ASAM American Society of Addiction Medicine

The ASAM Methodology for Clinical Practice Guidelines

Adopted April 12, 2023

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Introduction

In keeping with the American Society of Addiction Medicine's (ASAM) mission to define and promote evidence-based best practices in addiction prevention, treatment, remission, and recovery, ASAM Quality Improvement Council (QIC) sought to rigorously update and structure ASAM's Clinical Practice Guideline (CPG) methodology. The QIC recognized a need for ASAM's CPG methods to be more in line with international standards for CPGs such as:

- Establishing improved transparency
- Managing conflicts of interest
- Balancing guideline group composition
- Using a rigorous systematic review
- Establishing quality of evidence
- Determining strength of recommendations
- Articulating recommendations clearly and succinctly
- Engaging stakeholder review
- Promoting diversity, equity and inclusion
- Establishing a process for CPG updates[1]

Over a two-year process, ASAM worked to create this new methodology which will inform how future ASAM CPGs are conducted.

Methodology

In January 2021, the ASAM QIC developed the "Clinical Practice Guideline Methodology and Oversight Subcommittee" and chose Dr. Melissa Weimer to lead this subcommittee. The CPG-MOS was charged with providing strategic oversight to the development, implementation, education, and communication of CPGs. The goals of the CPG-MOS were to establish and publish a methodology for the development of CPGs and to develop a CPG strategic plan.

Through an open call process, ASAM members were invited to apply for consideration to serve on the CPG-MOS subcommittee. The seven members chosen represent individuals from diverse backgrounds, geographies, research experience, and clinical backgrounds. Several members lead or have led systematic reviews and participated in Clinical Practice Guidelines for ASAM or other organizations. See the list of CPG-MOS members, their biographies, and disclosure of interests in Appendix A.

Members of the CPG-MOS have been meeting monthly since March 2021 to develop and write the updated ASAM CPG Methodology (see Appendix B for a timeline). The following references were used as basis for the development of the CPG Methodology: the Institute of Medicine,[1] American College of Physicians,[2] Veterans Association/Department of Defense,[3] American Psychiatric Association,[4] Grading of Recommendations Assessment, Development and Evaluation (GRADE) Handbook,[5], COCHRANE Handbook,[6] U.S. Preventive Services Task Force (USPSTF),[7] Appraisal of Guidelines for Research and Evaluation II (AGREE II) Instrument,[8] World Health Organization,[9] and a comparative assessment of CPG handbooks.[10]

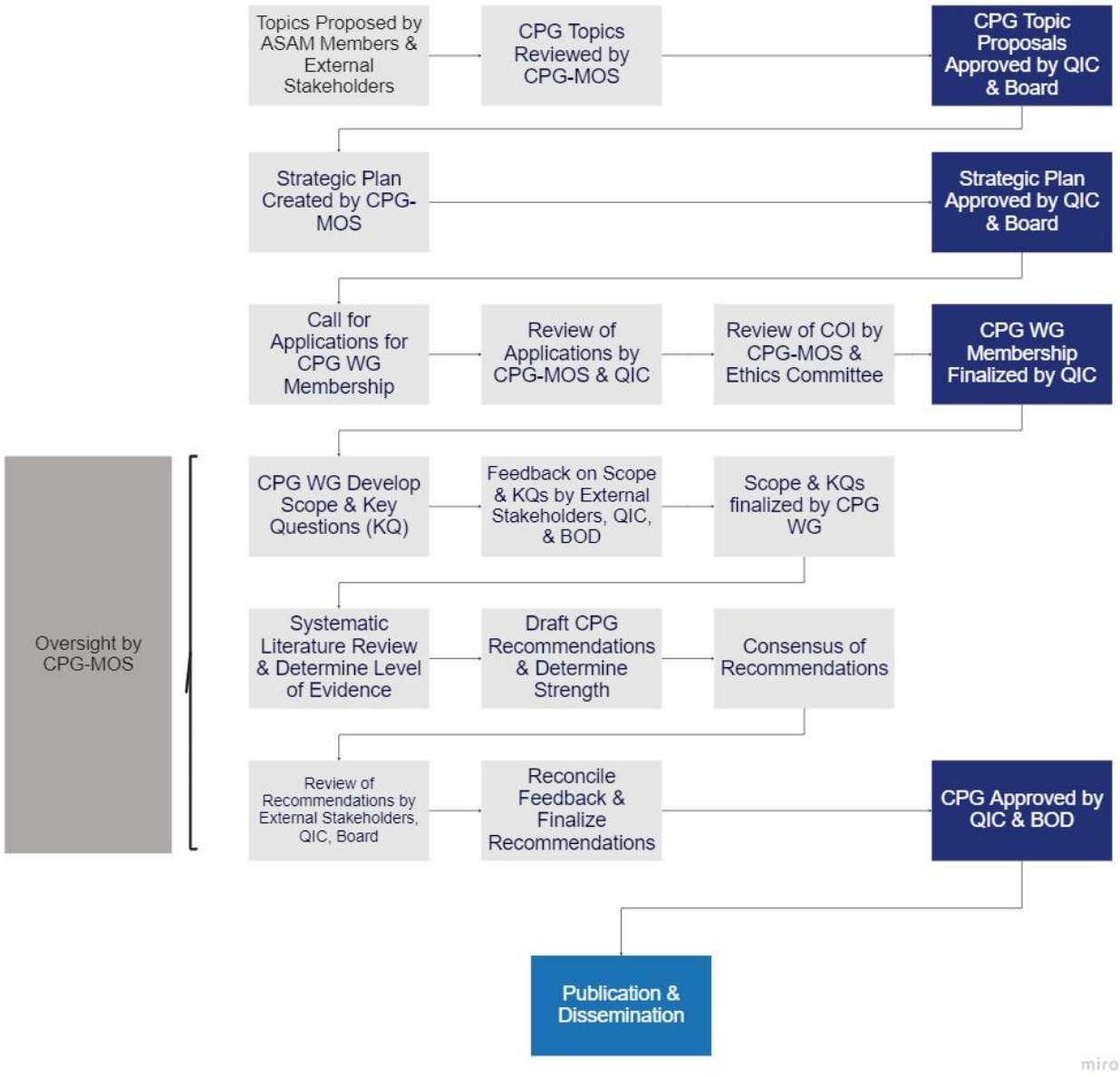
Each individual CPG methodology underwent evidence review, subcommittee deliberation, and consensus. The CPG-MOS subcommittee presented all proposed methodology for review, deliberation and approval to the ASAM QIC. When needed, other ASAM committees such as the ASAM Ethics Committee were engaged for review, deliberation and approval.

In the process of CPG methodology development, it became clear that other non-CPG clinical practice documents may be relevant for ASAM to develop. To promote best practices that remain evidence-based and can be more efficiently produced, the CPG-MOS and the QIC also developed a framework for new clinical documents described here as Clinical Guidance Statements and Clinical Considerations (see Table 1). These clinical documents will have less methodological rigor than the CPG, but will allow ASAM to respond in a timely manner to urgent clinical concerns from its members and the public.

Each section of the CPG methodology is outlined here. See Figure 1 for an overview of the process, and Appendix C for a more detailed overview.

The ASAM CPG Methodology will be reviewed every 5 years by the QIC for updates.

Figure 1. Overview of CPG Process



CPG	Clinical Practice Guideline	**COI**	Conflict of Interest
CPG-MOS	Clinical Practice Guideline Methodology and Oversight Subcommittee	**QIC**	Quality Improvement Council
CPG WG	Clinical Practice Guideline Workgroup	**COI**	Conflict of Interest

Health Equity

ASAM recognizes that the inclusion of diverse people, viewpoints, experiences, and research are key to our success in the development of structurally competent clinical practice guidelines (CPG) that promote health equity among all individuals. Structural competency is defined as “the

capacity…to recognize and respond to health and illness as the downstream effects of broad social, political and economic structures" including systemic racism.[11-14]

ASAM also recognizes that systemic racism disproportionately shapes the environment and life experiences of Black, Hispanic/Latinx, Asian, Pacific Islander, Native American, and other racially oppressed and disenfranchised people (hereinafter collectively referred to as Black, Indigenous, People of Color (BIPOC).[13] ASAM also recognizes that BIPOC and other racially, ethnically, and socioeconomically minoritized individuals have less access to addiction treatment and have historically been excluded from addiction research.

ASAM is committed to developing a systemic approach to diversity, equity, and inclusion (DEI) to confront and reduce racism, racial disparities, discrimination, bias, and health inequities in addiction health care and within our own organization.

ASAM utilizes GRADE methodology in the development of its CPGs. The GRADE Working Group has developed recommendations for considering health equity in GRADE-based guideline development.[15-19] ASAM will utilize this health equity framework in the ASAM CPG Development process.

ASAM is committed to explicitly addressing broad health inequities within their CPG Development and writing process. To achieve this goal, a health equity framework utilizing GRADE methodology will be integrated into the various components of the CPG Development Process and is included in the respective sections.

Definitions of Clinical Practice Guideline, Clinical Consensus Statement, and Clinical Consideration

The CPG-MOS developed definitions for:

- Clinical Practice Guideline (CPG)
- Clinical Consensus Statement
- Clinical Consideration

Clinical Practice Guidelines are the most scientifically rigorous, time-intensive documents, and require a formal systematic literature review to inform the recommendations.

Clinical Consensus Statements are informed by evidence, but may include a broader scope of evidence, such as case studies and reviews, including scoping literature reviews. Clinical Consensus Statements use expert clinical consensus on high-priority topics that may have conflicting or limited evidence.

Clinical Consideration documents address issues that are immediately clinically relevant, though they may have limited evidence. Clinical Considerations are typically informed by narrative literature reviews and based on expert clinical consensus.

Definitions and comparisons between these types of documents are shown in Table 1 below.

Table 1. Comparison between Clinical Practice Guidelines, Clinical Consensus Statements, and Clinical Consideration documents

	Clinical Practice Guideline	Clinical Consensus Statement	Clinical Consideration
Definition	The most rigorous clinical and scientific document ASAM develops informed by a formal systematic review and addresses prevention, screening, diagnosis, and treatment of conditions within the scope of Addiction Medicine. Clinical Practice Guidelines (CPG) include Full CPG Updates and Focused CPG Updates.	While remaining informed by evidence, these statements are more relevant to topics with observational evidence, case studies, and consensus agreement. These statements may also provide consensus agreement when several conflicting clinical guidelines are available. These statements are meant to have high clinical relevance.	Expert consensus-based clinical documents that discuss existing evidence for a focused topic. This document is based on less rigorous methods of development than a Clinical Practice Guideline or Clinical Consensus Statement. This document is meant to have high clinical relevance and address real-practice complexities of care.
Example	ASAM National Practice Guideline for the Treatment of Opioid Use Disorder[20]	ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine[21]	ASAM COVID Clinical Best Practices[22]
Scope	High priority, far reaching topics Addresses prevention, screening, diagnosis, and treatment of conditions within the scope of Addiction Medicine	Reconcile clinical guidelines Provides expert clinical consensus on topics with observational or limited evidence and/or where several conflicting clinical guidelines are available	Tackles issues that emerge as being clinically relevant at a given point in time
Methodology	Formal process. Recommendations follow a formal process with systematic review of evidence as outlined by the new 2023 ASAM methodology	Rigorous review of available evidence and/or existing CPGs and their evidence base is used to develop consensus statements based on reported benefits, harms, costs, patient preferences, and values	Incorporates some evaluation of evidence but can be a narrative review and involve consensus opinion

	Recommendations incorporate consideration of 1) benefits, 2) harms, 3) values and preferences, 4) cost/burden of treatment – and certainty about the estimates of each of these factors Recommendations include a strength of recommendation (strong or weak), and an assessment of the certainty of evidence on which the recommendations is based	Key questions may be developed but formal evidence assessment is not done	Evidence reviews and practice points are updated regularly
Evidence	A formal systematic review of empiric evidence serves as a foundation for recommendations For areas of low evidence, expert consensus may be needed to form CPG	A systematic review of empiric evidence Scoping Review Available CPGs and their evidence base	Narrative or rapid reviews of empiric evidence
Writing Group Selection	Follow pre-defined methodology	Follow pre-defined methodology	Expedited selection of writing group members are based on expertise Follows the same DOI/COI policy
CPG-MOS role	Follow pre-defined methodology	Follow pre-defined methodology	One-two members of the CPG-MOS involved in the oversight and writing
Timeline	12-24 months	6 months – 12 months	3-6 months
Output	Clinical Practice Guideline Full CPG Update	Consensus Statement	Clinical Consideration Practice Advisory

	Focused CPG Update		Best Practice Document
Pros/Cons	Pros: Rigorous, transparent, evidence-based, influential, strong recommendations can influence performance/quality standards Cons: expensive, time-consuming, unclear how best to update, may not be a relevant approach for many topics (e.g., those without good evidence, those requiring rapid turnaround)	Pros: More flexible, quicker, high-priority topics, reconcile conflicting existing CPGs, allows for focus on rationale and application Cons: In practice, important to note that many individuals may not understand the difference between a CPG and Clinical Consensus Statement (i.e., most do not understand nuances in methodology and probably receive these statements as a CPG) Not as clearly tied to discrete set of evidence/less transparent	Pros: Most flexible, clinically responsive, focused, some can be highly cited and often used in clinical practice Cons: Not as clearly tied to evidence, less transparent, theoretically more subject to bias

CPG Topic Identification and Selection

ASAM is the leading organization to inform the clinical practice for addiction medicine professionals. Development of ASAM CPGs requires careful demonstration of the need for new or updated CPGs. The ASAM CPG-MOS subcommittee recognizes that ASAM members constitute a brain trust of stakeholder and expert opinion holders who play an integral role in proposing topics that are meaningful and important to addiction medicine practice. The CPG-MOS also recognizes and values patient and non-ASAM voices to contribute to the field and identify topics that are most important. A formal and transparent process for topic identification and selection will foster interest with ASAM membership and provide an inclusive platform for topics most important to practicing addiction medicine professionals. Once topics are selected, it will be important to maintain a feasible scope for each CPG using a structured framework.

