

Revision #	1.0
Effective Date	04/04/2022
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# Society for Integrative Oncology (SIO) Guidelines Methodology Manual

*Date approved by SIO CPG Committee: 04/01/2022*

*Date approved by SIO Executive Committee: 04/04/2022*

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## 1. **Background**

The Society for Integrative Oncology (SIO) Guidelines Methodology Manual is designed to transparently communicate the methods in which SIO develops clinical practice guidelines. SIO clinical practice guideline development falls under the auspices of the SIO Clinical Practice Guidelines (CPG) Committee which acts on behalf of the SIO Executive Committee and the SIO Board of Trustees on matters of clinical guidance. The SIO CPG Committee oversees topic prioritization, development, the formation and progress of expert panels, and is the review and approval body of all guideline products. More details on the SIO CPG Committee's standard operating procedures can be found at <https://integrativeonc.org/practice-guidelines/guidelines-sops>.

This Methodology Manual is adapted from the [American Society of Clinical Oncology \(ASCO\) Guidelines Methodology Manual](#).

## 2. **Guideline Topics**

SIO clinical practice guidelines should address topics that are consistent with the mission of SIO, are novel, relevant, and will have significant impacts on the field of oncology practice. There should be consensus in the CPG Committee that there is a need for specific guidelines and due diligence review to avoid duplication of existing guidelines/recommendations.

Clinical practice guideline topics will be generated by the CPG Committee using the Topic Submission and Selection Guide (Appendix A) as well as guidance from the SIO Executive Committee, the SIO Board, SIO Committees, and the SIO membership, and priorities determined at SIO Board retreats and other policy/strategy initiatives. No set number of topics per year will be designated; instead, it will be dictated by the state of scientific evidence, the clinical/scientific need for a clinical practice guideline, the availability of necessary expertise, and resources to complete the guideline.

## 3. **Panel Composition**

Once a topic is approved for development by the SIO CPG Committee, a Clinical Practice Guideline (CPG) Panel is assembled – see Assembling the Panel (Appendix B). All SIO systematic review-based guideline products are developed by a multidisciplinary CPG Panel supported by SIO guidelines staff with health research methodology expertise. The CPG Panel Co-Chairs and SIO staff assemble a list of Expert Panel members which the SIO CPG Committee reviews and approves. Each CPG Panel should have at least one (1) expert with experience with the creation and/or evaluation of clinical practice guidelines, one (1) patient advocate familiar with the patient population of interest, one (1) clinician who is working with the patient population of interest, and one (1) person who has conducted studies (similar to or those actually being reviewed) included in the clinical practice guideline. Prospective members are sent an invitation to join the CPG Panel, along with the Expert Panel Roles and Responsibilities (Appendix C) document. In addition, a slide set has been developed for the roles of CPG Panel Co-

Chairs and CPG Panel members (Appendix D) to further explain the responsibilities and processes.

CPG Panels are assembled in accordance with SIO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines (Appendix E). SIO requires disclosure by individuals involved in drafting, reviewing, and approving guideline recommendations and sets limits on the financial relationships that panel members and reviewers can have with Companies that could reasonably be affected by care delivered in accordance with guideline recommendations. To carry out this policy, potential panel members must complete a conflict of interest disclosure form prior to formal invitation to serve on the panel. Following the COI policy, SIO develops a list of "affected companies" – see Conflict of Interest (COI) Frequently Asked Questions (FAQ) (Appendix F). A Company is an "affected Company" if there is a reasonable likelihood of direct regulatory or commercial impact (positive or negative) on the entity as a result of care delivered in accordance with guideline recommendations. Decisions to invite CPG Panel members and evaluations of any actual or perceived conflict of interest are made at the full discretion of SIO.

Once the CPG Panel is assembled, guideline development can begin. The work of a panel is confidential. The materials members receive, any discussions, and the decisions made by the panels are subject to SIO's policies on confidentiality and may not be shared with anyone outside the SIO CPC Committee, the CPG Panel, and SIO staff. Some of the materials may be highly sensitive and there could be legal penalties for using or disclosing the information inappropriately. Non-authors, including but not limited to third parties are not permitted prepublication access to SIO-approved clinical practice guidelines or related materials developed for SIO publication and public dissemination. An exception is individuals solicited by SIO for the purposes of invited and confidential peer review. In certain cases, SIO will share draft guideline documents with outside parties. In these select cases, the parties are required to sign a non-disclosure agreement.

#### **4. Protocol**

The Protocol specifies the purpose of the guideline product, target patient population, clinical outcomes of interest, and their importance for decision-making, key features of the systematic literature review, and a proposed timeline for completion. SIO methodologist, the CPG Panel Co-Chairs will typically draft the protocol for full panel review. For consistency, a Protocol Worksheet (Appendix G) is used. Once the CPG Panel Co-Chairs have approved a first draft of the Protocol, the Protocol will be shared with the full CPG Panel. The SIO CPG Committee may also review the Protocol to make suggestions for revision intended to clarify aspects of the plan for developing the guideline. These suggestions are sent to the CPG Panel Co-Chairs. Work on the systematic literature review can proceed upon the sign-off of the Protocol by the CPG Panel.

## **5. Systematic Literature Review**

Upon approval of the Protocol, a systematic review of the medical literature is conducted. The SIO methodologist uses the information entered into the protocol, including the clinical questions, inclusion/exclusion criteria for qualified studies, search terms/phrases, and range of study dates, to perform the systematic review. Literature searches of selected databases, including The Cochrane Library and Medline (via PubMed), are performed. Working with the CPG Panel, the methodologist completes screening of the abstracts and full text articles to determine eligibility for inclusion in the systematic review of the evidence.

## **6. Summarizing the Evidence**

After the systematic review is completed, evidence tables are generated by the SIO methodologist to capture a summary of the studies included. This summary also includes the quality appraisal of the studies. The AMSTAR II tool is used for assessing the quality of systematic reviews and meta-analysis, while the Cochrane Risk of Bias tool is used for randomized control trials. Example templates of these summary tables are provided in Guideline Manuscript Template (Appendix H).

## **7. Drafting the Recommendations**

After the systematic review of the literature is completed, CPG Panel members review the evidence profile and summary of findings and draft the guideline recommendations for clinical practice – see Drafting Recommendations and the Manuscript (Appendix I).

SIO guideline recommendations are crafted, in part, using the [Guidelines Into Decision Support \(GLIDES\)](#) methodology and accompanying BRIDGE-Wiz software. This method helps CPG Panels systematically develop evidence-based, clear, transparent, and implementable recommendations. In addition, a guideline implementability review is conducted. Based on the implementability review, revisions are made to the draft to clarify recommended actions for clinical practice. Ratings for type and strength of the recommendation and evidence quality are provided with each recommendation. The quality of the evidence for each outcome is assessed using the Cochrane Risk of Bias tool by the project methodologist in collaboration with the CPG Panel Co-Chairs and reviewed by the full CPG Panel.

## **8. Open Comment**

SIO guidelines are available for open comment for a 2-week period. Prospective reviewers must contact SIO to request to review the draft guideline recommendations and are required to sign a non-disclosure and confidentiality agreement before receiving the draft guideline recommendations. Reviewers must identify themselves by name and affiliation; anonymous comments will not be accepted. Guidelines staff review and

summarize comments and bring relevant comments to the CPG Panel Co- chairs, and to the entire panel if necessary. Any changes made from the open comment process will be reviewed by the entire panel prior to SIO CPG Committee approval. Comments are advisory only and SIO is not bound to make any changes based on feedback from open comment. SIO does not respond to reviewers or post responses to comments; however, major edits to the draft will be reflected in the open comment discussion.

## **9. Review Process**

SIO has a rigorous review process for guidelines. After the draft has been approved by the CPG Panel, the guideline is independently reviewed and approved by the SIO CPG Committee. All members of the SIO CPG Committee are asked to critically review the guideline prior to the next scheduled SIO CPG Committee meeting. The SIO CPG Committee members then present the results of their reviews and then vote on whether to approve the guideline (with recusals from members who have relationships with affected companies). If applicable, approved SIO guidelines are then submitted to any Participating Organization(s) for approval per their internal review processes.

Approved SIO guidelines are then submitted to targeted journals per the CPG Panel Co-Chairs' recommendation, taking input from the CPG Panel and the SIO CPG Committee, as well as the SIO Board of Trustees and equivalent leadership for any Participating Organization(s), and as appropriate querying editors for interest.

## **10. Dissemination and Implementation**

SIO produces Clinical Tools and Resources to more widely disseminate, in a practical and user-friendly form, the recommendations contained in the guidelines. A list of these CT&Rs is currently being developed.

## **11. Guideline Update Process**

SIO is committed to the currency and validity of its guidelines. A process for updating guidelines will be established.

