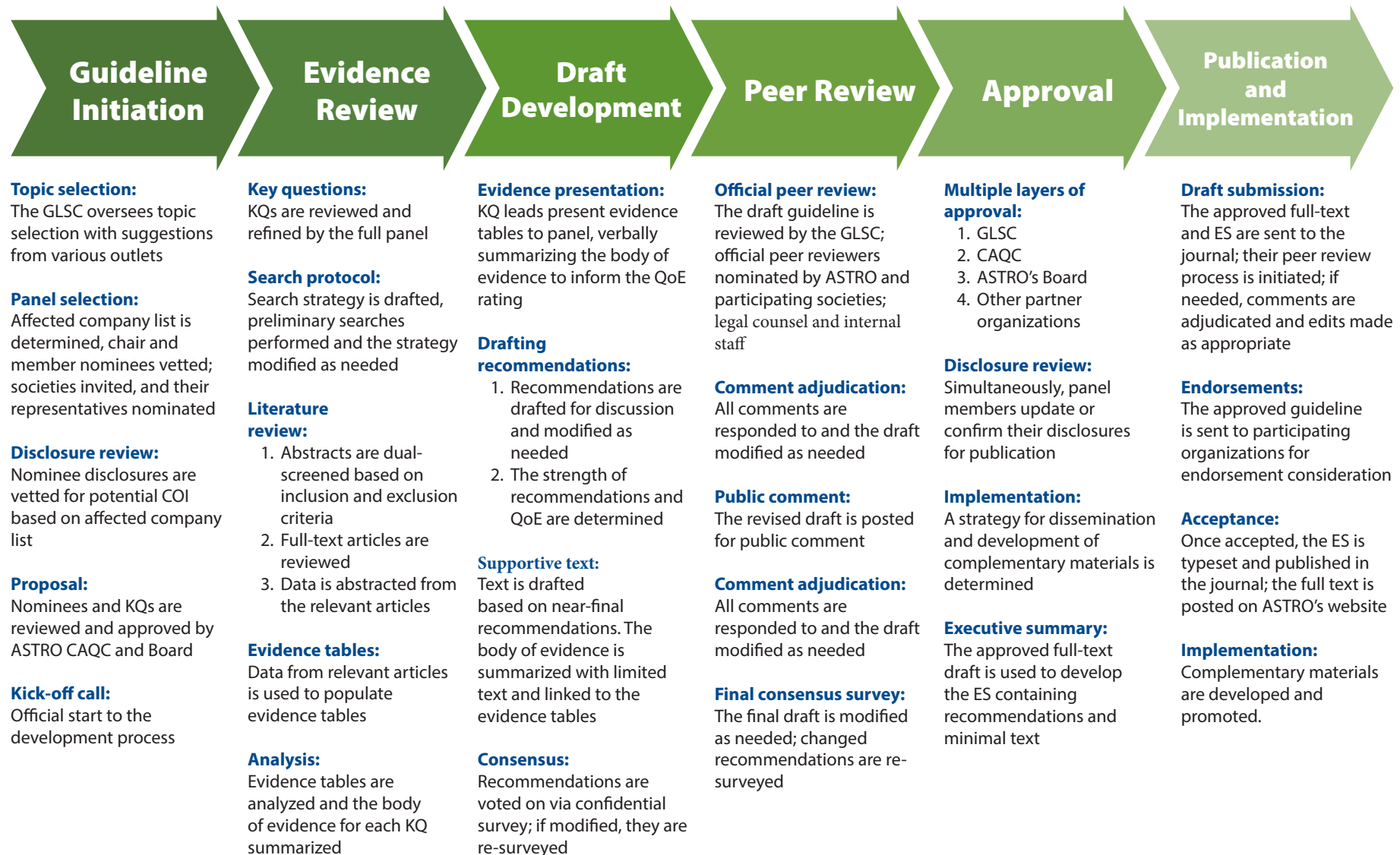
For topics selected for an update or replacement or that are approaching 5 years post-publication, an environmental scan of completed or in progress external guidelines and upcoming major trials is performed. A rapid literature review of evidence published since the last version of the guideline is also conducted. Based on the results, the GLSC makes a decision to:

1. Take no action and re-review the guideline during the next annual topic identification and prioritization process (or at the discretion of the GLSC),
2. Proceed with an update of the guideline (revising a portion of the original document) or replacement of the guideline with a completely new version,
3. Reaffirm the guideline,
4. Sunset the guideline due to outdated evidence or technology.

If the GLSC decides to reaffirm or sunset the guideline, the original task force members and ASTRO's Board of Directors are notified and a short article is published explaining the status of the guideline, which is linked to the original document. If the GLSC decides to update or replace the guideline, the project follows the standard process shown in Figure 1.

FIGURE 1. GUIDELINE DEVELOPMENT PROCESS

ASTRO Guideline Development Process Overview



CAQC, Clinical Affairs & Quality Council; COI, conflict of interest; ES, Executive Summary; GLSC, Guideline Subcommittee; KQ, key question; QoE, and quality of evidence.

References

1. Institute of Medicine. *Finding What Works in Health Care: Standards for Systematic Reviews*. Washington, DC: The National Academies Press; 2011.
2. Institute of Medicine. *Clinical Practice Guidelines We Can Trust*. Washington, DC: The National Academies Press; 2011.
3. Council of Medical Specialty Societies. Code for Interactions with Companies. April 2015. <http://cmss.org/wp-content/uploads/2016/02/CMSS-Code-for-Interactions-with-Companies-Approved-Revised-Version-4.13.15-with-Annotations.pdf>. Accessed June 1, 2018.
4. Council of Medical Specialty Societies. Principles for the Development of Specialty Society Clinical Guidelines. September 2012. <https://cmss.org/wp-content/uploads/2016/02/CMSS-Principles-for-the-Development-of-Specialty-Society-Guidelines-September-20122.pdf>. Accessed June 1, 2018.
5. International Committee of Medical Journal Editors. Defining the Role of Authors and Contributors. www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html. Accessed April 17, 2019.