Clinical Practice Guideline Topic Identification

ASAM CPGs address prevention, screening, diagnosis, and treatment of conditions within the scope of Addiction Medicine.

Topics for consideration can be nominated by any ASAM member, CPG-MOS member, ASAM committee and governance of ASAM via direct communication or online submission process once annually three months prior to the national ASAM Annual Conference. Non-ASAM

members including patients with addiction, external stakeholder groups, and other professional organizations may also nominate CPG topics once a year via the same online submission process. Non-ASAM members are encouraged to partner with current ASAM members for CPG recommendations, though this is not mandatory.

The ASAM website submission form will prompt the nominator to respond to the topic importance, relevance to addiction medicine practice, availability of evidence including a list of initial evidence to support the topic and a list of initial key clinic questions, likelihood that the CPG will improve addiction treatment, and need for CPG (see selection criteria below).

Clinical Practice Guideline Topic Selection

Nominated topics for ASAM CPGs will be compiled and reviewed on an annual basis by the CPG-MOS during the annual meeting via virtual or in person meeting.

CPG Topics will be initially selected by the CPG-MOS based on:

- Importance as determined by the prevalence of the condition, effect of the condition on morbidity and mortality.
- Relevance to Addiction Medicine practice by addressing addiction prevention, screening, diagnosis, and treatment of conditions within the scope of Addiction Medicine.
- Availability of evidence to guide development of the CPG.
- Likelihood that a CPG will improve addiction practice and care (e.g., Lack of consensus in the field or CPG do not already exist on the topic).
- Need for a CPG including evidence of a quality gap, time since publication of CPG on the topic by ASAM or other organizations, etc.

Topic Prioritization Process and formal ASAM adoption

Step 1: The CPG-MOS will internally review proposals and decide whether the topic is of potential interest within three months of the annual submission period after receiving the collated list of nominated topics from ASAM staff. When possible, the CPG-MOS will meet in person at the annual ASAM meeting to discuss and decide upon topics. The CPG-MOS will utilize a modified-Delphi process along with anonymous ranking to finalize topics for proposed ASAM CPGs. Topics that are not chosen as CPGs may be alternatively recommended by the CPG-MOS for Clinical Consensus Statements or Clinical Consideration documents.

Step 2: The CPG-MOS will present recommended and not recommended CPG topics to the QIC for approval along with their rank.

Step 3: The QIC will finalize the proposed CPG topics and present them to the ASAM Board for final approval within six months of CPG-MOS topic selection. The number of approved topics will consider ASAM staff capability and resource availability to complete the CPG.

Role of the CPG-MOS, CPG Writing Group Identification, CPG Writing Group Terms, and CPG Writing Group Composition

Structure and Role of CPG-MOS

As part of ASAM's mission to define and promote evidence-based best practices in addiction prevention, treatment, remission, and recovery, the CPG-MOS will provide strategic oversight to the development, implementation, education, and communication of CPGs. The goals of the CPG-MOS are to:

- Establish and publish methodology for the development of CPGs.
- Establish and publish topic selection process.
- Develop a CPG strategic plan.
- Develop methodology for how to manage stakeholder's involvement.
- Develop a process to address and manage conflicts of interest.

The CPG-MOS Committee will provide strategic oversight of several activities, including but not limited to:

- Establishing CPG methodology and ensure its adoption and evolution.
- Proposing CPG topics and present them to the QIC for approval.
- Proposing CPG Writing Group members and present them to the QIC for approval.
- Serving on CPG Writing Group and as a content and methodology experts.
- Guiding education, tool development, communications, and all CPG-derived activities.
- Reviewing disclosure of interest and determine a management strategy for conflicts of interest for potential members of CPG Writing Group along with the Ethics Committee.
- Overseeing the requests to participate on CPG from external organizations.

The CPG-MOS will report to the QIC, which reports to the ASAM Board of Directors. **See charter for composition and terms.**

CPG Writing Group

Composition

Each ASAM CPG will have a committee specific to that guideline called the CPG Writing Group.

The CPG Writing Group will be a multidisciplinary group of 10-14 members. The majority of members will be any of the following:

- Addiction medicine board certified physicians
- Physicians with expertise in treatment of addiction
- Advanced practice clinicians

- Other clinicians with expertise in the treatment of addiction
- Research scientists

To ensure a range of perspectives in the CPG development process, all CPG Writing Groups will strive for diversity in any of the following ways:

- Geographic location
- Training background
- Years of practice
- Race
- Ethnicity
- Gender identity
- Socieoeconomic status
- Immigration status
- Sexual orientation
- Population treated
- Lived experience either personally or family and/or friends impacted by addiction
- Individuals who have specific training in health equity

Depending on the content of a guideline, other experts may be included. The CPG Writing Group will aim to have members who have experience developing CPGs, evidence synthesis, and/or data methodologies. At least one member the CPG-MOS will serve on the CPG Writing Group to ensure fidelity the CPG methods; this member will be non-voting. One other member from the CPG-MOS may serve on the CPG Writing Group as a content expert; this member will be voting. Optimally, at least two members from the CPG Writing Group should also have expertise in epidemiology, public health, or health policy.

All members of the CPG Writing Group must be current ASAM members. The CPG Writing Group will be a standing committee to the QIC.

Additionally, all CPG Writing Group members will demonstrate their understanding of structural competency, health equity, and their commitment to DEI. Their involvement in these activities will be weighed heavily in their selection to be on the Writing Group. Examples of how this may be assessed include asking each CPG Writing Group applicant to describe training, past and current work activities, diversity of patient population served (specifically inquiring about work with racially, ethnically, and socioeconomically minoritized individuals with addiction), and efforts taken to promote health equity. All CPG Writing Group members will be required to complete a one hour training on racism (AMA Historical Foundations of Racism in Medicine)[24]. CPG Writing Group members will be required to review all current ASAM policy documents related to Advancing Racial Justice in Addiction Medicine.[13]

These efforts are iterative as ASAM continually assesses the best ways to promote health equity and continuously develops health equity understanding among CPG Writing Group members.

Terms

CPG Writing Group members will serve during the writing of the CPG. Writing Group members may serve consecutively on additional CPG Writing Groups when their expertise is necessary. There will be continuous attention focused on assuring diversity, equity, and inclusion among the CPG Writing Group membership.

Identification

Prospective participants for a CPG Writing Group will be recruited via open calls for applications distributed through various informal and formal professional networks. Applicants will be screened for conflicts of interest and ability to meet minimum time commitments. Prospective CPG Writing Group members will be evaluated and selected by the CPG-MOS who will then present their proposals of recommended participants for Writing Group membership to the QIC for final approval.

Disclosure of Interest and Management of Conflict of Interest

Policy Rationale and Key Principles

ASAM currently has a policy on conflict of interest that acknowledges the importance to "identify actual or potential conflicts of interest which might improperly affect ASAM activities and decisions. As the professional and business settings and relationships in which ASAM members play significant roles become increasingly varied and complex, informal means of identifying actual or potential conflicts of interest become increasingly inadequate." CPGs are one of the important roles ASAM plays in the treatment of individuals with substance use disorders (SUD). Disclosures of interest and management of conflicts of interest must be carefully and transparently completed. *This CPG COI policy is separate from and more stringent than the current ASAM COI policy, April 2020.*[25]

The intent of disclosure of any potential conflicts of interest is to ensure that the ASAM CPGs provides a balanced, independent, objective and scientifically rigorous product by understanding other interests that could potentially influence the work and decision-making of the CPG Writing Group. Disclosure of interests are not considered to be actual conflicts of interest until the value and nature of the disclosure is reviewed by the CPG-MOS and Ethics committee. When a disclosure of interest is deemed to be a conflict of interest, mitigation will occur as described below to prevent actual or perceived bias during CPG development and to ensure credibility and public trust in ASAM CPGs. The CPG's guiding principle for collection of Disclosure of Interest (DOI) and management of COIs is to prioritize the interests of the patient over any competing or professional interests via an evidence-based assessment of the benefits, harms and costs of an intervention.

The aim of managing conflicts related to organizations that stand to profit from guidelines is to insulate the development process fully from such influence, whereas the aim of managing conflicts related to intellectual and professional interests is to incorporate the perspective with checks and balances.[26]

There are three core tenets of COI management[7,27]:

- **Transparency**
  - Defined as operating in a way that makes it easy for ASAM members, key stakeholders, and the public to see what actions are performed.
  - The DOI/COI management methodology will be easily accessible on the ASAM CPG website and/or via accessible publication.
  - This DOI/COI management methodology will be an iterative process and will be reviewed every 5 years.
  - The DOI along with any COI mitigation plan, if needed, will be readily available for all members of the CPG committees to review in advance of meetings and at the time of meetings.
  - COI mitigation, if it occurs, will accompany all finalized CPGs and be available to the public.
- **Proportionality**
  - Not all relationships carry equal risk.
- **Consistency**
  - COI mitigation strategies should be impartial and consistently managed throughout the CPG writing and development process.

Disclosure of Interests (DOI)

Who Reports DOI?
DOI reporting is required of all those involved in the CPG process including committee members and supporting staff, to include:

- ASAM Board of Directors
- ASAM QIC
- ASAM Ethics Committee (Members Involved in the COI process)
- ASAM CPG-MOS
- ASAM CPG-Writing Group
- ASAM staff and supporting staff (including any commissioned staff from outside ASAM)

DOI Time Frame
DOI refers to active relationships within the last 24 months.

When are DOI collected?
DOI is a continual process. All individuals involved in the CPG process must provide complete, timely, accurate, and signed disclosure statements of their relevant relationships, and must update their DOI annually and prior to any critical meetings of the CPG. If major changes occur in the individual's affiliations, relationships, investments, compensation, and throughout the CPG development process, it is the responsibility of the individual to disclose these changes in a timely manner.

DOI will be updated, collected, and reviewed at the following times:

- Annually, ASAM DOI every January
- Prior to participation in a CPG Writing Group
- Within two weeks of any critical meeting of the CPG
- Prior to any review of the CPG, to include all ASAM Board of Directors, ASAM QIC, ASAM CPG-MOS, ASAM-ethics, and ASAM staff

What DOI are mandated?
DOI includes ALL financial, personal, and professional relationships with industry, individuals, or organizations in the last 24 months for themselves and their partner or spouse. Participants should err on the side of full disclosure if in doubt about whether an interest warrants reporting. All DOI will be obtained via current CV and the Individual filling out an online survey. When more information is needed to understand the disclosure, individuals may be asked to further explain their relationships. See Mandated List of Disclosures below. Each participant will provide the following:

- Updated and current CV.
- Disclosure of recent scholarly and non-scholarly publications.
- All employment (not just that related to health care and includes all employment, even if not related to the CPG).
- Research and consulting financial support related to addiction medicine and behavioral health, such as research funding, speaker's bureau participation, consulting or advisory roles, or expert opinion or expert testimony.
- Investments and proprietary interests related to addiction medicine and behavioral health, such as stocks, bonds, and securities; commercial business interests; and patents, trademarks, and copyrights (this does not include broadly diversified, externally managed investments, such as mutual funds).
- Membership of healthcare-related boards or panels.
- Formal advocacy or lobbying activities via testimony related to addiction medicine or behavioral health.

How is DOI reported?
DOI will be obtained electronically via survey and maintained by ASAM staff. Participants will sign and date DOI forms certifying their knowledge and belief that they have disclosed all financial and non-financial interests and will promptly disclose any changes.

DOI Review, COI Management, and COI Mitigation

DOI Review/COI Mitigation Committee

Two members of the CPG-MOS and three members from the ASAM Ethics Committee will be responsible to review all DOI during the CPG Writing Group selection process. The Chairs of the CPG-MOS and the Ethics Committee will independently nominate these members and the CPG-MOS and Ethics Committees will separately vote for the individuals to serve in this role. The five individuals who serve in this role will report his/her DOI and CVs. The chairs of the CPG-MOS and the Ethics Committee will independently review the DOI and deem the Individuals free of COI that would impact their ability to independently assess the COI of other CPG process members.