## Appendix A



### Topic Submission and Selection Guide

The CPG Committee will take the following information into account when considering topics:

- a. Is there a need for guidelines for the proposed topic that is appropriate for SIO to pursue?
- b. What is the proposed topic and scope, clinical population of focus, and period of time of literature to be reviewed to be addressed by the guidelines?
- c. The amount and quality of the available evidence on the proposed guideline topic
- d. Whether a clinical practice guideline has been previously published on the topic or a similar topic by SIO or another organization. If yes, the reference, scope and date of publication of that guideline will be considered. The new SIO guideline should advance knowledge and/or distinguish itself compared to any previous guidelines.
- e. Whether it is a new guideline or update/extension of an existing SIO guideline
- f. Proposed budget for the guideline, as applicable
- g. Source of funding (if any) for the guideline and related dissemination activities
- h. Other SIO resources (if any) that will be available for the development and dissemination of the guidelines (e.g., research assistant, communication expert)
- i. Potential partnering organizations interested in collaborating on the topic.

The topics will be generated and prioritized as follows:

- a. The CPG Committee, with guidance from the SIO Executive Committee and the SIO Board, will draft the list of topics.
- b. The CPG Committee will send the list of topics via an online survey to the SIO Executive Committee, the SIO Board, and the SIO membership for ranking by priority.
- c. The CPG Committee will review all results of the survey and will confer with any partnering organization(s).

Then, the CPG Committee will put forward a topic for recommendation, to be submitted to the Liaison to the SIO Executive Committee for review and approval by the SIO Executive Committee.

## Appendix B



### Assembling the Panel

#### Affected companies

- a. Once a topic is selected and approved, the guideline methodologist works with the CPG Committee to collect any pertinent information on the topic. Pertinent information on the topic means any detail that could help clarify the topic (e.g., population, interventions, outcomes, etc.).
- b. The guideline methodologist, the project administrator, and the CPG Committee Co-Chairs develop a preliminary affected companies list. The list is finalized upon CPG Committee approval. Please see Appendix C for the most updated list of the affected companies.

#### CPG Panel Co-Chair(s) Selection

- a. SIO and the Participating Organization(s) will put forth one (1) Co-Chair each. The CPG Committee will request input from both SIO and the Participating Organization(s) on the selection of the appointed CPG Panel Co-Chairs.
  - i. If SIO is serving as the Participating Organization, SIO may or may not provide a CPG Panel Co-Chair but will still provide panel representation.
- b. The CPG Panel Co-Chairs need to jointly have a track record of publications, organizing people, and must make a clear time commitment and give priority to the project.
- c. The CPG Committee Co-Chairs will solicit nominations for the SIO CPG Panel Co-Chair from the SIO Executive Committee, the SIO Board, and SIO Committee Co-Chairs.
- d. All nominations will be evaluated by the CPG Committee. Nominees should have a proven track record of working on and publishing guidelines and be considered national and/or international leaders in their field; they will be asked to submit their CV.
  - i. The guideline methodologist provides the CPG Committee with the list of nominees, reiterating the COI Policy that CPG Panel Co-Chairs must be free of conflicting relationships with affected companies (see Appendix C), although one (1) CPG Panel Co-Chair may have research funding only.
  - ii. The guideline methodologist ensures the CPG Committee is aware of any conflicts of proposed CPG Panel Co-Chairs and requests approval of proposed CPG Panel Co-Chairs that are likely to be unconflicted (if not done already as above).



- e. Once a nominee is selected, the guideline methodologist invites the nominee to serve as the SIO CPG Panel Co-Chair using standard email, including any pertinent information on the topic if applicable.
  - i. This invitation contains a survey link where the nominee can formally accept or decline the invitation. If accepted, the nominee continues the survey to submit their COI disclosures.
  - ii. The guideline methodologist, the project administrator, and the CPG Committee Co-Chairs conduct the initial COI review.
    - 1) If the initial review is satisfactory, a summary is prepared for review and approval by the CPG Committee.
    - 2) If the initial review warrants further investigation, the guideline methodologist informs the nominee to provide more details to confirm the disclosures.
- f. Upon CPG Committee approval, the Liaison to the Executive Committee will put forth the SIO CPG Panel Co-Chair nomination to the SIO Executive Committee for approval.
- g. Upon SIO Executive Committee approval, the guideline methodologist sends the welcome package to the SIO CPG Panel Co-Chair.
- h. Once SIO has completed this process, the Participating Organization(s) will identify their CPG Panel Co-Chair according to its own internal process.

### **Panel membership where SIO is the Lead Organization**

- a. Prior to soliciting panel nominations, the CPG Committee will meet with the CPG Panel Co-Chairs to:
  - i. Discuss finalization of affected companies list
  - ii. Discuss panel membership using the panel composition criteria template
    - 1) In some cases, a COI pre-check should be conducted prior to sending the invitations.
  - iii. Discuss if any other organizations should provide representatives
    - 1) If there are other organizations providing representatives, their representatives will follow the same process as outlined below.
- b. The CPG Committees (SIO and the Participating Organization(s)) will consider CPG Panel nominations based on the following:
  - i. All SIO-representing Panel members must be SIO members in good standing, and Participating Organization(s)-representing Panel members may need to be members of the Participating Organization(s) if deemed necessary (e.g., Panel members nominated by the ASCO Panel Co-Chair do not need to be ASCO members to be on the panel). Outside Panel members may be invited if required critical expertise is not represented in the SIO or Participating Organization(s) membership.
  - ii. All CPG Panel members must agree to contribute to the guidelines according to ICJME guidelines (<http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>).

- iii. CPG Panel members will include the following:
  - 1) The CPG Panel should include at least one (1) expert with experience with the creation and/or evaluation of clinical practice guidelines, one (1) patient advocate familiar with the patient population of interest, one (1) clinician who is working with the patient population of interest, and one (1) person who has conducted studies (similar to or those actually being reviewed) included in the clinical practice guideline.
  - 2) Ideally, the CPG Panel should also include individuals who have previously published at least one (1) meta-analysis, systematic review, or clinical practice guideline; integrative/complementary practitioners of the modalities being included in the guideline (if relevant), and researchers, clinical researchers, and clinicians who have expertise in central clinical issues being addressed in the guideline.
  - 3) CPG Panel members should also be constituted of a diverse representation of professions (e.g., nurses, social workers, medical/radiation oncologists, licensed acupuncturist); geographic locations within the US (e.g., Midwest, East Coast, Mountain, West Coast, etc.); gender, and have at least two (2) international members (note: the number of international members can be greater than two (2) if there is appropriate expertise).
  - 4) The CPG Panel may include up to two (2) trainee members. These could include postdoctoral fellows or junior faculty, either clinical or research, with a focus on integrative oncology.
  - 5) CPG Panel members may not serve on more than one (1) guideline at a given time.
- iv. There should be approximately sixteen (16) members on each CPG Panel, with approximately ten (10) of those being SIO members and/or being members of the Participating Organization(s) inclusive of the two (2) Co-Chairs, one (1) patient representative, one (1) community oncologist, and up to two (2) SIO CPG Committee members. This number may fluctuate depending on the specific guideline. Moreover, the CPG Panel Co-Chairs will include one (1) SIO member and one (1) member of the Participating Organization(s).
- c. CPG Panel solicitation will be conducted as follows:
  - i. The CPG Panel Co-Chairs use the information above, plus their own knowledge of leaders in the field, to draft a list of potential panelists, representing both SIO and the Participating Organization(s). The CPG Panel Co-Chairs email the list of suggested panelists to the CPG Committee, which is available to provide feedback and input as will be helpful.
  - ii. The CPG Committee engages the SIO membership to solicit nominations or self-nominations to be put forth to the CPG Panel Co-Chairs for

consideration. Nominees are asked to complete an online survey to collect information on the following eligibility categories and are also asked to submit a copy of their CV.

- 1) Demonstrated history of leadership skills (required)
  - 2) Strong track record of excellence in integrative oncology (research or clinical) (required)
  - 3) Experience developing clinical practice guidelines (preferred)
  - 4) Conduct and publication of research in the specified guideline topic (preferred)
  - 5) Past/current involvement with SIO (required)
  - 6) Any conflicts of interest that would prohibit participation
- d. CPG Panel nominations will be first reviewed by the CPG Panel Co-Chairs and the guideline methodologist per CPG Committee procedures. Then, the final list of nominations will be put forward to the CPG Committee for review and final approval.
- e. Once nominees are selected, the guideline methodologist sends invites to serve on the CPG Panel using standard email, including any pertinent information on the topic if applicable.
- i. This invitation contains a survey link where the nominee can formally accept or decline the invitation. If accepted, the nominee continues the survey to submit their COI disclosures.
  - ii. The guideline methodologist, the project administrator, and the CPG Panel Co-Chairs conduct the initial COI review.
    - 1) If the review is satisfactory, the nominee is confirmed and a summary is prepared for review by the CPG Committee.
    - 2) If the review warrants further investigation, the guideline methodologist informs the nominee to provide more details to confirm the disclosures.
- f. The guideline methodologist and the project administrator will be responsible for communicating progress to the CPG Committee. The Liaison to the Executive Committee will then convey progress to the SIO Executive Committee.
- g. In the event that the CPG Panel Co-Chairs identify deficiencies in panel membership, they will be allowed to add new panel member(s) through an expedited process under the condition that it must be done before the systematic review is completed.
- i. The CPG Panel Co-Chairs will work with the CPG Committee Co-Chairs to resolve any deficiencies.
  - ii. The CPG Panel Co-Chairs may refer to the existing list of names that have been put forth as well as consider names who were not already included.
  - iii. The CPG Committee engages the SIO Executive Committee to solicit nominations or self-nominations to be put forth for consideration.
  - iv. Nominees must still submit their information as outlined in 7.3.c.ii.

## **Panel membership where SIO is the Participating Organization**

- a. Panel membership qualities and qualifications will be determined by the Lead Organization.
- b. SIO CPG Panel members to be considered will be put forward to the CPG Panel Co-Chairs by the CPG Committee per CPG Committee procedures.
- c. The CPG Committee will consider all potential SIO CPG Panel members based on the following (note: this process is under development and will be refined; we may develop a selection committee.)
  - i. SIO-representing Panel members must be SIO members in good standing. Outside Panel members may be invited if required critical expertise is not represented in the SIO membership.
  - ii. All Panel members must agree to contribute to the guidelines according to ICJME guidelines (<http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>).
  - iii. SIO Panel members may not serve on more than 1 (one) guideline at a given time.
- d. CPG Panel solicitation will be conducted as follows:
  - i. The CPG Committee engages the SIO membership to solicit nominations or self-nominations to be put forth to the CPG Panel Co-Chairs for consideration. Nominees are asked to complete an online survey to collect information on the following eligibility categories and are also asked to submit a copy of their CV.
    - 1) Demonstrated history of leadership skills (required)
    - 2) Strong track record of excellence in integrative oncology (research or clinical) (required)
    - 3) Experience developing clinical practice guidelines (preferred)
    - 4) Conduct and publication of research in the specified guideline topic (preferred)
    - 5) Past/current involvement with SIO (required)
    - 6) Any conflicts of interest that would prohibit participation
  - ii. The CPG Committee reviews all nominations, keeping in mind that there are a set number of panel slots available. The CPG Committee selects the final candidates, which can include no more than two (2) CPG Committee members as outlined in 7.5.
  - iii. The CPG Committee then puts those names forward as recommendations to the Lead Organization, who will make the final decision.

## **CPG Committee members serving on CPG Panel**

- a. Up to two (2) CPG Committee members may serve on an SIO guideline panel. CPG Committee members can serve as CPG Panel Co-Chairs. CPG Committee members who serve on the panel will fully participate as CPG Panel members.

- b. CPG Committee members who are interested in serving on the panel may submit their names and expertise to the CPG Committee Co-Chairs for review.
- c. The CPG Committee Co-Chairs will review the candidates' credentials and expertise and will put forward two (2) names to the CPG Panel Co-Chairs for consideration to be included in the panel.
- d. If a CPG Committee Co-Chair submits their name for consideration, they will be recused from the discussion and decision-making process, and another member of the CPG Committee will be asked to participate in the decision-making process.
- e. When it comes time for the CPG Committee to review and approve the guideline, they will be recused from the CPG Committee vote.
- f. CPG Committee members cannot participate on multiple panels at the same time or on consecutive guideline panels (beginning in March 2020).

## Appendix C



### Expert Panel Roles and responsibilities

#### Co-Chairs

Work with methodologist/SIO staff/SIO leadership in identifying potential panel members.

#### **Role in the Conduct of the Systematic Review of the Literature**

- a. Work with methodologist/SIO staff in developing the guideline protocol, which includes specific inclusion/exclusion criteria, search terms, and other information for the systematic review.
- b. Collaborate with the methodologist/SIO staff to develop a systematic review.
- c. Plan a strategy for the Panel to complete and review the results of the systematic review, as well as a plan for the formulation of recommendations.

#### **Meeting Attendance and General Responsibilities**

- a. Depending on the scope of the project, Panel co-chairs may hold regular meetings with methodologist (outside of the full Panel meeting) in order to move the project to completion.
- b. Work with methodologist to set and enforce deadlines.
- c. As the leaders of the effort, Co-Chairs are expected to meet the commitments and timelines that they establish at the onset of the project during protocol development.
- d. Assure meetings and discussions take place in an environment that welcomes opposing views and allows for evidence-based resolution of disagreements in a respectful manner.

#### **Manuscript Development, Guideline Authorship Policies, and Dissemination**

- a. Assume primary responsibility for drafting the manuscript but may divide the work by having specific panel members draft some sections. It is recommended that no more than three to four people assume responsibility for initially drafting the manuscript.
- b. Typically serve as first and last authors of the finished product, although there can be exceptions to this at the discretion of the Co-Chairs.
- c. Determine order of authorship.
- d. All authorship determinations must meet journals' requirements for authorship.

- e. Will be asked to provide feedback or input into the development of clinical tools and resources such as decision aids, algorithms, or flow charts that are designed to facilitate adherence to the guideline.
- f. Will be asked to interface with the media at the time of publication and to assist in the development of press releases. Co-Chairs are not expected to draft these documents, but to critically review them to ensure that the content is accurate and clear.
- g. Acknowledge that participation on Expert Panel does not confer authority to speak or provide communication on behalf of SIO without express permission from SIO.

### **Role in Guideline Updates**

- a. May be asked to review abstracts from an updated literature search to identify potentially practice-changing data based on defined criteria. These data represent “signals” for updating a guideline.
- b. Work with methodologist to decide when to reconvene the panel and have responsibility for updating the guideline recommendations and for developing the manuscript that results from any changes to these recommendations.

### **Confidentiality Policy and Disclosure of Potential Conflicts of Interest**

- a. Must observe a strict policy of confidentiality of documents, draft and final, pending publication and are required to keep content of panel deliberations confidential.
- b. Must adhere to the SIO Conflict of Interest Policy Implementation for Clinical Practice Guidelines by disclosing all conflicts of interest, including commitments that might be perceived as conflicts prior to initiating work on the guideline; and are asked to apprise methodologist of any changes that arise over the course of the project.
- c. Refrain from initiating new relationships with companies that may create a conflict under SIO’s Conflict of Interest Policy Implementation for Clinical Practice Guidelines for the duration of the panel term.

### Panel members

#### **Role in the Development of the Systematic Review of the Literature and Formulation of Recommendations**

- a. Are expected to substantively contribute to the development of the guideline protocol
- b. Should attend and participate in webinars/teleconferences to synthesize the results of the systematic review, discuss the structure of the guideline, and to formulate recommendations.
- c. Are expected to critically edit and review drafts of the documents (protocol and

recommendations).

### **Meeting Attendance and General Responsibilities**

- a. Attend Expert Panel meetings to synthesize the results of the systematic review, discuss the structure of the guideline, and to formulate consensus recommendations.
- b. Be prepared for the meeting by reviewing the materials in advance.
- c. Meet deadlines for literature review, manuscript drafting, and manuscript editing within a reasonable timeframe.
- d. Members who are unable for whatever reason to adhere to the project timeline/work schedule are asked to notify methodologist and Panel Chairs. They may be asked to resign to ensure the timely development of guideline product and to allow for recruitment of an alternate member to prevent an additional workload burden on the remaining panel members.

### **Manuscript Development, Guideline Authorship Policies, and Dissemination**

- a. Actively participate in the development of recommendations
- b. Critically edit and review manuscript drafts.
- c. Panel members who have attended meetings, participated in the review of evidence and helped draft and edit the guideline are eligible to serve as authors on the published product provided they meet the journal's authorship policies.
- d. May be asked to provide feedback or input into the development of clinical tools and resources such as decision aids, algorithms, or flow charts that are designed to facilitate adherence to the guideline.
- e. May be asked to interface with the media at the time of publication and to assist ASCO in the development of press releases. Panel members are not expected to draft these documents, but to critically review them to ensure that the content is accurate and clear

### **Confidentiality Policy and Disclosure of Potential Conflicts of Interest**

- a. Are required to observe a strict policy of confidentiality of guideline documents, draft and final, pending guideline publication; and are required to keep content of panel deliberations confidential.
- b. Are required to disclose any potential conflicts of interest, including commitments that might be perceived as conflicts prior to initiating work on the guideline; and are asked to apprise the methodologist of any changes that arise over the course of the project.
- c. Should refrain from initiating new relationships with companies that may create a conflict under SIO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines for the duration of the panel term.