For a framework that can serve as a guide to describe COI and various mitigation strategies, see Ngo-Metzger et al., 2018.[23]

Levels of COI

The DOI Review/COI Mitigation Committee will review all DOI and determine a level of COI as none, low, moderate, or high on an individual basis for each participant. When more Information Is needed to determine a level of COI, the DOI Review/COI Mitigation Committee may ask Individuals for more Information about their DOI.

Examples of Potential COI

Final determination of COI level Is made by the DOI Review/COI Mitigation Committee.

High-Level COI

- Any active financial relationship (including employment, stock ownership, excluding mutual funds) with a high-risk entity defined below as a Healthcare Company/Commercial Entity (e.g., an entity that has a direct financial stake in the clinical conclusion of the CPG) are high-level conflicts.
- Involvement with a patient or disease advocacy organizations whose mission is clinically relevant to the topic under discussion.
- Recipient of research funding directly from a pharmaceutical company in the last 24 months.

Moderate-Level COI

- Relationships with entities that may seek to profit by association with guidelines but are not vested in clinical conclusions of guidelines (e.g., proprietary interest in health Information software related to clinical decision making).

Low-Level COI

- Inactive high-level conflict (e.g., served on advisory board for a pharmaceutical company, but stepped down 12 months ago and has no ongoing relationship, paid or unpaid)
- Financial relationships with non-commercial entities (e.g., expert testimony in legal proceedings related to the CPG).
- Non-financial interests may at times be considered a COI. Examples which may be COI may Include depending on the subject matter, person's level of Involvement and other factors to be adjudicated on by the DOI Review/COI Mitigation Committee
    - Authored a manuscript or commentary related to the CPG in the last 24 months (based on publication date).
    - Participated in clinical research related to the CPG as a principal investigator (PI), co-PI, or consultant in the last 24 months (includes federally funded grants and non-federally funded grants) – (e.g., for a CPG on opioid use disorder, served as investigator evaluating medications for opioid withdrawal within previous 24 months).
    - Developed national educational curriculum for a disease process related to the CPG in the last 24 months.

Management of COIs

The DOI Review/COI Mitigation Committee will acknowledge, assess, and manage COI over the course of the CPG development process, as follows:

- **Chairs and Co-Chairs**
  - CPG-Chairs and Co-Chairs will be individually assessed for COI. Each participant will have a mitigation strategy recommended by the DOI Review/COI Mitigation Committee as needed.
  - CPG-Writing Group Chair and Co-Chair (if there is one) are required to be free of high or moderate level COIs relevant to the subject matter of the document during the term of service.
  - Disputes about COI mitigation will be referred to the Ethics Committee for final mitigation determination and adjudication.

- **CPG-Writing Group Members**
  - CPG-Writing group members will be individually assessed for COI. Each participant will have a mitigation strategy recommended by the DOI Review/COI Mitigation Committee as needed.
  - Members who are deemed to have significant COI may be recused from participation in the CPG process, which will be determined by the DOI Review/COI Mitigation Committee.
  - Disputes about COI mitigation will be referred to the Ethics Committee for final mitigation determination and adjudication.

- **ASAM Board of Directors and Quality Improvement Council**
  - Members of the ASAM BOD and QIC will be individually assessed for COI. Each participant will have a mitigation strategy recommended by the DOI Review/COI Mitigation Committee.
  - Participants who are deemed to have moderate and high COI may be recused from participation in the CPG process.
  - Disputes about COI mitigation will be referred to the Ethics Committee for final mitigation determination and adjudication.

- **Serving on other CPG Writing Groups**
  - CPG-Writing Group members (excluding reviewers) cannot serve on the clinical document writing group of another addiction related organization on the same or similar topic for the duration of his or her service on the ASAM CPG Writing Group, unless the Volunteer Leader is serving as an official ASAM Representative.

Report of COIs in the final CPG

Only moderate and high-level COIs will be reported in the final CPG. When COI mitigation strategies are necessary, it will be reported in the final CPG.

Definitions

Disclosure of Interest
A signed declaration of financial and non-financial interests with industry, individuals, or organizations in the last 24 months for person involved in CPG process and their partner or spouse; the person reporting does not make judgments about whether an interest represents a conflict of interest. The DOI Review/COI Mitigation Committee ultimately decides the level of COI for each disclosure.

Conflict of Interest
Any declared interest that may affect or be perceived to affect objectivity and independence in the CPG development and writing process.

Healthcare Company/Commercial Entity
Any for-profit organization that is involved in the production, marketing, distribution, or reselling of health care goods, services, or information consumed by patients, clinicians, and/or support staff. For editors, commercial entities also include publishers. This excludes entities through which the member provides clinical services to patients.

> Note: Types of these companies include, but are not limited to, medical device manufacturers and distributors, pharmaceutical, pharmacy, laboratory testing, electronic health records, hospitals, outpatient care centers, wearable devices for health and fitness, billing services, apps, etc.

Associated Healthcare Organizations
Any non-profit, government, or academic institutions that represent, advocate, legislate, educate, and/or provide treatment for stakeholders of the healthcare system(s). Excludes entities through which the member provides clinical services to patients and/or conducts research.

Direct Financial Relationship
A relationship held by an individual that results in wages, consulting fees, honoraria, or other compensation (in cash, in stock or stock options, or in kind), for the individual's services or expertise.

ASAM staff
Refers to ASAM employees at the level of manager or above.

Determining the Scope of the CPG and Key Questions

ASAM CPGs address prevention, screening, diagnosis and/or treatment of conditions within the scope of Addiction Medicine. Once a CPG topic is selected, the scope of the topic and approach to review will be defined jointly by the CPG-MOS and the CPG Writing Group.

Key questions will be developed by the CPG Writing Group that address prevention, screening, diagnosis, and/or treatment framed in terms of Populations, Interventions, Comparators,

Outcomes, Timing and Settings (PICO-TS). The PICO-TS framework is consistent with the standard approach for systematic reviews, as adopted by the Agency for Healthcare Research and Quality,[23] the American College of Physicians,[2] the American Psychiatric Association,[4] and the U.S. Preventive Services Task Force,[7] among others.

CPG key questions will consider health equity as an outcome and consider patient-important outcomes relevant to health equity.

Key questions will undergo stakeholder review prior to finalization. Final key questions for the CPG will be approved by the CPG-MOS prior to initiation of the formal literature review.

Systematic Review

Background

A quality clinical practice guideline should be based on a systematic review of the literature.[6] This critical initial step helps ensure that all relevant evidence is identified, critiqued, and synthesized using methods that help reduce the likelihood of bias. Typically, the systematic review is done prior to initiating work on the CPG by a group separate from the CPG Writing Group.

Systematic reviews use well-established methods to search, identify, appraise, and synthesize the literature examining prespecified key questions of interest.[6] Systematic reviews can contain a qualitative synthesis of evidence, a quantitative synthesis of evidence, or a combination of both. A meta-analysis is simply the term given to the quantitative synthesis of evidence: all meta-analyses are based on a systematic review of the literature, but not all systematic reviews include a meta-analysis. Narrative reviews are often used to broadly summarize a topic of interest, but do not adhere to strict inclusion and exclusion criteria and search parameters nor use explicit criteria to evaluate the quality of evidence.

Broadly speaking, a systematic review includes the following six processes[6,28]:

1. Define the question(s) of interest and methods
2. Conduct literature search
3. Identify studies and other sources of information for inclusion
4. Data abstraction
5. Critical appraisal
6. Synthesis of evidence

Topic/Scope development

As with any research project, a systematic review should start with one or more key questions of interest and an established set of criteria to guide the inclusion or exclusion of studies. The systematic review team would work with the CPG Writing Group to define the questions and

criteria of interest. The key questions and inclusion and exclusion criteria should define the scope according to a "PICOTS" framework as follows[23]:

- Population (e.g., adults with opioid use disorder)
- Intervention (e.g., office-based buprenorphine treatment)
- Comparator (e.g., placebo, other drugs, non-pharmacologic interventions)
- Outcome(s) (ideally prioritize no more than 5-7 outcomes of interest)
- Timing – (i.e., is there a minimum study follow-up period that would be meaningful? For instance, the CPG Writing Group may not want to provide recommendations for a years-long treatment based on evidence from very short-duration studies)
- Setting – (e.g., office-based, inpatient, community-based)
- Study design (for some questions, limiting the review to randomized controlled trials may be appropriate, while for others – such as questions about harms – the inclusion of observational studies may be appropriate)

A protocol that details these questions and the inclusion/exclusion criteria along with the proposed study plan should be developed utilizing the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) framework.[29,30] The finalized protocol should be uploaded to a site such as PROSPERO[31] prior to work beginning on the review (many journals require reviews to have been registered, similar to requirements that trials are registered in trial registries).

Literature Search

An important first step in systematic reviews, is a quality literature search. There are various nuances to the design of a complex literature search, and seemingly minor differences can influence the literature yield. The search should be guided by someone trained in literature search methodology (such as a research librarian). Depending on the topic, several literature databases may need to be included in the search including PubMed, OVID MEDLINE, PsycINFO, AHRQ, and the Cochrane Library to name a few. Also, depending on the topic, it may be appropriate to include "gray literature" which might include information from websites, governmental reports, conference abstracts and so forth.

Identify Studies for Inclusion

Unfortunately, there is not currently a well-validated method for computerized identification of studies to include in a systematic review. Typically, a search would include a relatively large number of titles and abstracts which are reviewed by study team members. There is no "correct" number of titles/abstracts that a literature review should identify, but a small yield (e.g., 100-200 or less) may indicate that the search strategy was too narrow while a very large yield (e.g., 5000-7000 or more) may indicate that the search strategy is too broad.

The initial review of titles and abstracts is used to very quickly identify studies that are clearly irrelevant and can be safely excluded at the abstract level, as well as potentially promising studies that would need to be reviewed in greater depth at the "full-text" level. Typically, teams will use a reference manager and/or systematic review organizational platform to help track studies.

There is debate as to whether titles and abstracts should be reviewed blindly by two different study team members. If there is not time or staffing to do so, it is still important to conduct an initial training review to ensure study team members are interpreting and applying inclusion/exclusion criteria consistently. This can be done by randomly selecting a small set of abstracts and asking study team members to independently review them.

It is standard practice for studies that move on to "full-text" review to be independently reviewed by two study team members. If there is disagreement about the inclusion of a given study, this is typically resolved through discussion with a third study team member. It is good practice to track the reasons for exclusion at the full-text level according to pre-specified criteria since this information will be used in the review publication's literature flow diagram (which is analogous to the study flow diagram that might accompany a clinical trial).

Data Abstraction

The study team will develop a data abstraction template to guide the process of extracting discrete data elements from each included study which can then be used to synthesize, compare, and contrast data across studies. Typically, the data abstraction elements will mirror the pre-specified "PICOTS" criteria (see above). To ensure that data extraction is accurate, it is useful to have at least two people involved with data abstraction from each study. This can be done by having two people independently abstract data from each study and then reconciling any differences through discussion, or by having one-person abstract data and having a second person look over the entries for accuracy.

Critical Appraisal

One of the most important elements of a systematic review – and one of the key differences between systematic and narrative reviews – is the critical appraisal of each included study. Quality assessment and risk of bias evaluation are other commonly used terms for critical appraisal. Critical appraisal is a systematic evaluation of the methodologic strengths and weaknesses of each study. There are many potential forms of bias that can systematically threaten the validity of a study's results.

There are many tools available to guide the critical appraisal of individual studies.[32] One of the most commonly used tools is the "risk of bias" tool developed by the Cochrane Collaborative to assess the internal validity of trials (there is an updated version of this tool called ROB 2.0).[33,34] A trial that is determined to have a "high risk of bias" has certain key methodologic flaws that have the potential to introduce systemic bias into a study and, therefore, threaten the believability of its results.[34] The critical appraisal of each study is typically done independently by two study team members – any discrepancies are resolved through discussion, or by a third independent appraisal.

Tools such as a funnel plot may be used to consider the potential impact of non-reporting biases on the results of a systematic review as well.

There are also tools available to guide the critical appraisal of observational studies.[35,36] The assessment of observational study quality is, in some respects, more challenging than the quality assessment of trials and a detailed discussion of this is beyond the scope of this section. There are several tools available for different types of observational study designs, for example:

- ROBINS-I for non-randomized studies of interventions[37,38]
- SIGN and Newcastle-Ottawa for cohort studies[39,40]
- SIGN, Newcastle-Ottawa, and CASP for case-control studies[39-41]
- AHRQ and Johanna Briggs Institute tools for cross-sectional studies of prevalence[35,42]
- QUADAS-2 for studies of diagnostic tests[43]

Synthesis of Evidence

One of the most important aspects of a systematic review is the synthesis of evidence across a body of literature. It is critical that individual studies are contextualized within the larger body of evidence examining a given question of interest. All systematic reviews include a qualitative synthesis of evidence, which is a narrative description of what the evidence shows at a high level. The synthesis includes information about similarities and differences of findings across studies, key studies that contribute the most to the understanding of a given question, and information about the applicability of the evidence to different population or settings. It is as important for these syntheses to clarify what is known from the evidence as it is to clearly delineate gaps in evidence.