## Appendix D



### Guideline Process



### Steps in Creating an SIO Guideline

1. Protocol developed to act as a road map for guideline development
2. Systematic review conducted by methodologist and panel (searches, abstract review, full text review, data extraction, evidence table development)
3. Panel meets, reviews evidence, develops recommendations
4. Draft manuscript assembled by the Co-Chairs (with some/all panel members) and methodologist
5. Panel reviews and approves the first draft
6. Draft recommendations posted for open comment period
7. Reviews incorporated into revised draft
8. Panel reviews and approves revised draft
9. Draft submitted to CPG committee for review and approval
10. Panel revises draft based on CPG committee review
11. Panel reviews and approves final draft.
12. Draft returned to CPG committee for review and approval (if required)
13. Draft submitted to select journal for publication



### Guideline Steps



## Overview of Responsibilities

### Co-Chairs

### Responsibilities Systematic Review Development

- Co-Chairs work with the methodologist in developing the Guideline Protocol, which includes specific inclusion/exclusion criteria, search terms, and other information for the systematic review.
- Panel Co-Chairs collaborate with the methodologist to develop a systematic review. The systematic review is what ensures that the Guidelines are “evidence based.”
- Co-Chairs plan a strategy for the Panel to review the results of the systematic review. They assume responsibility for deciding if the panel work can be conducted via webinar/teleconference or if a face to face meeting is needed.



## Responsibilities for Guideline Development

- Panel Co-Chairs assume primary responsibility for drafting the manuscript, but may divide the work by having specific panel members draft some sections. It is recommended that no more than three to four people assume responsibility for initially drafting the manuscript.
- Co-Chairs work with methodologist to set and enforce deadlines.
- Co-Chairs typically serve as first and last authors of the finished product, although there can be exceptions to this at the discretion of the Co-Chairs.
- Co-Chairs may be asked to review abstracts from an updated literature search to identify potentially practice-changing data based on defined criteria. These data represent “signals” for updating a guideline.



## Additional Responsibilities

- Co-Chairs will be asked to provide feedback or input into the development of “clinical tools and resources” such as decision aids, algorithms, or flow charts that are designed to facilitate adherence to the guideline.
- Co-Chairs will be asked to interface with the media at the time of publication and to assist SIO in the development of press releases, and of materials suitable for use with patients. Co-Chairs are not expected to draft these documents, but to critically review them to ensure that the content is accurate and clear.



## Panel member nominations: Things to consider

- Are all of the relevant specialties and disciplines represented?
- Is there a balance between senior leaders in the field and up and coming clinicians?
  - 0-3 years post fellowship is considered to be early career, between 3-10 is mid-career, and beyond 10 would be senior.
- Is the proposed panel geographically diverse (i.e. not dominated by one area or institution)?
- Are there international members?
- Is there a balance between known intellectual points of view?
- Is there sufficient patient and/or advocate representation?
- Is there representation from current or past CPGC members?
- 10-16 members including co-chairs and patient/advocate representation



## Overview of Responsibilities

### Panel Members



## Protocol and Systematic Review Development

- Work with methodologist in developing the guideline protocol, which includes specific inclusion/exclusion criteria, search terms, and other information for the systematic review.
- All panel members must approve final draft of protocol before literature search can commence
- Review identified studies after methodologist completes screening of literature
- Suggest any missing study that is not captured by literature search. Preferably before data extraction/creation of evidence tables



## Guideline Recommendations & Manuscript Development

- Must be involved in drafting and reviewing of recommendations and manuscript.
- Assigned into writing groups by the co-chairs.
- Keep to established deadlines during the different phases of guideline development.
- Inform methodologist of any new practice changing study published during the guideline development process.
- Update COI disclosures as necessary
- Respond to email correspondence in a timely fashion

## Writing Groups

- Can be groups of 3 or 4 panel members
- Tasks include reviewing evidence tables and drafting recs for specific intervention assigned
- Drafting sections in the manuscript
- Schedule bi-weekly/monthly calls to work on group assignment
- Group lead will be assigned by co-chairs
- Co-chairs will check in on group meetings to provide support intermittently

## Panel tasks

- Work in assigned groups
- Review list of included studies assigned to group
- Determine what needs to be removed or what might be missing
- Send any missing citation to methodologist for review
- Group lead should ensure group work is done within the set timelines

## Drafting Recommendations

Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.



## Statement of fact is not a recommendation

- Acupressure in patients experiencing pain during breast cancer therapy improved patient's QOL and reduced pain intensity in the long term.  
[FACT based on clinical/scientific evidence]
- Clinicians should perform/administer/offer acupressure to patients experiencing pain during breast cancer therapy.  
[ACTIONABLE Recommendation]



## GLIDES approach and BRIDGE-WIZ software

- Yale University guideline developers created BRIDGE-Wiz based on a body of guideline development literature
- Other medical societies have used and evaluated this process positively<sup>1</sup>
- Systematically develop clear, translatable, and implementable recommendations using natural language, based on the evidence and assessment of its quality to increase usability for end users

<sup>1</sup>Shiffman RN, Michel G, Rosenfeld RM, Building better guidelines with BRIDGE-Wiz: development and evaluation of a software assistant to promote clarity, transparency, and implementability, Journal of the American Medical Informatics Association, (2011). doi:10.1136/amiainf-2011-000172



## Explicit

- **WHEN** {under what circumstances}
- **WHO** {in the Intended Audience}
- **Ought** to {with what level of obligation}
- **DO WHAT**
- {To **WHOM**} {which members of the target population}
- **HOW**
- **WHY**

- For an intervention define:
  - Action and actors
  - Population and circumstances
  - Benefits?
    - Benefit > harm
    - Balance/equilibrium
    - Harm > benefit
- Cost???



Panel determines

- Rating quality of evidence for recommendations
  - High
  - Intermediate
  - Low
  - Insufficient
- BRIDGE-Wiz provides:
  - Suggested strength of recommendation
  - Suggested terms of obligation



Quality or Strength of Evidence

The overall strength of the total body of evidence is rated as:

- **High** (Convincing)
  - High confidence that available evidence reflects true effect
- **Intermediate** (Adequate)
  - Moderate confidence that available evidence reflects true effect
- **Low** (Inadequate)
  - Little confidence that available evidence reflects true effect
- **Insufficient/Inconclusive**
  - Evidence is insufficient to discern net effect

## Type of Recommendation and its Strength

- **Evidence-based**
  - Sufficient evidence to inform recommendation
- **Formal Consensus**
  - There is insufficient evidence and expert panel uses formal consensus process to reach recommendation
- **Informal Consensus**
  - There is insufficient evidence, so recommendation is considered best current guidance based on informal consensus of Expert Panel
- **No recommendation**
  - Insufficient evidence, confidence, or agreement to provide a recommendation

## Recommendation Strength

Evidence Quality	Net Benefit	Net Harm	Balance
<b>High Quality</b> - High confidence in evidence of effect. Further research is very unlikely to change effect's magnitude or direction	Strong	Strong	Moderate Weak
<b>Intermediate Quality</b> - Moderate confidence in evidence of effect. Further research is unlikely to change effect's direction, but may change magnitude	Strong Moderate	Strong Moderate	Moderate Weak
<b>Low Quality</b> - Low confidence in evidence of effect. Further research may change effect's direction and/or magnitude	Weak	Weak	Weak

With **Intermediate** Evidence Quality and a Balance of Benefits and Harms  
this key action statement should have a Recommendation Strength of

Moderate    Weak

The level of obligation should be  Should    May

**DO:**

- Think about if everyone will understand the recommendations in the same way.
- Make sure that if you say “contraindications,” “exceptions,” “selected patients,” etc. that you define what that means, explicitly.
- If applicable, a list of the most common side effects should also be included in the manuscript.

**DON'T:**

- Include statements of fact in recommendations – this can be included in literature review and/or clinical interpretation sections.
- Use words for non-measurable actions, e.g. “consider”
- Use words that different people may interpret differently, e.g. “accessible”

- Population: patients experiencing anxiety from breast cancer therapy
- Intervention: music therapy
- Comparator: no music therapy
- Benefit: High – reduction in anxiety, increased QOL and other clinical benefits
- Harms: Low – no differences in adverse events
- Balance of benefits and harms: benefits > harms
- Evidence quality: one or more RCT = High quality
  
- BRIDGE-Wiz suggestions
  - Strength of recommendation: **High**
  - Term of obligation: **“should”** {offer}



## Draft recommendation

Music therapy should be offered to patients experiencing anxiety during breast cancer therapy.

(Type: Evidence based; Benefits outweighs harms; Evidence quality: High; Strength of recommendation: Strong)

- Note: Specific benefits, harms, exceptions, unclear areas of evidence, etc. are described in the text



## Publications

## SIO SOCIETY FOR Integrative Oncology® Publication

- Full guideline is published in select journal
  - Authorship: all Panel members that contribute to either writing/reviewing the manuscript, participate on Panel calls or email discussions.
    - Note: All COI/authorship confirmation should be completed as soon as requested by journal.

## SIO SOCIETY FOR Integrative Oncology® Timeline

Mo 1	Mo 2	Mo 3	Mo 4	Mo 5	Mo 6	Mo 7	Mo 8	Mo 9	Mo 10	Mo 11	Mo 12	Mo 13	Mo 14	Mo 15
Protocol & Planning														
Systematic Review														
					Recommendations & Guideline Draft									
									Revisions, Reviews, & Approval					
													Comms & Publication	

## Appendix E



### **Conflict of Interest Policy Implementation for Clinical Practice Guidelines of the Society for Integrative Oncology<sup>1</sup>**

The Society for Integrative Oncology (SIO) is dedicated to improving the lives of people affected by cancer through research, education, prevention and delivery of high-quality patient care. One of the primary ways in which SIO fulfills this responsibility is through the development of clinical practice guidelines. Provider and public confidence in these guidelines depend on the cultivation of expert opinions based on the best available evidence and in a manner designed to minimize actual and perceived conflicts of interest.

For SIO, guideline development is a multi-step process. Once drafted by a diverse panel of experts, guidelines must be approved by SIO's Clinical Practice Guideline (CPG) Committee (Committee) and peer-reviewed in accordance with rigorous standards set by high impact journals. The following procedures provide strategies for managing potential conflicts of interest (COI) through each phase of guideline development.

#### **I. General Policy**

SIO requires COI disclosure by individuals involved in drafting, reviewing, and approving guideline recommendations and sets limits on the financial relationships that panel members and reviewers can have with Companies that could reasonably be affected by care delivered in accordance with guideline recommendations.

SIO will also be adopting the Council of Medical Specialty Societies Code (CMSS) for Interactions with Companies<sup>2</sup> that requires the majority of panel members (51%), including the panel chair, to be free of certain relationships with affected Companies. The remaining 49% of panel members may be appointed to a panel if they hold some relationships with affected Companies. SIO defines a "Company" as a for-profit entity that develops, produces, markets, or distributes drugs, devices, services, products or therapies used to diagnose, treat, monitor, manage, and alleviate health conditions. The CMSS code was developed to ensure that societies' interactions with companies are independent and transparent, and advance medical care for the benefit of patients and populations.

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<sup>1</sup> The SIO's Conflict of Interest Policy Implementation for Clinical Practice Guideline for Panel Co-Chairs and Expert Panel Members was adapted from ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines in March 2020.

<sup>2</sup> Council of Medical Specialty Societies, Code for Interactions with Companies.  
[www.cmss.org/codeforinteractions.aspx](http://www.cmss.org/codeforinteractions.aspx)

## II. Identifying Affected Companies

Companies with products and/or services affected by a guideline are considered “affected Companies” for purposes of determining whether a COI exists in the development of SIO guidelines. A Company is an “affected Company” if there is a reasonable likelihood of *direct regulatory or commercial impact (positive or negative)* on the entity as a result of care delivered in accordance with guideline recommendations. Affected Companies will generally be identified at the time of development of the guideline protocol, prior to selection of panel members, chairs or co-chairs.

Affected Companies will generally be identified by members of the SIO CPG Committee and the SIO Executive Committee. In some cases, where identification is straightforward, an SIO guideline methodologist may identify affected Companies using criteria approved by the SIO CPG Committee. The list of affected Companies should remain consistent throughout guideline development and adoption. If changes in the marketplace or in the focus of the guideline make revisions necessary, a modified list may be developed or reviewed by the independent party. The list of Companies affected by a guideline will be made available to prospective guideline panel chairs and panel members and the Clinical Practice Guideline Committee.

## III. Disclosure

SIO’s policy is to promote the development of clinical practice guidelines in a manner that minimizes the risk of actual and perceived bias. Disclosure of relationships with Companies is the first step in SIO’s process of evaluating and managing relationships that could result in actual or perceived bias.

### a. General COI Disclosure Additional Disclosure

All prospective panel members, including prospective panel chairs and co-chairs, will disclose financial interests and other relationships with Companies in accordance with SIO’s Policy. All Committee members disclose the same information. These disclosures are general and may or may not identify relationships with affected Companies.

Disclosure categories include compensation received for employment, leadership positions, consulting activities, speaking engagements, and expert testimony; as well as ownership interests, research funding (to the individual or the institution), and licensing fees and royalties associated with intellectual property interests received by panel or Committee members themselves and their immediate family members.<sup>3</sup>

An individual’s COI disclosures must be current in SIO’s electronic system prior to appointment to a panel. Panel members and Committee members must keep their COI disclosures up to date.

### b. Additional Disclosure

After reviewing the general disclosures and the list of affected Companies, the Committee Chair or SIO guideline methodologist may request more detailed information from an individual about the nature, value, or extent of his or her disclosed relationship with an affected Company in order to apply this Policy.

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<sup>3</sup> American Society of Clinical Oncology, Policy for Relationships With Companies 2013 JCO2013.49.5002 <http://jco.ascopubs.org/content/early/2013/04/22/JCO.2013.49.5002>



Occasionally, an individual may have a relevant indirect or non-financial interest or relationship that is not covered by SIO's general COI disclosure, such as an intellectual property interest from which no royalties or other payments have yet been received; a strong professional or research opinion; or an outside affiliation. In these situations, the interest should be disclosed to the panel chair, co-chair or SIO guideline methodologist. Disclosure reports identifying panel members' relationships with affected Companies will be available to panel members throughout the guideline development process. The Committee will have this information available when considering guideline recommendations.

#### **IV. Guideline Panels**

SIO's goal is to assemble a diverse and well-qualified group of experts to develop, approve, and adopt guideline recommendations in a manner that minimizes the risk of actual and perceived bias.

##### **a. Not Eligible to Serve on Panel Additional Disclosure**

Having a relationship with a Company does not necessarily mean an individual is biased or has a COI. However, SIO's policy is that certain financial relationships give rise to COIs that are not capable of being effectively managed and are, in fact, inconsistent with actual and perceived independence in the guideline development process. An individual is not eligible to serve on a clinical practice guideline panel if he or she:

1. participates in a speakers' bureau<sup>4</sup> (on any subject) on behalf of an affected Company;
2. is employed by an affected Company, or has been employed by an affected Company at any time during the year prior to appointment to the panel and to continue for one year after the publication of the guideline; or
3. holds a significant ownership interest in an affected Company<sup>5</sup>; or
4. holds a financial or other relationship whether with an affected Company or another interest that, in SIO's discretion, presents a risk of actual or perceived bias that cannot be effectively managed or could undermine public confidence in the guideline.

##### **b. Eligible to Serve as Panel Chair or Co-Chair**

Generally, individuals who have disclosed financial interests in or relationships with affected Companies will not be appointed as panel chairs or co-chairs. A panel chair or co-chair must have been free of all interests and relationships for one year prior to appointment as chair and remain free of these interests and relationships at all times during the panel's work and through one year after the guideline is published.

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<sup>4</sup> "Speakers' bureau" means a compensated role as a presenter for which any of the following criteria are met: (a) a Company has a contractual right to dictate or control the content of the presentation or talk; (b) a Company creates the slides or presentation material and has final approval of the content and edits; or (c) the presenter is expected to act as a Company's agent or spokesperson for the primary purpose of disseminating company or product information. SIO recognizes that some activities called "speakers' bureaus" may not meet these criteria and, conversely, that activities may meet these criteria and not be termed "speakers' bureaus." SIO will rely on the judgment and integrity of disclosing individuals to determine whether an activity constitutes a speakers' bureau under this Policy. This definition of "speakers' bureau" does not extend to employees of a Company who make presentations as part of their employment.

<sup>5</sup> "Significant ownership interest" means shares of a publicly traded Company greater than \$50,000 in value or an equity interest in a privately held Company greater than 5% at the time of disclosure. This does not include interests invested in diversified funds whose holdings cannot be controlled by the disclosing individual.

However, the Committee may appoint one panel chair who receives research funding from an affected Company, if doing so would ultimately help the panel develop a higher quality guideline. In this case, the Committee must appoint a co-chair who has no relationships with affected Companies, including research funding.

If a panel chair or co-chair wants to continue to serve as chair for future guideline updates, he or she must remain eligible as described above. If, at the time of update, an individual is no longer eligible to serve as a chair, he or she will be eligible to serve as a panel member at the discretion of the Clinical Practice Guideline Committee and in accordance with this Policy Implementation.

**c. Eligible to Serve in the Panel Majority**

In accordance with the CMSS Code, a majority of SIO guideline panel members must be free of conflicts of interest relevant to the subject matter of the guideline. All relationships with Companies must be disclosed as described in Section IIIa. The Committee Chair or SIO guideline methodologist may ask for additional information about a relationship with an affected Company, as described in Section IIIb, to apply this Policy Implementation.