Some systematic reviews may also include a quantitative synthesis of evidence also known as a meta-analysis. There are several things to consider when deciding whether a meta-analysis is appropriate. For example, clinical trials lend themselves more readily to meta-analysis than observational studies of treatment effects (with some exceptions). The study team will also need to determine whether there is too much clinical heterogeneity across studies to conduct a meta-analysis. Clinical heterogeneity refers to differences in populations, interventions, study follow-up, outcome definitions and so forth across studies. If there are many meaningful differences in these factors across studies, a meta-analysis of their results could be misleading. On the other hand, assessing results across a body of studies that have some small differences can be an advantage since it allows for the examination of a body of literature that may be more broadly applicable than a very narrowly defined one. The study team – usually in consultation with a statistician with expertise in meta-analysis – can also explore heterogeneity in statistical terms and can evaluate sources of heterogeneity by conducting subgroup and sensitivity analyses (and even meta-regression analyses for larger bodies of literature).

The systematic review team will also note the certainty of evidence supporting each finding using well-established criteria such as those proposed by the GRADE working group (see subsequent section on GRADE rating).

Methodology

ASAM will utilize the systematic review methods described above in their CPGs including clearly defined key questions following the PICO-TS framework, literature search, identification of studies for inclusion, data abstraction, critical appraisal of the literature, and qualitative and

quantitative synthesis of the literature. To ensure quality CPG, ASAM will seek staff or contractors who are trained in systematic search strategies and systematic review methods.

Health Equity & Systematic Review

The systematic review team (ASAM staff or contractors) will search selected databases for health equity, DEI, and social determinants of health related to the CPG topic. When synthesizing the literature, we will utilize the PROGRESS-plus elements outlined by GRADE as appropriate.[15-18] Data extraction tables will summarize patient characteristics who were involved in clinical research and report inclusion of racially, ethnically, and socioeconomically minoritized populations. When there is a notable lack of inclusive research populations, this will be highlighted and considered in the CPG recommnendation and strength of evidence statements. Evidence gaps related to race, ethnicity, socieoeconomic disadvantage and other health inequities will be highlighted.

Grading Quality of Evidence and Strength of Recommendations

Background

CPGs are one way to translate evidence into clinical practice. Ideally, a CPG is based on a systematic review of the evidence conducted by a group with experience in evidence synthesis. The CPG Writing Group is to use its expertise and perspective to translate evidence into practical recommendations that can be used by clinicians, policymakers, and the public. There are four elements to consider when translating evidence from the systematic review into recommendations:

- Benefits and harms of the intervention or diagnostic test in question
- Certainty of evidence about these benefits and harms
- Values and preferences of the populations affected by the guideline
- Costs and/or burden of the intervention or diagnostic test

The systematic review will outline estimates of the benefits and harms of a given intervention or diagnostic test for each outcome of interest. The systematic review will also qualify how convincing the body of evidence is that underlies each effect estimate. The degree to which a body of evidence is convincing or unconvincing is most commonly referred to as the "certainty of evidence" (which is synonymous with previously used terms like strength of evidence or quality of evidence).

The most commonly used framework to assess the certainty of a body of evidence was initially developed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) working group in 2000.[5,44-47] The certainty of evidence is typically assessed by the investigators who conduct the systematic review on which the guideline is based. There is also a GRADE framework for assessing the strength of recommendation – this step, which is covered in

a subsequent section of this guide, is typically under the purview of the CPG writing group and is done while or after the guideline recommendations are being drafted.[46,47]

The certainty of a body of evidence is assessed for each intervention/diagnostic test and outcome pair, and it is based on consideration of several concepts: the quality or risk of bias of the individual studies that comprise the body of evidence, the consistency of findings across these studies, the precision of effect estimates, the directness of the outcomes and populations assessed in the pool of studies to those that are of most interest to the guideline developers, and reporting bias (such as publication bias).

The certainty of evidence is rated as high, moderate, low, or very low/insufficient. The GRADE working group labels the last category "very low", while the modified method used by the Agency for Healthcare Research and Quality (AHRQ) and the American College of Physicians (ACP) labels the last category "insufficient".[5,35,46-48] The ASAM CPG will use the AHRQ/ACP modification for its certainty of evidence ratings. Conceptually, certainty of evidence categories connotes the relationship between the effect estimates in the published literature and the "true" estimate of effect as follows:

- **High:** Raters are very certain the estimate of the effect of the intervention on the outcome lies close to the true (unbiased) effect. When an outcome is rated as "High," additional studies would not change the estimate of the effect of the intervention on that outcome.

- **Moderate:** Raters are moderately certain in the estimate of the effect of the intervention on the outcome. The true effect is likely to be close to the estimate of the effect, but there is a possibility it is different. When an outcome is rated as "Moderate," additional studies would slightly change the estimate of the effect of the intervention on the outcome, but it is unlikely to change the direction of the effect.

- **Low:** Raters have low certainty in the estimate of the effect of the intervention on the outcome. The true effect might be substantially different from the estimate of the effect. When an outcome is rated as "Low," additional studies will likely change the estimate of the effect of the intervention on the outcome and could change the direction of the effect.

- **Insufficient evidence:** Raters have no certainty in the estimate of the effect of the intervention on the outcome. When an outcome is rated as "insufficient" additional studies will very likely change the estimate and direction of the effect.

Reviewers methodically consider [49]each GRADE factor when arriving at a certainty of evidence rating. A body of evidence in which, say, most studies are methodologically flawed (i.e., have high risk of bias) may be "downgraded" for this reason. Or if there are several well-done studies with conflicting results, the certainty of evidence may be downgraded for inconsistency. Even though there are well-established methods for GRADE-ing the certainty of a body of evidence, the summary ratings still carry a degree of subjectivity, so it is important that the rationale for a given certainty of evidence rating is articulated. Each of the factors considered in establishing a certainty of evidence rating is described in more detail in Table 2 below.

Table 2. ASAM Guideline Grading System

Strong **Strength of Recommendation**	**Weak** **Strength of Recommendation**
-Benefits outweigh risks OR Risks outweigh benefits -High Quality Evidence	-Benefits are similar to risks -High Quality of Evidence
-Benefits outweigh risks OR Risks outweigh benefits -Moderate Quality Evidence	-Benefits are similar to risks -Moderate Quality of Evidence
-Benefits outweigh risks OR Risks outweigh benefits -Low Quality Evidence	-Benefits are similar to risks -Low Quality of Evidence
Insufficient Evidence to Support Recommendation Strength	

Risk of Bias (Study Quality/Internal Validity)

Flaws in a study's design or the way it is reported can reduce confidence in its findings. In fact, one of the most important aspects of a systematic review is the critical appraisal of each individual study's risk of bias.[49] The ASAM CPG will use systematic reviews which use a risk of bias assessment tool developed by the Cochrane collaboration (the Cochrane ROB 2.0 tool). This is the most commonly used standardized instrument for assessing the quality of randomized controlled trials. The methodology for examining the quality of observational studies is less well-established, but there are several instruments available. The ASAM CPG will use an instrument developed by the Scottish Intercollegiate Guidelines Network (SIGN) for cohort and case-control studies. It is standard practice for systematic review teams to have 2 investigators independently assess each study's risk of bias (disagreements are resolved by involving a third researcher when necessary).

Randomized Controlled Trials (RCT)

Within Cochrane's RoB 2.0 tool, a rater must evaluate each risk of bias domain and select an overall rating of:

- Low risk-of-bias
- Moderate risk-of-bias (Cochrane defines as "Some concerns")
- High risk-of-bias

Low-risk-of-bias RCTs generally include a clear description of the population, setting, intervention, and comparison groups; a random and concealed allocation of participants to study groups; low dropout rates; and intention-to-treat analyses (i.e., an analysis based on group assignment at baseline).

Moderate-risk-of-bias RCTs have incomplete information about methods that might mask important limitations or other biases such as moderate dropout rates.

High-risk-of-bias RCTs have clear flaws that could introduce significant bias, which might include an insufficient approach for randomization or allocation concealment, high rates of attrition without intention-to-treat analysis, or differences between personal characteristics between groups at baseline.

Observational Studies

For observational (cohort and case-control) studies, using SIGN's forms, a rater must also evaluate each risk of bias domain and select an overall rating of:

- Low risk-of-bias (SIGN defines as "High quality")
- Moderate risk-of-bias (SIGN defines as "Acceptable")
- High risk-of-bias (SIGN defines as "Unacceptable")

Cohort Studies

Low-risk-of-bias cohort studies include a sample representative of the source population, have low loss to follow-up, and measure and consider relevant confounding factors (e.g., age, income, health status).
`

Moderate-risk-of-bias cohort studies might not have measured all relevant confounding factors or adjusted for them in statistical analyses, have loss to follow-up that could bias findings, consist of a sample not representative of the source population, or have potential conflicts of interest that are not addressed.

High-risk-of-bias cohort studies have clear and serious bias that would affect findings, which might include not adjusting for all major confounders or have high loss to follow-up.

Case-Control Studies

Low-risk-of-bias case-control studies include appropriate and clear consideration and selection of cases and controls, valid measures of exposures in both groups, and statistical adjustment for all major confounding variables.

Moderate-risk-of-bias case-control studies might not have measured all relevant confounding factors or adjusted for them in statistical analyses, might include controls not fully representative of cases, or might not have addressed potential conflicts of interest.

High-risk-of-bias case-control studies have clear and serious bias that would affect findings, which might not be adjusted for all major confounders or selection of controls from a highly different population than cases.

The other main categories for GRADE-ing the certainty of a body of evidence include:

- **Imprecision:** The variation or spread in the data as generally indicated by a 95% confidence interval. If the 95% confidence interval is wide, the rater might downgrade the outcome 1 level.

- **Indirectness:** The generalizability of body of evidence of the outcome to the intended population. For example, modern recreational cannabis might not be applicable to cannabis used in studies completed in the past. In this scenario, the rater might downgrade the outcome 1 level.

- **Inconsistency:** The between group differences in the estimate of the effect of the intervention. This might be shown through measures of heterogeneity in a meta-analysis (e.g., I^2 statistic) or through observed clinical heterogeneity between studies. An example of clinical heterogeneity would be differences in health status in participants between studies. If heterogeneity is observed and cannot be explained by other study factors, then the rater might downgrade the outcome 1 level.

- **Publication bias:** A bias in which positive studies (i.e., showing a significant benefit of an intervention) are more likely to be published. If a funnel plot or a review of the literature shows negative (i.e., showing no significant benefit of an intervention) and smaller studies are not a part of the literature base, then the rater might want to downgrade the outcome 1 level.

For all the reasons above, if the issue is particularly severe, then the rater might downgrade the outcome by 2 levels instead of 1 (from high to low certainty of evidence).

GRADE criteria can upgrade the certainty of the evidence for an outcome. Upgrading is generally reserved for observational studies. Unlike RCTs, which start at "High," observational studies start at "Low" certainty of evidence. The following are criteria to consider for upgrading the evidence:

- **Large effect**: The effect of the intervention on an outcome and if the magnitude of the effect is large (e.g., a risk ratio greater than 3), then a rater might increase the certainty of evidence by 1 level.

- **Dose-response relationship:** A scenario when an intervention increases or decreases in dose or frequency, then the outcome also increases or decreases. If this type of relationship is observed, then a rater might increase the certainty of evidence by 1 level.

- **All plausible confounding:** A scenario where all relevant confounding variables (i.e., a variable that distorts the relationship between the intervention and outcome) are accounted for in a statistical analysis. If this is observed in the analysis, then a rater might increase the certainty of evidence by 1 level.

Similarly, to downgrading the certainty of the evidence, if one of the above criteria to consider for upgrading is also substantial, then a rater might upgrade the rating by 2 levels.

GRADE can be applied to outcomes with data from a meta-analysis or through a qualitative (or narrative) synthesis.

Insufficient evidence and Expert Opinion

There are many areas of addiction medicine in which the evidence base is still accumulating, but the urgency and severity of addiction-related issues demand that clinicians and public health officials act even in the face of imperfect empirical evidence. For this reason, ASAM feels it important to issue expert-opinion based recommendations when the certainty of evidence for a given question is insufficient.