For the purpose of appointing at least 51% of guideline panel members who are free of COI, SIO defines the following relationships as COIs:

1. Research funding from an affected Company, paid to the individual or his or her practice or institution if:
  - a. research payments are made directly from the affected Company to the individual;
  - b. the individual's salary is supported (in whole or part) through a research grant from an affected Company;
  - c. the individual is a national or overall principal investigator for a study funded by an affected Company;
  - d. the individual is a member of a steering committee of a study that does not have a principal investigator.<sup>6</sup>
  - e. in kind donations of products being tested by the manufacturers.
2. Compensation (including honoraria) from any one affected Company that equals, in aggregate, \$5,000<sup>7</sup> or more in a calendar year.
  - a. This includes fees and honoraria for leadership positions, consulting activities, speaking engagements, expert testimony, and patent or other licensing fees.
  - b. This excludes any compensation provided under any of the circumstances described in Section IVa.

Individuals with any of these relationships are not eligible to serve in the panel majority, but may be eligible to serve in the panel minority. A member of the panel majority must remain free of these COIs from the time of his or her appointment to the panel through the end of the calendar year in which the guideline is published. If an individual's relationships change during that period such that he or she is no longer eligible to serve in the panel majority, the Committee chair will shift the individual to the panel minority. If that is not feasible given the panel composition, the individual must resign from the panel.

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<sup>6</sup> Serving as a site or local PI, or a consortium PI without salary support are not considered conflicts of interest.

<sup>7</sup> This dollar value may be updated periodically to keep pace with current standards.

If an individual holds a patent in a technology that could be part of a guideline recommendation, the individual may be eligible to serve on the panel minority as described in Section IVc with special requirements for COI management, or SIO may find the individual ineligible to serve on the panel under Section IVa.4 above.

If an individual holds stock options in an affected Company, as defined in Section II above, the individual may be eligible to serve on the panel minority as described in Section IVc with special requirements for COI management, or SIO may find the individual ineligible to serve on the panel under Section IVa above.

#### **d. Voting**

At in-person and/or virtual meetings, panel recommendations must be adopted by a 75% majority of panel members in attendance at a meeting where a simple majority of panel members are present. When the panel votes electronically, recommendations must be adopted by a 75% majority of the entire panel.

Because of the supermajority voting standard, panel members who have disclosed financial relationships with affected Companies do not need to recuse themselves from discussing and voting on guideline recommendations on these grounds.

### **V. Clinical Practice Guideline Committee**

The roles and responsibilities of the Clinical Practice Guideline Committee is to identify and prioritize topics for guideline development, provide strategic direction in the development of guidelines, review and approve final drafts of the guidelines and provide recommendations regarding possible third-party guideline endorsement and joint guideline endeavors.

#### **a. Disclosure**

Committee members will generally disclose financial relationships with Companies as described in Section IIIa and make additional disclosures as described in Section IIIb. These disclosures will be compared with the list of affected Companies before a guideline is reviewed by the Committee.

Committee members' general disclosure reports, identifying relationships with affected Companies, will be available to Clinical Practice Guideline Committee members prior to Committee discussion of a guideline.

#### **b. Clinical Practice Guideline Committee Reviewers**

From time to time, the Committee Chair appoints Committee members to serve as reviewers of a guideline. Generally, the Committee Chair will select Committee members who have no financial relationships with affected Companies or products to serve as guideline reviewers.

#### **c. Recusal**

To underscore the independence and integrity of the guideline adoption process, guidelines will be approved only by Committee members who do not have financial relationships with affected Companies or products. Therefore, disclosure of any financial relationship with an affected Company should be cause for recusal. Whether a relationship relates to the subject matter of the guideline is not a relevant consideration for purposes of determining recusal.

A Committee member recused from voting may take part in initial Committee discussion of

the guideline manuscript, recognizing that there may be additional discussion by remaining Committee members after recusal and before the vote.

#### **d. Voting**

Generally, guidelines will be reviewed and approved by a vote of the Committee at a meeting where a quorum is present. However, if the quorum is lost by virtue of recusals as described in Section Vc, the remaining Committee members in attendance will constitute a quorum as long as at least three voting members are present. Approval by majority vote of this group will be considered approval by the Committee.

### **VI. Publication and Peer Review**

When SIO publishes a guideline, all disclosures of panel members will generally be published concurrently. This Policy Implementation is also posted publicly on SIO's website. Panel members will be required to disclose COIs to the journal in which the guideline will be published, in accordance with the journal's policies.

### **VII. Joint Guidelines and SIO-Endorsed Guidelines**

From time to time, SIO may join another organization to create a guideline or may endorse a relevant guideline produced by another organization. In these instances, the COI management procedures used for the development of the joint or endorsed guideline must meet the requirements of CMSS Code for Interactions with Companies, as a baseline.<sup>2</sup>

### **VIII. Exceptions**

SIO's goal is to assemble a diverse and well-qualified group of experts to develop, approve, and adopt guideline recommendations. If required to achieve this goal, these procedures may be adapted by the SIO on a case-by case basis to the extent necessary.

### **IX. Decisions**

Questions about the application of this Policy Implementation will be decided by SIO. SIO will consider recommendations from the panel chair and co-chair and the Committee Chair (unless the question concerns their roles). SIO decisions can be made by the SIO CPG Committee and the SIO Executive Committee. Questions and decisions may concern, for instance, whether an individual is eligible to serve on a panel, or as a panel chair or co-chair, or in a panel majority, or as a Committee reviewer; whether an individual should be recused from voting; or whether an exception is warranted.

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**Application:** *Applies to SIO*

**History:** *Based upon the ASCO Guidelines Committee COI Policy and adopted by the SIO Guidelines Committee on April 3, 2020*

## Appendix F



### **Conflict of Interest (COI) Frequently Asked Questions (FAQ)**

This document answers some common questions about the SIO Conflict of Interest (COI) policy. Please feel free to contact the guideline methodologist (Dr. Nofisat Ismaila, [oismaila@fredhutch.org](mailto:oismaila@fredhutch.org)) and/or the SIO Clinical Practice Guidelines Committee Co-Chair (Dr. Heather Greenlee, [hgreenlee@fredhutch.org](mailto:hgreenlee@fredhutch.org)) if you have additional questions or concerns.

#### **1. What is an affected company? How are the affected companies identified?**

Answer: A Company is considered an “affected Company” if there is a reasonable likelihood of direct regulatory or commercial impact (positive or negative) on the entity as a result of care delivered in accordance with clinical practice guideline recommendations. In cases where identification of affected companies is straightforward, the guideline methodologist will identify affected Companies using criteria approved by an independent party. Categories of affected Companies will generally be identified at the time of development of the guideline protocol, prior to selection of panel members, chairs or co-chairs. Identification is done by using both private and public search engines. For the purposes of SIO Clinical Practice Guidelines, affected Companies extend beyond pharmaceutical companies and can also include companies, and products and clinical practices in a for-profit clinical setting, which could be impacted by clinical practice guideline recommendations.

#### **2. What is the list of affected companies?**

<b>Companies, Products and Practices</b>
Pharmaceuticals and Diagnostic/Health Equipment companies
<ul style="list-style-type: none"><li>• Any pharmaceutical or health care supply/service company</li></ul>
Companies related to Complementary, Alternative and Integrative Medicine (CAIM) Practices and Products
<ul style="list-style-type: none"><li>• Acupressure</li></ul>
<ul style="list-style-type: none"><li>• Acupuncture</li></ul>
<ul style="list-style-type: none"><li>• Biofeedback</li></ul>
<ul style="list-style-type: none"><li>• Cannabis</li></ul>
<ul style="list-style-type: none"><li>• Dietary supplements</li></ul>
<ul style="list-style-type: none"><li>• Energy therapies, including but not limited to: Reiki Qigong</li></ul>
<ul style="list-style-type: none"><li>• Herbs/botanicals</li></ul>
<ul style="list-style-type: none"><li>• Laser therapy</li></ul>
<ul style="list-style-type: none"><li>• Manipulation</li></ul>

**3. What sorts of relationships are considered conflicts that would preclude me from serving on a panel?**

Answer: SIO's policy is to promote the development of clinical practice guidelines in a manner that minimizes the risk of actual and perceived bias. Having a relationship with an affected Company does not necessarily mean an individual is biased or has a conflict of interest. However, some relationships cannot be managed and are inconsistent with reducing actual or perceived bias. Please refer to the COI Policy for an explanation of prohibited relationships for panel members and chairs. Generally, employees or major owners/stockholders of affected companies are not permitted to participate on guideline panels.

Individuals who receive research grant funding from an affected Company or in kind donations of products being tested by manufacturers must report the potential conflict, which will be evaluated on a case-by-case basis. In general, research involving human trials would be considered a COI, however in vitro and animal studies would not be considered conflicted.

Individuals who receive income royalties, consulting fees, clinical fees from a for-profit clinic, and/or other financial benefits from any potentially affected Company must report the potential conflict and whether the income is greater or less than \$5,000 USD.

SIO requires that panel Co-Chairs be free of conflicts with affected Companies, and one of the Co-Chairs can receive research funding from an affected Company. SIO requires the majority of panel members (51%), including the panel chairs, to be free of certain relationships with affected Companies. The remaining 49% of panel members may be appointed to a panel if they hold some relationships with affected Companies. The guideline methodologist can answer questions about your particular circumstances, if you have questions.