Like other recommendations, these expert-based recommendations would follow a period of open debate among CPG Writing Group members. Recommendations based solely on clinical judgement and clinical experience will be thoroughly scrutinized to eliminate bias and self-interest. ASAM will strive for consensus among experts for these recommendations. In cases where this is not possible, ASAM will articulate points of disagreement and their rationale alongside the CPG recommendation. Recommendations based on low or insufficient evidence will require >=70% consensus from the CPG Writing Group (see consensus methods).

It is important to clearly distinguish expert-based recommendations from those that are based on evidence. ASAM will have a separate section for expert-only based recommendations and consider other ways of identifying them (e.g., using a different background color).

The Strength of Recommendations

The GRADE working group has also developed methods for determining the strength of a clinical guideline recommendation.[46,47] This is done by the guideline group and is distinct from and distal to the step of GRADE-ing the certainty of a body of evidence. By assigning a strength of recommendation, the guideline group can distinguish recommendations that are important to apply to many or most patients from those that might be important in some circumstances but not others. In practical terms, strong recommendations are those that might be applied for many or most patients in many or most circumstances. These are recommendations that might apply without extensive shared decision making; they are also recommendations that might serve as the basis for performance or quality metrics. Weak recommendations (also known as conditional recommendations) are important to know about but may not apply to or be of interest to everyone.

As described above, there are four factors that are considered when translating evidence to practice, and these same factors apply to strength of recommendation discussions: the benefits and harms of an intervention or test; the certainty of evidence about these benefits and harms; the values and preferences of the target population; and the cost and/or patient (or societal) burden of the intervention or test. Interventions for which the benefits and harms are finely balanced might deserve a weak recommendation. Similarly, if the body of evidence is weak (of low certainty), it would be very unusual to issue a strong recommendation. When the values and preferences about a given intervention are likely to be highly variable across a population a weak recommendation is likely more appropriate. For more information on factors that affect the strength of recommendations, see Guyatt et al.[47]

The ASAM CPG Writing Group will use GRADE methodology to both determine the certainty of evidence and strength of recommendations for each clinical practice recommendation. The ASAM CPG Writing Group will adopt the modified GRADE methodology used by the ACP (see ACP modified GRADE methodology)[48] to rate the certainty of evidence for each key question in

the CPG as high, moderate, or low based on factors detailed above. The factors that support each quality rating will be summarized in standardized GRADE evidence summaries (evidence profiles or summary-of-findings tables), which report both relative and absolute outcome effects. Two independent assessors will determine the quality of each study. A third assessor with extensive methodologic experience will resolve disagreements among the assessors, when needed.

Expert-opinion based recommendations may be needed based on insufficient evidence. In these situations, ASAM CPG Writing Group will clearly distinguish expert-based recommendations from those that are based on evidence. ASAM will have a separate section for expert-only based recommendations.

Table 3. GRADE methodology in practice (adapted from Qaseem, et al. Ann Internal Medicine, 2010)

<table>
<tr><th>Grade of Recommendation</th><th>Benefit Versus Risks and Burdens</th><th>Methodological Quality of Supporting Evidence</th><th>Interpretation</th><th>Implications</th></tr>
<tr><td>Strong recommendation, high-quality evidence</td><td>Benefits clearly outweigh risks and burden or vice versa</td><td>RCTs without important limitations or observational studies with significant treatment effect</td><td rowspan="2">Strong recommendation; can apply to most patients in most situations without reservation</td><td rowspan="3">For patients, most would want the recommended course of action and only a small number would not; a person should request discussion if the intervention was not offered.

For clinicians, most patients should receive the recommended course of action.

For policymakers, the recommendation can be adopted as policy in most situations.</td></tr>
<tr><td>Strong recommendation, moderate-quality evidence</td><td>Benefits clearly outweigh risks and burden or vice versa</td><td>RCTs with important limitations or strong evidence from observational studies</td></tr>
<tr><td>Strong recommendation, low-quality evidence</td><td>Benefits clearly outweigh risks and burden or vice versa</td><td>Observational studies or case series</td><td>Strong recommendation but may change when high quality evidence is available</td></tr>
<tr><td>Weak recommendation, high-quality evidence</td><td>Benefits closely balanced with risks and burdens</td><td>RCTs without important limitations or observational studies with significant treatment effect</td><td rowspan="2">Weak recommendation; best action may differ depending on patient values</td><td rowspan="3">For patients, most would want the recommended course of action but some would not depending on their circumstances and values.

For clinicians, different choices will be appropriate for different patients and patient-centered decision making should be the goal based on patient values, preferences and circumstances.

For policy makers, policymaking will require substantial debate and involvement of many stakeholders.</td></tr>
<tr><td>Weak recommendation, moderate-quality evidence</td><td>Benefits closely balanced with risks and burdens</td><td>RCTs with important limitations or strong evidence from observational studies</td></tr>
<tr><td>Weak recommendation, low-quality evidence</td><td>Uncertainty in the estimates of benefits, risks, and burden; benefits, risks and burden may be closely balanced</td><td>Observational studies or case series</td><td>Very weak recommendations, other alternatives may be equally reasonable</td></tr>
</table>

Insufficient	Balance or benefits and risks cannot be determined	Evidence is conflicting, poor quality, or lacking	Insufficient evidence to recommend for or against routinely providing the care	For patients, clinicians and policy makers, decisions based on evidence for scientific studies cannot be made

Clinical Recommendation Development

Consensus Building

CPGs that integrate diverse opinions and subject matter expertise are required to produce optimal recommendations. CPG writing groups have grown to be more diverse and inclusive and as such, this can present challenges for decision making and consensus, such as ensuring that all writing group members have a voice and can influence the results of the guideline recommendation development process, ensure transparency, deal with disagreement, achieve consensus, and resolve situations where consensus is not possible.

The WHO handbook notes[50]:
"By dictionary definitions, the term consensus means "general agreement." However, dictionaries do not clarify whether unanimity is required or whether agreement among a large majority suffices for consensus to be present. In some cases, consensus is interpreted to mean general acceptance by a group rather than agreement by all its members. These differences point to the fact that the process of reaching consensus, regardless of the definition used, always involves discussion and compromise to arrive at a decision that is acceptable to all parties."

CPG Writing Groups sometimes use informal processes to deal with challenges toward consensus, but this can be inefficient and ineffective in certain groups. Time pressures, lack of leadership and dominance by individuals with powerful personalities and intimidating reputations can threaten the integrity of the process. Therefore, it is important to employ strategies to effectively address the complexities of developing sound and well-respected clinical practice guidelines that are based on true consensus.

Consensus Methodologies

The first component for developing consensus involves use of a structured methodology to collect, analyze, and summarize relevant evidence to produce and grade the Certainty of Evidence for each Clinical Practice recommendation. This is done via the systematic review and GRADE framework and will be integrated into the ASAM Clinical Practice Guideline (CPG) methodology. The second component relies on processes to encourage CPG Writing Group consensus for the determination of the Strength of each CPG Recommendation, and encourages CPG Writing Group members to contribute equally for this consensus determination.

A common technique to develop consensus is the "Delphi method", which is used in the healthcare setting as a reliable means of determining consensus for a defined clinical problem.[51] This method is an iterative process that uses a systematic progression of repeated rounds of voting and is an effective process for determining expert group consensus. Recent adaptations of the Delphi method allow for virtual Input ("e-Delphi") and mix qualitative and quantitative approaches to Identify best practices.

Another method is the “Nominal Group Technique.” This approach elicits opinions from a small group of people who meet in person and have an equal opportunity to talk. There is formal feedback, structured face to face interactions, ranking of opinions, and an explicit method for final decision making that may also involve ranking of options from most to least acceptable by CPG Writing Group members. When needed, the Delphi and Nominal Group techniques can be combined.

Another approach, which was initially developed by the United States National Institutes of Health, is a “Consensus Development Conference”. This approach involves bringing together a selected group of people (as few as 10) to reach consensus about an issue during a two- to three-day meeting. Various interest groups or experts who are not on the decision-making panel present the evidence they have gathered on an issue. The panel then retreats to consider the evidence presented and attempts to reach a consensus. Both the open conference and the private group discussion are facilitated by a chair. In the Consensus Development Conference method, no formal guidance is given as to how consensus is ultimately reached. Thus, the method serves to exemplify the overlap between formal and informal consensus methods. Voting can be a used to achieve consensus: A show of hands or an anonymous vote might be used during the Consensus Development Process to assess progress and identify diverse viewpoints.

Consensus Decision Making

In CPG Writing Groups, consensus decision-making is a process whereby the consent of all committee members is pursued. When consensus has been reached, it generally means that every committee member finds the proposed resolution acceptable – or at least lends it support, even if less than wholeheartedly.

The level of agreement necessary to finalize a decision is known as a “decision rule”. Decision rules for consensus vary across a broad range: unanimous agreement; unanimous consent; unanimous agreement minus one or two votes; unanimous consent minus one or two group members; supermajority or simple majority. The thresholds for defining supermajority can vary in themselves, with some of the most common being 90%, 80%, 75%, two thirds and 60%. A simple majority is reached when more than 50% of group members support a given decision.

Unanimity is desirable but may be difficult to achieve, especially in large and diverse groups. Hence, before starting the decision-making processes, all CPG Writing Groups should have a plan as to how to move forward when unanimity cannot be achieved. This plan should encompass specific decision rules and should be discussed a priori to ensure that unanimity will be genuine and not the result of pressure, coercion, fear, undue influence, failure of group members to comprehend alternatives, or fatigue with the debate.

The results of the systematic review and certainty of evidence for each key question of the CPG are presented to the CPG Writing Group members by non-voting members of the CPG team (i.e. ASAM staff or independent contractors) two weeks prior to a planned Consensus Development Conference meeting. CPG Writing Group members are expected to formulate their own, independent opinions for each CPG Recommendation and strength of recommendation based on this information.

CPG Writing Group members meet for a Chair-moderated and facilitated face to face (in person or virtual) meeting utilizing Consensus Development Conference methodology. CPG Recommendations and strength of recommendations consensus are sought at this meeting via moderated and time-limited discussion. Each member of the CPG Writing Group has an equal opportunity to speak to each CPG recommendation (wording and content) and strength of recommendation determination. Following discussion, a formal voting process takes place among CPG Writing Group voting members for the CPG recommendation followed by a formal vote for the strength of recommendation determination. Votes are submitted as “agree,” "disagree", “abstain,” or “absent.” Open votes are taken by voice or hand, without anonymous ballots. Members recused from voting for reason of potential conflict of interest are recorded as "recused" and do not vote; these members may participate in the CPG deliberation discussion.

Each CPG recommendation and strength of recommendation determination will require a minimum of ≥70% of CPG Writing Group voting members to "agree" for consensus to be reached. *(This requires ≥70% CPG Writing Group members to be voting members based on CPG COI mitigation methodology AND confirmation of ≥70% attendance of CPG Writing Group voting members at the Consensus Development Conference).*

Motions on procedural or methodological decisions requiring a vote are passed when a simple majority (>50%) of CPG Writing Group voting members vote “agree.”

When consensus is not reached during the Consensus Development Conference, the conference may be followed by a virtual, modified online e-Delphi process for purposes of recommendation "word-smithing" revisions and additional deliberation time. Recommendation revisions will be shared with CPG Writing Group members via survey software and sent to CPG Writing Group members via email for a provisional vote. CPG Writing Group voting members will have a limited time to respond to the survey via "agree", "disagree", or "abstain". Lack of response will be counted as "absent". Members recused from voting for reason of potential conflict of interest are recorded as "recused" and do not vote. Consensus will be defined as ≥70% of CPG Writing Group voting members "agree".

The e-Delphi process will be followed by a second (or third) Consensus Development Conference meeting for final approval of CPG Recommendations and strength of evidence determinations. Confirmation of ≥70% attendance of CPG Writing Group voting members at the Consensus Development Conference will need to occur for the meeting to proceed. Final consensus will be reached when ≥70% of CPG Writing Group voting members "agree".

If consensus is not achieved by the above processes, a GRADE grid methodology (see Table 4)[52] will be implemented to facilitate consensus during a face to face (virtual or In person) Consensus Development Conference.

All CPG Recommendations and Strength of Evidence require face to face (virtual or in person) voting for final adoption.

If consensus Is not achieved through the above processes, the CPG recommendation will not be adopted.

Table 4. GRADE grid for recording CPG Writing Group members' views in development of guidelines

(adapted from, Jaeschke, et al. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive, BMJ 2008; 337:a744, https://www.bmj.com/content/337/bmj.a744.long##)

	GRADE score*				
Balance between desirable and undesirable consequences of intervention	Desirable clearly outweigh undesirable	Desirable probably outweigh undesirable	Trade-offs equally balanced or uncertain	Undesirable probably outweigh desirable	Undesirable clearly outweigh desirable
Recommendation	Strong: definitely do it	Weak: probably do it	No specific recommendation	Weak: probably do not do it	Strong: definitely do not do it

*CPG Writing Group Members mark an "X" In the cell which best corresponds to their assessment of the available evidence, In terms of benefits versus disadvantages.

Final voting results for each CPG recommendation and strength of recommendation are documented and shared as a supplement to the CPG.

Consensus by ASAM Quality Improvement Council and Board of Directors

Final CPG recommendations require a simple majority (≥50%) consensus by eligible voting members of the ASAM Quality Improvement Council (QIC) and the ASAM Board for final approval. Members of the QIC and BOD recused for reasons of potential conflicts of interest are recorded as recused and do not vote; these members may participate in deliberation.

Votes are submitted as “yes,” “no,” “abstain,” or “absent.” Open votes are taken by voice, hand, or email, without anonymous ballots.

Health Equity

CPG guidance statements will include specific recommendations or considerations that address health equity. They will acknowledge:

- “Are there groups or settings that might be disadvantaged in relation to the problem or interventions that are considered?
- Are there plausible reasons for anticipating differences in the relative effectiveness of the intervention for disadvantaged groups or settings?
- Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention or the importance of the problem for disadvantaged groups or settings?
- Are there important considerations that should be made when implementing the intervention to ensure that inequities are reduced, if possible, and that they are not increased?”

The CPG recommendations will consider accessibility of the recommendation in diverse settings and populations. Each CPG will include a section of the CPG that addresses concerns related to the equity of the CPG for racially, ethnically, and socioeconomically minoritized populations.

Finally, the CPG will avoid language that may stigmatize already racially, ethnically, and socioeconomically minoritized populations.

Internal and External Review Procedures

The CPG Writing group will engage a full spectrum of **internal and external stakeholder reviewers** prior to finalization of the CPG to ensure the CPG is balanced, inclusive, and relevant.

Stakeholders are separately engaged in the CPG Topic Nomination process which is outlined in that methodology (see below outlined stakeholder list).

The CPG Writing Group will demonstrate open, systematic, and fair processes for receiving and responding to reviewer comments. Feedback gathered from stakeholders may highlight points of divergence and agreement with existing evidence and expert recommendations and guidance.

The CPG Writing group may decide to maintain a database in which it documents every criticism or comment it receives from every reviewer, how the guideline was or was not modified, and the rationale for actions or inactions taken. Making such a document available to the public is important for transparency, and the group may decide to post this document on the ASAM website."[53]

The CPG Methodology and Oversight committee procedures for review and oversight of the CPG process is outlined in separate methodology.

Stakeholders

A stakeholder is any individual or group who has an interest in the guideline; or who is responsible for implementing the guideline; or is affected by the research-informed decisions of the guideline (e.g. ASAM members, people with lived experience (PWLE), clinicians, public and private funders, and policy makers).[54,55]

The inclusion of stakeholders in research and guideline development has been recommended by the Substance Abuse and Mental Health Services Administration, the World Health Organization (WHO), the US Food and Drug Administration, and the National Institute for Health and Care Excellence (NICE).[9,56-60]

People with lived experience (PWLE) of a health issue, including patients and family members, are a key stakeholder group that should be included in the design, implementation, and translation of health research within and outside addiction medicine.[61,62] The US Department of Health and Human Services recently recognized the importance of this topic and released a report on methods to engage PWLE.[60] The report noted that "lived experience" helps to develop a deeper understanding of the conditions affecting certain populations, the solutions that are most appropriate for those impacted by the issue, and the potential harmful unintended consequences of the current and past actions taken by the existing system on the people it aims to serve.

ASAM will engage the Internal and External stakeholders listed below in the CPG Writing process. Efforts will be made to meaningfully engage stakeholders affected by the recommendations, especially those who are underrepresented in research, health policy, or experience systemic barriers to access to care.

Stakeholder review will strive to engage representatives of diverse backgrounds including:

- Geographic location
- Training background
- Years of practice
- Race
- Ethnicity
- Gender identity
- Socieoeconomic status
- Immigration status
- Sexual orientation
- Population treated
- Lived experience either personally or family and/or friends impacted by addiction
- Individuals who have specific training in health equity

The external review processes will balance the science of CPG development with practical implications for how these CPG affect stakeholders and stakeholder groups.

Procedures for stakeholder engagement are outlined below.

<u>Stakeholder groups (one stakeholder can fit under multiple categories):</u>

- ASAM leadership including Board of Directors, Quality Improvement Council
- ASAM members
- People with lived experience (PWLE)
    - *Attention will be paid to inclusion of individuals typically underrepresented in research and healthcare policy such as individuals who use substances with criminal legal involvement or those who experience systemic barriers in access to care.*
- Families and friends of PWLE
- Clinicians and other health care professionals (Individuals and organizations that provide medical care: physicians, nurse practitioners, addictions counselors, peer/recovery coaches, etc.)
- Payers (pays for or reimburses for addiction-specific interventions/treatment, governments, health insurers, the public)
- Purchasers (employers, governments, entities responsible for underwriting the cost of care)
- Policymakers (government agencies, professional associations, quality assurance/accrediting organizations like The Joint Commission)
- Product makers or manufacturers (pharmaceutical companies)

- Principal investigators (e.g., researchers or research groups such as NIDA)
- The press (e.g., publishers, news media)
- Accreditors (those who monitor care, quality assurance organizations)

Inclusion of People with Lived Experience

PWLE is vital to confirm that "values and preferences" in CPG recommendation development are adequately addressed by the patient perspective. Currently, there is no standard approach for including people with lived experience (PWLE) in CPG development.[57] However, a range of options for supporting PWLE engagement have been identified:[56,63,64]

- Nomination, prioritization, or selection of CPG topics
- Participation on a pre-specified PWLE stakeholder panel
- Scoping of CPG and development of key questions to guide the systematic review
- sharing of evidence related to the CPG topic (e.g., first-person experience, grey literature, peer-reviewed publications)
- Feedback on systematic review protocol
- Commenting on recommendations before and/or during public comment periods
- Dissemination and implementation of the CPG
- Development of patient-facing materials that summarize final CPG recommendations

When PWLE are engaged in the CPG Writing process, attention will be made to the following:

- Compensation for time investment contributing to CPG
- Tokenism, meaning: "Lack of meaningful engagement can result in "tokenism" when stakeholders are left with the sense that their engagement is for "checking a box" rather than for true partnership and collaboration"[65,66]
- Communication and engagement approaches based on foundational principles of respect, equitable power, and trust[66]
- Deliberate and ongoing actions aimed at establishing and improving trust by building relationships prior to the start of the CPG
- Deliberate and ongoing communications engaging in the communities were PWLE live[67]
- Continuous sensitivity and awareness that PWLE involving substance use and addiction may be apprehensive about contributing due to historical mistrust and/or stigma

Procedure for External Stakeholder Review

External stakeholders will be invited to review and comment on the CPG. All external reviewers will be required to disclose potential financial conflicts of interest in keeping with ASAM general COI policy. External review comments received in the absence of a disclosure form will not be considered.

Feedback from people with lived experience (PWLE) will be sought during the external review process. The CPG-MOS will iteratively explore different ways to obtain this feedback via direct outreach, surveys or other strategies because engagement from people with lived experience may not respond to traditional methods of stakeholder review (see Boot Camp Translation as an

example).[68] Specifically, the "values and preferences" of PWLE as they pertain to each CPG recommendation will be sought.

Invited reviewers and public commenters review the document at the same time, as opposed to having two separate review periods for each group. Reviewers will have approximately one month to review and submit comments. Reviewers' comments/criticisms with relevant scientific evidence and citations will be given higher priority, though all comments will be reviewed by the CPG Writing Group.

Once the review period is over, ASAM staff will consolidate comments in a standard format for the CPG Writing Group to review.

The CPG Writing Group will review all comments, revise the CPG as needed, and vote to accept, reject, modify or request further information. All revisions to the CPG recommendations will be reviewed by the ASAM CPG-MOS prior to movement to the next step of the CPG review process to ensure fidelity and quality of the CPG recommendations.

Procedure for Internal Stakeholder Review

Throughout the CPG writing process, the CPG-MOS will update the ASAM QIC at its regularly scheduled meetings on the progress of the CPG Writing Group.

After External Stakeholder Review and incorporation of modifications, the ASAM Quality Improvement Council and Board of Directors will be invited to participate in a formal internal review process of the CPG prior to finalization. All internal reviewers will be subject to the DOI/COI methodology per the previously described CPG-MOS DOI/COI methodology.

Once the Internal Review period is over, ASAM staff will consolidate comments in a standard format for the CPG Writing Group to review. The CPG Writing Group will review all comments, revise the CPG as needed, and vote to accept, reject, modify or request further information. All revisions to the CPG recommendations will be reviewed by the ASAM CPG-MOS prior to movement to the next step of the CPG review process to ensure fidelity and quality of the CPG recommendations.

The ASAM QIC and BOD will review the final CPG product and approve it prior to finalization.

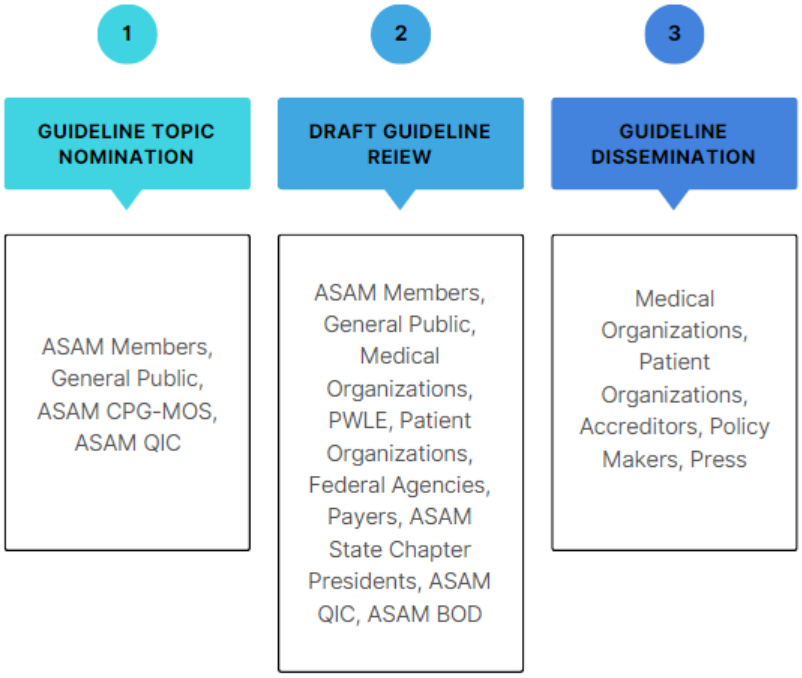
Written Record of All External and Internal Reviewer Comments

All reviewer comments and the CPG Writing Group's responses to comments will be kept in a written record form with the rationale for modifying or not modifying a CPG in response to reviewer's comments. This document of comments and responses to comments (e.g. how they were addressed) will be included in the final CPG materials. Comments and response to comments will be available to the public upon request.

Procedure for External Review after Finalization and Publication

Dissemination of the CPG will be shared with key stakeholders.

Figure 2. Stakeholder Engagement Stages



Approval and Dissemination

Background

The approaches of medical society to approve CPGs vary in regard to the level of external/independent review, incorporation of suggestions, approach to consensus determination and inclusiveness.

ACP is perhaps the most "top-down" process in which ACP Board of Regents and Board of Governors approves and sends back to CPG Writing Group or incorporation of Public Panel reviews and comments prior to journal submission and publication.[2.]

The APA are in line with Institute of Medicine and Council of Medical Specialty Societies standards.[1,4,69.] The Committee on Practice Guidelines (CPG) is primarily tasked with development and managing review of the guideline. The APA Board of Trustees (BOT) and APA Assembly provide final review and approval after the development and review process has been completed. The process allows for further rounds of review and revision if there is a failure of consensus within the Assembly or BOT if the CPG determines that the evidence warrants further review.

The VA/DoD process involves submission of new practice guidelines to the Evidence Based Practice Work Group (EBPWG) through VA or DoD.[3.] The EBPWG votes to approve a CPG and the CPG workgroup/clinical champions are tasked with the review and development process. Final approval by the EPBWG comes after:

1. The third draft of the guideline is reviewed by "outside national experts" who have agreed to perform an independent external peer review
2. VA/DoD solicit feedback from "a broader group of end users, to include patients."
3. VA/DoD end users provide feedback to guideline contractor and/or directly to the VA/DoD program to evaluate the "content and the logic and flow of the guideline."
4. VA/DoD Program offices review independent reviewer comments and incorporate appropriate suggestions
5. Champions and guidelines contractor present guideline to EBPWG and respond to EBPWG comments and feedback

A recent publication[70] analyzing a cross section of 43 specialty society CPGs and guideline procedure manuals noted, "Among the 36 (of 43) specialty societies that published evidence-based Clinical Practice Guidelines, 27 (75%) required approval by a committee representing the society. None specified the criteria used for approval decisions. Six specialty societies (17%) required approval. but included procedures to maintain some editorial independence for the guideline development group, such as approval by a guideline committee not an executive committee or approval dependent on fidelity to established guideline methodology, not content. One society required Board review, but not approval. The approval process was not reported by 2 (6%) of the specialty societies."