**4. Must all panel members be completely free of relationships with affected Companies?**

Answer: No, but a majority of panel members must be free of relationships with affected Companies. In addition, panel chairs must be free of all relationships with an affected Company, except in instances where one of two co-chairs may receive research funding from an affected Company.

**5. Are there any exceptions?**

Answer : Yes. SIO's goal is to assemble a diverse and well-qualified group of experts to develop, approve, and adopt clinical practice guideline recommendations. If required to achieve this goal, these procedures may be adapted by SIO on a case-by case basis to the extent necessary. All decisions about exceptions are made at the discretion of SIO.

**6. Are COIs made public?**

Answer: Yes. Any COIs will be disclosed in the journal where the guidelines are published.

Appendix G



**SIO Clinical Practice Guideline Development Protocol Worksheet**

**A. Title of Guideline**

**B. Overarching Guideline Question**

Guideline question:	
---------------------	--

**C. Overarching Inclusion Criteria** (criteria that would apply to all research questions)

Inclusion Criteria:	
---------------------	--

**D. Overarching Exclusion Criteria** (criteria that would apply to all research questions)

Exclusion Criteria:	
---------------------	--

**E. Definition of Terms**

Term	Definition

**F. Searching the Literature**

Generally speaking, only the top three tiers of evidence should be considered in an SIO guideline product to make strong evidence-based recommendations (this includes evidence-based practice guidelines from other guideline development organizations). Inclusion of evidence below that threshold should to be justified with a compelling rationale (e.g. inclusion of cohort studies for diagnostic utility guidance) and generally should be followed by lower strength recommendations.



**Question 1**

<b>Research Question:</b>	
Population:	
Intervention:	
Comparison:	
Outcomes:	
• Primary	
• Secondary	
Time:	
Health setting:	
Study designs:	

<b>Publication date from:</b>	<b>to:</b>
Languages:	
<b>Study Selection Criteria:</b> (applies only to this research question)	
Inclusion Criteria:	
Exclusion Criteria:	
<b>Concepts:</b>	
<b>Evidence sources:</b>	
PubMed:	
Cochrane:	
GIN:	
ECRI:	
AiCPG:	
Other (specify):	
Other (specify):	



## Question 2

<b>Research Question:</b>	
Population:	
Intervention:	
Comparison:	
Outcomes:	
• Primary	
• Secondary	
Time:	
Health setting:	
Study designs:	

<b>Publication date from:</b> <b>to:</b>	
Languages:	
<b>Study Selection Criteria:</b> (applies only to this research question)	
Inclusion Criteria:	
Exclusion Criteria:	
<b>Concepts:</b>	
<b>Evidence sources:</b>	
PubMed:	
Cochrane:	
GIN:	
ECRI:	
AiCPG:	
Other (specify):	
Other (specify):	

## Question 3

<b>Research Question:</b>	
Population:	
Intervention:	
Comparison:	
Outcomes:	
• Primary	
• Secondary	
Time:	
Health setting:	
Study designs:	

<b>Publication date from:</b> <b>to:</b>	
Languages:	
<b>Study Selection Criteria:</b> (applies only to this research question)	
Inclusion Criteria:	

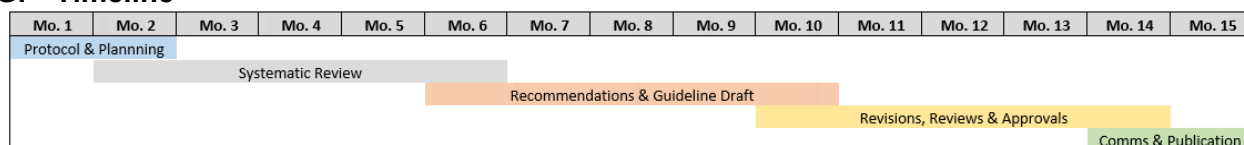
Exclusion Criteria:	
<b>Concepts:</b>	
<b>Evidence sources:</b>	
PubMed:	
Cochrane:	
GIN:	
ECRI:	
AiCPG:	
Other (specify):	
Other (specify):	

#### Question 4

<b>Research Question:</b>	
Population:	
Intervention:	
Comparison:	
Outcomes:	
• Primary	
• Secondary	
Time:	
Health setting:	
Study designs:	

<b>Publication date from:</b>	<b>to:</b>
Languages:	
<b>Study Selection Criteria:</b> (applies only to this research question)	
Inclusion Criteria:	
Exclusion Criteria:	
<b>Concepts:</b>	
<b>Evidence sources:</b>	
PubMed:	
Cochrane:	
GIN:	
ECRI:	
AiCPG:	
Other (specify):	
Other (specify):	

#### G. Timeline



<b>Development Step</b>	<b>Target Date</b>
• Expert Panel Assembled	
• Initial Panel meeting - Protocol Finalized	
• Systematic Review draft completed	
• Second Panel Meeting – Draft recommendations	
• Open Comment	
• Manuscript draft- first complete version	
• Revisions to Manuscript Draft	
• Panel Approval	
• Internal & CPGC Review	
• Final report with revisions completed	
• Manuscript Submission to Journal	
• Manuscript Publication	

**H. Additional topics for discussion (no formal literature search to be performed)**


**I. List of Affected Companies**

<b>Class of drug</b>	<b>Agent (generic/trade)</b>	<b>Affected company</b>

Date search for affected companies completed: \_\_\_\_\_

**A. Expert Panel Membership**

## Appendix H



### Guideline Manuscript Template

**[Insert Guideline Title]: SIO Guideline [Update]**

**Authors:** *[Insert author list i.e. first name, middle initial, last name, designation<sup>1</sup>;*

**Author Institutions:** *[Insert institution information i.e. <sup>1</sup>Organization, City, State;]*

*[(Insert initials of co-chairs) were Expert Panel Co-chairs]*

**Corresponding Author:**

Society for Integrative Oncology

Address: 4301 50<sup>th</sup> Street NW, Suite 300 PMB 1032, Washington DC 20016;

email: [guidelines@integrativeonc.org](mailto:guidelines@integrativeonc.org).

**Running Head:** *[Insert abbreviated title ≤ 65 characters including spaces]*

Published online ahead of print at [www.xxx.xxx](http://www.xxx.xxx) on [add DATE]

**Other organization Committee approval:** [add DATE]

***Editor's note***

This Society for Integrative Oncology (SIO) Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a supplement with additional evidence tables, slide sets, clinical tools and resources, and links to patient information at <https://integrativeonc.org/knowledge-center/patients> and [www.cancer.net](http://www.cancer.net), is available at <https://integrativeonc.org/practice-guidelines/guidelines>.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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**ABSTRACT**  
*[Text ≤ 275 words]*

**Purpose:**

**Methods:**

**Results:**

**Recommendations:**

Additional information is available at <https://integrativeonc.org/practice-guidelines/guidelines>.

## INTRODUCTION

The purpose of this guideline [update] is to

### The Bottom Line

**[Insert Guideline Title]: SIO Guideline [Update]**

#### **Guideline Question**

[Insert the overarching question(s) – if there are multiple questions or sub-questions, they should **not** be listed in the bottom-line box]

#### **Target Population**

[Insert all of the specific target populations that this manuscript applies to]

#### **Target Audience**

[Insert all of the specific health providers and patients that this guideline applies to]

#### **Methods**

An Expert Panel was convened to develop [update] clinical practice guideline recommendations based on a systematic review of the clinical oncology literature.

#### **Recommendations**

*Recommendation 1.1* [insert specific and actionable recommendation – e.g. must offer, should offer, may offer]

Using GLIDE

- Type of recommendation: Evidence based, informal consensus
- Quality of evidence: Low, intermediate, high
- Relationship between benefits and harms: harm outweighs benefit, benefit outweighs harm
- Strength of recommendation: Weak, moderate, strong

*Recommendation 1.2*

#### **Additional Resources**

Definitions for the quality of the evidence and strength of recommendation ratings are available in Appendix Table A2, online only. More information, including a supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at <https://integrativeonc.org/practice-guidelines/guidelines>. The SIO Guidelines Methodology Manual (available at <https://integrativeonc.org/practice-guidelines/sio-guidelines-guidelines-methodology>) provides additional information about the methods used to develop this guideline. Patient information is available at <https://integrativeonc.org/knowledge-center/patients>.

**SIO believes that cancer clinical trials are vital to inform clinical decisions and improve cancer care, and that all patients should have the opportunity to participate.**

## GUIDELINE QUESTIONS

This clinical practice guideline addresses four overarching clinical questions: (1) [clinical question 1]? (2) [clinical question 2]? (3) [clinical question 3]? (4) [clinical question 4]?