Another publication[10] reviewing 19 guideline development handbooks enumerated 17 "necessary tasks". *Interestingly, none of the necessary tasks included detailed guidance on the final approval process but* did promote "a systematic and transparent approach to move from evidence to recommendations."

"Most medical specialty societies in the U.S. require approval of guidelines by a board that represents the society as whole. Since medical specialty societies have loyalties to the patients they serve and to their physician members, and because the interests of those two groups may differ, such an approval process introduces a potential conflict of interest into the guideline development process."[2]

Methodology

The ASAM approval process should meet existing standards for medical society clinical guideline publications and promote "a systematic and transparent approach to move from evidence to recommendations."[2]

Per ASAM stakeholder review process, a rigorous method for internal and external stakeholder review will occur to ensure broad and inclusive feedback on the CPG prior to the final approval process which will streamline and facilitate the final approval process.

1. After stakeholder review by both external and internal ASAM stakeholders, the CPG-MOS with the CPG Writing Group chair will present the final CPG to the ASAM QIC for approval.

2. The ASAM QIC will present their approved CPG to the ASAM Board of Directors for final approval.
3. Once approved by the ASAM BOD, the CPG will be submitted to the Journal of Addiction medicine for external review and potential publication.
4. Additional dissemination of the CPG will occur via posting on the ASAM website.
5. Additionally, the Quality Improvement Council and BOD will identify other dissemination methods such as presenting the CPG in collaboration with the Education Council at the ASAM national meeting and other national educational conferences.
6. CPG writing group members are discouraged from using their participation on the CPG writing group for their own monetary gain by ineligible companies. At a minimum, members should decline financial offers from affected companies to speak about the CPG for one year after approval and publication.

Methodology to Update Clinical Documents

The CPG-MOS and the QIC are responsible for inventorying ASAM Board-approved clinical practice guidelines, clinical consensus statements, and clinical considerations. Annually, any necessary updates will be considered as warranted. At a minimum, Board-approved CPGs and clinical consensus statements will be reaffirmed, updated, or retired at least every five years.

The CPG-MOS will make a recommendation to the QIC each year as part of their CPG Topic Selection process regarding the need for existing CPG and clinical consensus statement updates and the type of update recommended (see Table 6 below for differentiation between focused vs. full update). Considerations by the CPG-MOS and QIC that drive this decision include:

- New literature as determined by annual literature surveillance
    - ASAM will determine the best strategy for the performance of literature surveillance on a regular basis
- Significant practice or policy developments
- FDA decisions (e.g., new product approvals or labelling changes)
- Strengths/weaknesses of existing CPG research methodology and findings
- Time and sense of urgency
- Requests and requirements for review and update from the practice community, key stakeholders, and other sources (which are free of relationships with industry or other potential bias)
- Need for consistency with a new guideline or guideline revision
- Implication for changes in the guideline (small vs. large)
- Budgetary constraints
- Competing clinical topics

In cases of ASAM CPGs that involve other organizations, the other organization will need to confirm their interest in a CPG Update. The CPG-MOS recommends that discussion for the CPG Update process occur at the time the original CPG is written.

CPGs should go through a "Full CPG Update" when the above factors suggest the need for modification of clinically important recommendations and all original CPG key questions need review. An updated review would be necessary whenever new evidence shows that a recommended intervention causes previously unknown substantial harm or that a new intervention is significantly superior to a previously recommended intervention.

CPGs can be considered for a "Focused CPG Update" which involves updating the evidence related to a limited subset of the original CPG key questions. A focused update would be appropriate when new practice advances or policies relate to one to two of the original key questions.

When it is not clear if the entire CPG needs revision, the CPG-MOS and QIC may request ASAM staff perform an updated literature review and ask members of the original CPG writing group to review this literature for key gaps in the CPG. The writing group's consensus will be presented to the QIC by the CPG-MOS for consideration of next steps.

When clinical guidance, clinical consensus, or practice clarification is needed or requested related to a CPG or Focused CPG Update, alternative methods of update may be considered such as a "Clinical Consensus Statement" or "Clinical Considerations" document which are defined elsewhere.

The following scenarios can be used for the determination of the extent of CPG updates. Ultimately, the final determination of a "Full CPG Update", "Focused CPG update", "Clinical Consensus Statement", or "Clinical Consideration" will first be recommended by the CPG-MOS to the QIC. The QIC will present their recommendation for next steps to the ASAM Board of Directors as delineated in the CPG Topic Selection methodology. All CPGs and clinical documents will follow defined CPG methodology and will require consensus and approval as defined in CPG methodology.

Table 5. Clinical Document Update Plans

	Recommended Response / Clinical Document Plan
Scenario 1: No New Evidence/Development, CPG within 5 years of publication	No changes to CPG recommended.
Scenario 2: CPG > 5 years since publication	Consider the need for a Full CPG Update versus Focused CPG Update based on factors listed above.
Scenario 3: Limited new evidence/development but request for additional key questions, CPG within 5 years of publication	Consider publication of a "Clinical Consensus Statement" or "Clinical Considerations" document to address new evidence or developments and share clinical guidance. Consider adding new key questions to a Full or Focused CPG update in the future.
Scenario 4: New Evidence/development and possible need for CPG change, CPG within 5 years of publication	Plan a Full CPG update versus Focused CPG update related to the breadth of the new evidence/developments and factors above within a certain timeframe.

	Consider publication of a "Clinical Consensus Statement" or "Clinical Considerations" to share key new evidence.
Scenario 5: New Evidence/Developments and clear need for CPG update	Plan a Full CPG Update versus Focused CPG Update related to the breadth of the new evidence or developments and CPG recommendation change.

The CPG Writing Group for Full CPG updates and Focused CPG updates may consist of previous members of the original CPG Writing Group; however, all writing group members will need to have DOI/COI screened in accordance with updated CPG DOI/COI methodology and new membership is encouraged. Final membership will be determined via the Writing Group Membership methodology.

Table 6. Standard Formats for ASAM CPG Full Updates and CPG Focused Updates

	Focused Update	**Full CPG Update**
Scope	Rewrite of specific sections or statements within the document Limited number of revised guidance related to the original CPG Key questions	Substantial rewrite of entire document All Original CPG Key Questions are reviewed and/or replaced
Methodology	2023 ASAM CPG Methodology	2023 ASAM CPG Methodology
Publication	Literature review to Journal of Addiction Medicine (JAM) that includes why the update was performed and mentions the guideline has been partially updated with a link to the revised guideline. *(Note that there is no guarantee that the update will be published. If not accepted for JAM publication, the literature review will be self-published by ASAM on its website.)* Summary article to JAM in a table format which contains all recommendations that have been deleted and/or modified as well as all new recommendations. Every attempt is made to match each deleted, changed, and new recommendation. Updated and new statements will	Literature review to Journal of Addiction Medicine that includes why the update was performed and mentions the guideline has been fully updated with a link to the revised guideline. *(Note that there is no guarantee that it will be published. If not accepted for JAM publication, the literature review will be self-published by ASAM on its website.)* Executive summary submitted to JAM for consideration which includes all recommendations and substantive comments regarding document. No track changes shown in full-text guideline, pocket guide, phone app nor slide deck. The prominent locations in the guideline will indicate the year that the

	be clearly identified in the full-text guideline, pocket guide, phone application, and training material. The prominent locations in the guideline will indicate the year the guideline was updated in a way that is easily understood by the reader (e.g., “Originally adopted [year], Focused Update [year]”).	updated guideline was adopted, as it normally does (e.g., “Adopted [year]”), and the year it was archived (e.g. “Archived [year]”).

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Appendix A: CPG-MOS Member Bios and Disclosures

CVs for all CPG-MOS members are available upon request.

Melissa B. Weimer, DO, MCR, DFASAM (*Chair*)

Dr. Weimer is an Associate Professor of Medicine and Public Health at Yale University. She is board certified in Internal Medicine and Addiction Medicine and has a clinical and research focus on expanding access to substance use disorder treatment, particularly in the hospital setting. She also has training in the management of complex pain, particularly for patients with concomitant opioid use disorders. She is the Medical Director of the Yale Addiction Medicine Consult Service (YAMCS), a multidisciplinary, hospital-based program to address the substance use disorder needs of patients admitted to Yale New Haven Hospital. She is also an Associate Program Director for the Yale Addiction Medicine Fellowship program.

Dr. Weimer is experienced in clinical research and serves as co-principal investigator on several NIH grants. She has led or participated in several systematic reviews and clinical practice guidelines through the Pacific Northwest Evidence-based Practice Center and Yale University.

Dr. Weimer received her DO from Virginia College of Osteopathic Medicine and completed Internal Medicine residency and fellowship training in General Internal Medicine at Oregon Health & Science University. She received her Master's in Clinical Research from Oregon Health & Science University.

Disclosures: Dr. Weimer is an employee of Yale School of Medicine. In the last 24 months, she has received grant funding from the National Institutes of Health (National Institute on Drug Abuse; National Institute on Alcohol Abuse and Alcoholism), the Health Resources Services Administration, and Massachusetts Medical Society. She has stock options with Path CCM, Inc., and has served as a consultant for CVS Health. Dr. Weimer has performed legal consulting in the last 2 years. She serves on the National Board of Directors for ASAM and has participated in lobbying efforts with ASAM. A list of publications can be found here. She reports no DOI for her spouse or children.

Emily Brunner, MD, DFASAM

Dr. Brunner is board certified in family medicine and a distinguished fellow in the field of addiction medicine. She has experience treating addiction in both inpatient and outpatient settings. She is an experienced speaker and specializes in trauma-informed clinical treatment of substance use disorders with a comprehensive and compassionate approach.

Dr. Brunner has been involved in leadership of the Minnesota Society of Addiction Medicine and is now on the national board of the American Society of Addiction. She is a passionate advocate for improving the care of patients with substance use disorder across the healthcare system, and

specifically in advocating for increased utilization of medications for opioid use disorder across all levels of care.

Dr. Brunner received a B.S. from MIT, and then did medical school and residency at the University of Michigan. She also has a strong interest in behavioral addiction and has begun treating internet gaming disorder. She is medical director of Gateway Recovery, sees patients at Elite Recovery and Recovering Hope and does trainings on behalf of Hazelden Betty Ford Foundation.

Disclosures: Dr. Brunner is employed by Gateway Recovery, Elite Recovery, Recovery Hope, and Hazelden Betty Ford Foundation. She was also employed briefly with Workit Health within the last 24 months. She has not received grant funding. She serves on the national board of ASAM and has participated in lobbying on behalf of ASAM. She has not published anything in the last 24 months. She reports no DOI for her spouse or children.

Devan Kansagara, MD, MCR

Dr. Kansagara is a Professor of Medicine, Division of General Internal Medicine and Geriatrics at Oregon Health & Science University. He practices internal medicine in the VA Portland Health Care System. One of his areas of interest is evidence-based medicine, and the use of evidence to guide health policy.

Dr Kansagara directed the Portland Evidence-based Synthesis Program for ten years, one of four sites nationally responsible for developing evidence syntheses to help guide VA policy. He previously served as the Vice Chair of the American College of Physicians Clinical Guidelines Committee, and currently serves on the ACP Scientific and Medical Policy Committee. He also currently works on health policy for the Oregon Health Authority. Dr. Kansagara's other main area of interest is health systems redesign. In particular, he has done intervention and implementation work with hospital to home care transitions and the patient centered medical home.

He received an MD from the University of Connecticut School of Medicine and completed residency training at Yale University. He received his Master's in Clinical Research from Oregon Health & Science University.

Disclosures: Dr Kansagara is an employee of the Veterans Affairs Portland Health Care System. Over the last 24 months he has received funding from the Veterans Health Administration, the American College of Physicians, and the Agency for Healthcare Research and Quality. He has no financial conflicts of interest to disclose. He serves on the American College of Physicians' Scientific Medical Policy Committee, and on the Health Evidence Review Commission for the state of Oregon. A list of publications can be found here. He has no disclosures of interest to report on behalf of his spouse or children.

Todd Korthuis, MD, MPH, FASAM

Dr. Korthuis is a general internist, addiction medicine specialist, and clinician-scientist. He began his clinical career treating patients living with HIV and has practiced addiction medicine since 2004. He is Professor of Medicine and head of the Section of Addiction Medicine at Oregon Health & Science University.

His research focuses on integration of addiction treatment and prevention in diverse health care settings. He serves as Co-Principal Investigator of the National Drug Abuse Treatment Clinical Trials Network (CTN) Western States Node that tests new treatment strategies for opioid, methamphetamine, and cocaine use disorders. He has served as Principal Investigator for multiple NIH-funded research studies including the CTN-0067 trial of extended-release naltrexone in North American HIV clinics, the BRAVO implementation trial of buprenorphine for OUD in Vietnam HIV clinics, the Oregon HOPE peer engagement intervention to decrease overdose in rural Oregon, the PEER-CM trial of peer-facilitated contingency management for harm reduction to reduce overdose, and the PROUD-R2 peer intervention to improve retention of people who use drugs in clinical trials in rural America.

Honors include the 2008 Lawrence S. Linn Award for research that improves the lives of people living with HIV, a 2012-2013 Fulbright Scholar award to study integration of HIV and addiction care in Vietnam, and a 2022 Fulbright Senior Scholar Award to study the intersection of harm reduction and substance use disorder treatment in Spain.

Disclosures: P. Todd Korthuis is an employee of Oregon Health & Science University. In the last 24 months, he has received grant funding from the National Institutes of Health (National Institute on Drug Abuse; National Center for Advancing Translational Sciences) and the Health Resources Services Administration. He has no investments or other interests. He is a member of the National Institute on Drug Abuse Study Section and serves on the Oregon Governor's Psilocybin Advisory Board. A list of publications can be found here. He reports no DOI for his spouse.

Lewis S. Nelson, MD, MBA, FASAM

Dr. Nelson is Professor and Chair of the Department of Emergency Medicine and Chief of the Division of Medical Toxicology at Rutgers New Jersey Medical School in Newark, NJ. He is the incoming President of the Association of Academic Chairs in Emergency Medicine and was a member of the Board of Directors of the American Board of Emergency Medicine, the Accreditation Council for Continuing Medical Education, and President of the American College of Medical Toxicology.

Dr. Nelson is a consultant to CDC, FDA, DHS, and has worked closely with several professional medical organizations such as ACEP, ACMT, ASAM, and SAEM. He is an editor of the textbook Goldfrank's Toxicologic Emergencies and on the editorial boards of several journals.

Dr. Nelson provides direct clinical care to patients in the ED and serves as a consultant on hospitalized and ambulatory patients with substance use disorder, overdose, and withdrawal. He is a senior consultant to the New Jersey Poison Information & Education System. He completed a residency in emergency medicine at Mount Sinai School of Medicine and a fellowship in medical toxicology at New York University School of Medicine.

Disclosures: Lewis S. Nelson, MD, MBA is an employee of Rutgers University. In the last 24 months, he has received grant funding from SAMHSA. He has performed expert legal consulting in the last 2 years. He is a member of the board of the Association of Academic Chairs in Emergency Medicine. A list of publications can be found here. He reports no DOI for his spouse or children.

Darius Rastegar, MD, FASAM

Dr. Rastegar is an Associate Professor of Medicine at the Johns Hopkins University School of Medicine. His areas of clinical expertise include primary care internal medicine, addiction medicine, and HIV/AIDS. He serves as medical director of the Inpatient Addiction Medicine Unit at Johns Hopkins Bayview Medical Center and the program director for the Johns Hopkins Addiction Medicine Fellowship.

Dr. Rastegar earned his MD from the University of Pennsylvania. He completed his internal medicine residency at Johns Hopkins Bayview Medical Center.

Disclosures: Darius Rastegar is an employee of Johns Hopkins University. In the last 24 months, he has received grant funding from NIDA. He is a member of the Maryland-DC Society of Addiction Medicine board of directors. Dr. Rastegar has performed legal consulting in the past 2 years. A list of publications can be found here. He reports no DOI for his spouse or children.

Audra Stock, LPC, MAC

Ms. Audra Stock is a Licensed Professional Counselor and Master Addiction Counselor with over 20 years of experience working with diverse populations treating mental health, substance use, and co-occurring disorders. She is currently serving as the Clinical Director for the Army's Substance Use Disorder Clinical Care programs responsible for managing the clinical programs across the European Region encompassing 5 clinics and virtual-telebehavioral health care programs spanning 3 continents and 30 countries.

Prior to this position, Ms. Stock served as the Deputy Director for the Center for Substance Abuse Treatment (CSAT) for the Substance Abuse and Mental Health Services Administration (SAMHSA). In this role, she led programs focused on bridging the gap between research and implementation of evidence-based practices resulting in increased access to behavioral health and addiction care nationwide. She has served as a key informant in the development of systematic reviews, has convened technical expert panels, and led the development and dissemination of multiple clinical practice tools and treatment improvement protocols. Ms. Stock has also served in senior leadership roles for other military and community mental health organizations responsible for the full continuum of triage services and outpatient psychiatric, behavioral health, and addiction care.

Disclosures: Ms. Audra Stock is an employee of the Department of Army, Medical Readiness Command-Europe. In this role, she provides behavioral health and substance use disorder specific consultation and clinical guidance. She has developed updated addiction treatment standards of care

for the European region. She has also provided expert witness testimony specific to the risks associated with substance use and adolescents. Ms. Stock is a member of American Society of Addiction Medicine. Ms. Stock is a contributing author for the Outpatient Alcohol Withdrawal Management: A Tool for Global Practice Settings. Ms. Stock is a certified professional coach and is the principal for Audra Stock and Associates, LLC providing leadership coaching, team effectiveness workshops, and consultation for improving organizational culture. She reports no DOI for her spouse or immediate family members.

Carlos F. Tirado, MD, MPH, FASAM

Dr. Tirado is Founder and CEO of CARMAhealth and Associate Professor of Practice at the University of Texas School of Pharmacy PhARM program.

Dr. Tirado is board certified in general and addiction psychiatry by the American Board of Psychiatry and Neurology. Dr. Tirado earned his MD and MPH degrees from the McGovern Medical School at UTHealth, completed residency at University of Texas Southwestern Medical Center and clinical-research fellowship at the University of Pennsylvania.

Dr. Tirado is an expert in medication treatment for addiction, primary care and behavioral health integration, peer recovery support models, and tele-behavioral health.

Disclosures: Dr. Carlos F. Tirado is Founder and CEO of CARMAhealth. In the last 24 months, Dr. Tirado has received grant funding from NIDA and Spark Biomedical. Dr. Tirado has stock options with Spark Biomedical. Dr. Tirado has served as a consultant for Pear Therapeutics and Alkermes in the past 2 years. Dr. Tirado is a member of the Subcommittee of Mental Health with the Texas Medical Association. A list of publications can be found here: Tirado CF - Search Results - PubMed (nih.gov). Dr. Tirado reports no DOI for his spouse.

Appendix B: CPG-MOS Charter

Clinical Practice Guidelines Oversight and Methodology Work Group (CPG-OMG) Charter

1. **Mission**
    a. **Primary Functions of the Committee**
    As part of ASAM's mission to define and promote evidence-based best practices in addiction prevention, treatment, remission, and recovery, this committee will provide oversight to the development, implementation, education, and communication of clinical practice guidelines (CPG).
    b. **Committee Goals 2020-2023**
        1. Establish and publish methodology for the development of CPGs.
        2. Establish and publish topic selection process.
        3. Develop a clinical practice guideline strategic plan.
        4. Develop methodology for how to manage stakeholder's involvement.
    c. **Responsibilities**
    The CPG Committee will provide strategic oversight to the following activities, including but not limited to:
        1. Establish methodology and ensure its adoption and evolution.
        2. Selecting CPG topics, writing subcommittee members, and expert panel members.
        3. Serve on writing groups of CPGs as liaison to the CPG-OMG, and as a content and methodology expert.
        4. Guide education, tool development and communications and all CPG derived activities.
        5. Review Conflict of Interest of potential members of writing groups and expert panels.
        6. Oversees the requests of participation on Clinical Practice Guidelines from external organizations.
2. **Governance**
    a. **Relationship between Committee and Organization Governance**
    The CPG-OMG will report to the Quality Improvement Committee, whom reports to the board.
    b. **Subcommittee Descriptions and Purpose**
    Subcommittees will be created as needed to develop CPGs. All CPG writing group subcommittees will have a member of the CPG-OMG to act as a liaison to the CPG-OMG, and as a methodology and content expert.
    c. **Conflicts of Interest**
    All members of the working on CPGs will follow the ASAM policy on reporting conflicts of interest policy. In addition to the ASAM policy, members of the CPG-OMG will be prohibited in participating in the development of a CPG or quality improvement policy, on the same topic for any non-ASAM organization.

The members of the CPG-OMG will be required to review and assess the conflict of interest disclosures, prior to appointing a member to any role. The CPG-OMG will ensure that Chair(s) of writing subcommittees have no conflicts of interest and will define what is relevant conflicts for the remaining members of the subcommittees.

3. Committee Composition

a. Qualifications

All qualifications must be met to have a complete group. Considerations will be giving to have diverse group. A member may meet more than one qualification.

1. Experience in developing CPG(s)
2. Knowledge of CPG methodologies, e.g., GRADE, RAM etc. Statistics, data methodologies Experience in CPG implementation or tool development Expert in Addiction Medicine

b. Appointments (process, nominations, and renewals)

All members of ASAM committee severe at the pleasure of the ASAM President. Members will be asked to apply or self-nominate to join the committee. The QIC will select members who meet the qualifications and make recommendations to the ASAM President for appointment.

CPG-OMG contain five-nine members, who will serve a term of two years with the option for renewal once. Members may serve no more than three terms in their lifetime. The standard appointment period will start and end at the ASAM annual meeting. No more than one-third of the CPG-OMG can be new members in a year. Considerations for diversity are encouraged, parameters to consider are not limited to: gender, race/ethnicity, age, location (rural vs. urban), career status (Fellows, early career, vs late career), and role (care team roles).

4. Activities

a. Meetings

1. The CPG-OMG will meet no less than once a month, most likely meet every fortnight via conference call and will hold at least one in-person meeting per year. During writing activities, this committee will likely meet weekly (as determined by the CPG-OMG) until publication. Meetings can be canceled, with the permission of the Chair, if deemed necessary. The CPG-OMG must meet at least 6 times per year to retain its status as an active committee, if it meets less than 6 times a year, it will be reevaluated on if it should be considered an advisory group.
2. Quorum will be reach when two-thirds of the committee is present. Members may miss up to four meetings per year, but no more than two consecutive meetings. Members should notify the ASAM staff liaison and chair(s) of their absence.

b. Policies and Procedures

1. The CPG-OMG will be responsible for the developing and publishing the CPG develop methodology. They will be responsible for the adheres and evolution of the ASAM CPG methodology. They will ensure that any deviation from said methodology is approved prior to the divergence occurs and is proper documented in the CPG publication.

2. The CPG-OMG will review and update the policies on the development of CPG, which include but are not limited to: Topic Selection, CPG COI, Subcommittee Member Selection, Partnerships, Endorsement and Review of external CPGs to ASAM.

c. <u>Deliverables and Guidance</u>

1. CPG-OMG will develop and publish the ASAM Clinical Practice Guidelines Methodology
2. CPG-OMG will have knowledge of the 2011 Institutes of Medicine's "Guidelines We can Trust," Rand/UCLA Appropriateness Method Manual, World Health Organization's Handbook for Guideline Development, Council of Medical Specialty Societies policy on Code for Interactions with Companies and Principles for the Development of Specialty Society Clinical Guidelines. CPG committee members will need to be aware of current trends in CPG development.
3. CPG-OMG members will have access and cognizant of all applicable ASAM policies and procedures.

Appendix C: CPG Methodology Topics and Timeline

TOPIC	Authors	Approved by CPG-MOS	Presented to QIC	Approved by QIC	Approved by BOD
Definitions of clinical documents	Melissa Weimer		9.28.22	9.28.22	
CPG Topic identification and selection	Todd Korthuis Darius Rastegar	4.20.21	4.28.21	9.22.21	10.23.21
Determining scope of the CPG	Todd Korthuis Darius Rastegar	4.20.21	4.28.21	9.22.21	
Committee identification, terms, and composition	Lewis S. Nelson Emily Brunner	5.18.21	5.26.21	8.25.21	
DOI/Conflicts of Interest	Melissa Weimer Lewis S. Nelson Emily Brunner ASAM Ethics Committee	6.15.21	7.28.21	5.11.22	
Stakeholder Engagement and Addressing Values and preferences	Audra Stock Carlos Tirado Annie Kleykamp	9.21.21, 2.14.23	6.22.22, 2.22.23	6.22.22, 2.22.23	
Updates to the guidelines	Audra Stock Carlos Tirado Melissa Weimer	9.6.22	11.16.22	11.16.22	
Systematic Review Methods	Devan Kansagara Melissa Weimer	2.14.23	2.22.23	2.22.23	
GRADE for Quality of evidence and strength of recommendations	Melissa B. Weimer Devan Kansagara	12.6.22	12.21.22	12.21.22	
Clinical recommendation development (consensus)	Emily Brunner Melissa Weimer Lewis Nelson	1.3.23	1.25.23	1.25.23	
Approval and Dissemination	Melissa Weimer	8.8.22	8.24.22	8.24.22	
Diversity, Equity and Inclusion in CPGs	Audra Stock Carlos Tirado Melissa Weimer	2.7.23	2.22.23	2.22.23	

Appendix D: Detailed Overview of CPG Process