## **METHODS**

### ***Guideline Development Process***

This systematic review-based guideline product was developed by an international multidisciplinary Expert Panel, which included a patient representative and an SIO guidelines staff member with health research methodology expertise (Appendix Table A1, online only). The Expert Panel met via webinar and corresponded through e-mail. Based upon the consideration of the evidence, the authors were asked to contribute to the development of the guideline, provide critical review, and finalize the guideline recommendations. The guideline recommendations were sent for an open comment period of two weeks allowing the public to review and comment on the recommendations after submitting a confidentiality agreement. These comments were taken into consideration while finalizing the recommendations. Members of the Expert Panel were responsible for reviewing and approving the penultimate version of the guideline, which was then circulated for external review, and submitted to [target journal(s)] for editorial review and consideration for publication. All SIO guidelines are ultimately reviewed and approved by the Expert Panel and the SIO Clinical Practice Guidelines Committee before publication. All funding for the administration of the project was provided by SIO.

The recommendations were developed by using a systematic review of evidence identified through online searches of PubMed [insert dates; update databases searched if applicable] and Cochrane Library [insert dates] of phase III randomized clinical trials (RCTs), [some observational studies], and clinical experience. Articles were selected for inclusion in the systematic review based on the following criteria:

- Population: [insert patient population]
- Interventions: [insert interventions of interest]
- Comparisons: [insert comparisons of interest]

- Outcomes: [insert outcomes of interest]
- Sample size: [insert sample size]

Articles were excluded from the systematic review if they were (1) meeting abstracts not subsequently published in peer-reviewed journals; (2) editorials, commentaries, letters, news articles, case reports, narrative reviews; (3) published in a non-English language. The guideline recommendations are crafted, in part, using the *Guidelines Into Decision Support* (GLIDES) methodology and accompanying BRIDGE-Wiz software. [Shiffman 2012] In addition, a guideline implementability review was conducted. Based on the implementability review, revisions were made to the draft to clarify recommended actions for clinical practice. Ratings for type and strength of the recommendation, and evidence quality are provided with each recommendation. The quality of the evidence for each outcome was assessed using the Cochrane Risk of Bias tool by the project methodologist in collaboration with the Expert Panel co-chairs and reviewed by the full Expert Panel.

The SIO Expert Panel and guidelines staff will work with co-chairs to keep abreast of any substantive updates to the guideline. Based on formal review of the emerging literature, SIO will determine the need to update the guideline. MEDLINE was searched from [insert dates]. The updated search was restricted to articles published in English, and to systematic reviews, meta-analyses, and randomized controlled trials.] The SIO Guidelines Methodology Manual (available at <https://integrativeonc.org/practice-guidelines/sio-guidelines-guidelines-methodology>) provide additional information about the guideline update process. This is the most recent information as of the publication date.

### ***Guideline Disclaimer***

The Clinical Practice Guidelines and other guidance published herein are provided by the Society for Integrative Oncology (SIO) to assist providers in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the



standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations specify the level of confidence that the recommendation reflects the net effect of a given course of action. The use of words like “must,” “must not,” “should,” and “should not” indicates that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating clinician to select other courses of action in individual cases. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. SIO does not endorse third party drugs, devices, services, therapies, apps, or programs used to diagnose, treat, monitor, manage, or alleviate health conditions. Any use of a brand or trade name is for identification purposes only. SIO provides this information on an “as is” basis and makes no warranty, express or implied, regarding the information. SIO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. SIO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.

### ***Guideline and Conflicts of Interest***

The Expert Panel was assembled in accordance with SIO’s Conflict of Interest Policy Implementation for Clinical Practice Guidelines (“Policy,” found at <https://integrativeonc.org/practice-guidelines/sio-guidelines-guidelines-methodology>). All members of the Expert Panel completed SIO’s disclosure form, which requires disclosure of

financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

## RESULTS

### ***Characteristics of Studies Identified in the Literature Search***

A total of [insert the total number of hits found by the literature search] were identified in the literature search. After applying the eligibility criteria, [insert the number and type of studies comprising the entire body of evidence] remained, forming the evidentiary basis for the guideline recommendations. [insert the references to the studies]

The identified trials were published between [insert dates]. The randomized trials compared similar interventions. The primary outcome for [#] of the trials for Clinical Question [#] was therapeutic efficacy, as were [#] of the trials for Clinical Question [#]. Morbidities and QoL were the primary outcome for the [#] other studies, though they were framed in a variety of ways such as recurrence-free survival, event-free survival, all-cause mortality. The cohort studies for Clinical Question [#] reported a mix of efficacy and adverse events-related outcomes. Table 1 presents the included articles from the literature search pertinent to the development of the recommendations. Characteristics of the studies' participants are in Data Supplement X.

**EXAMPLE Table 1.** Characteristics of Studies Identified in the Literature Search

Author, Year Country	# of Included Studies; Study Type	# of Included Patients	Cancer Type and/or Pain Condition	Comparisons	Primary outcome Measure used
Acupuncture					

<b>SRs</b>					
Chien 2019	5 studies	386	Multiple cancer types; CIPN	<ul style="list-style-type: none"> <li>• Acupuncture</li> <li>• Sham/waitlist</li> </ul>	Pain Severity VAS
Li 2019	3 studies	203	Multiple cancer types; CIPN	<ul style="list-style-type: none"> <li>• Acupuncture</li> <li>• Sham</li> </ul>	
<b>RCTs</b>					
Bao 2013 United States	RCT	47	Breast cancer; AI-induced joint muscle pain	<ul style="list-style-type: none"> <li>• 8 weekly acupuncture</li> <li>• Sham acupuncture</li> </ul>	
Crew 2010 United States	RCT	38	Breast cancer; AI-induced joint muscle pain	<ul style="list-style-type: none"> <li>• Acupuncture twice weekly for 6 weeks</li> <li>• Sham acupuncture</li> </ul>	

NOTE: (if needed)

Abbreviations: # of Pts. Number of Patients Randomly Assigned

Author/ year Location	N Sites	Institution Setting	Intervention/ Control	N of Participants	Age Gender	Race Ethnicity	Eligibility criteria	Cancer type	Primary outcome Measure

### ***Key Outcomes of Interest***

**EXAMPLE Table 2.** Key Outcomes of Interest

Author/ year	Intervention/ Control	Follow up duration	Outcome 1	Outcome 2	Outcome 3	Averse events	Any other relevant data

NOTE:

Abbreviations: # of Pts. Number of Patients Randomly Assigned

### ***Study Quality Assessment***

Study design aspects related to individual study quality, quality of evidence, strength of recommendations, and risk of bias were assessed. Refer to the Methodology Manual for more information and for definitions of ratings for overall potential risk of bias.

[Insert brief summary paragraph(s) on study quality here]

As seen in Table 3, study quality was formally assessed for the [#] RCTs identified using the Cochrane Risk of Bias tool (ROB). Design aspects related to the individual study quality were assessed by one reviewer, with factors such as blinding, allocation concealment, selective outcome reporting, etc., generally indicating a low to high ROB for one or more key domains in most of the identified evidence. Follow-up times varied between studies, lowering the comparability of the results.

**EXAMPLE Table 3.** Study Quality Assessment

Refid	Was the allocation sequence adequately generated?	Was allocation adequately concealed?	Blinding: Was knowledge of the allocated interventions adequately prevented?	Were patients blinded?	Were healthcare providers blinded?	Were data collectors blinded?	Were outcome assessors blinded?	Were data analysts blinded?	Was loss to follow-up (missing outcome data) infrequent?	Are reports of the study free of suggestion of selective outcome reporting?	Was the study apparently free of other problems that could put it at a risk of bias?	Assessment of Bias
792	Definitely no (high risk of bias)	Probably no	Definitely no (high risk of bias)	Definitely no (high risk of bias)	Definitely no (high risk of bias)	Definitely no (high risk of bias)	Definitely no (high risk of bias)	Definitely no (high risk of bias)	Definitely yes (low risk of bias)	Probably yes	Probably no	High risk of bias for one or more key domains.

## RECOMMENDATIONS

### CLINICAL QUESTION 1

[Insert clinical question one]

#### *Recommendation 1.1*

[Insert recommendation 1.1] (Type: evidence based; benefits outweigh harms; Evidence quality: high, intermediate or low; Strength of recommendation: strong, moderate, or weak)

*Literature review [update] and analysis.* X randomized trials were identified by the systematic review: list of studies.<sup>ref</sup> X systematic review and meta-analysis of topic was also identified.<sup>ref</sup> Dosing information is provided in [Table X](#).

*Clinical interpretation.* The inpatient trials enrolled [patient population]. To date, no trials have evaluated [intervention] in a cancer-only population. These recommendations were formulated by extrapolating the best available data. All RCTs included [criteria] as an eligibility criterion, but the definitions of [criteria] were not explicit or consistent.

### *Recommendation 1.2*

[Insert recommendation 1.2] (Type: evidence based; benefits outweigh harms; Evidence quality: high, intermediate or low; Strength of recommendation: strong, moderate, or weak)

*Literature review [update] and analysis.* The updated systematic review identified X systematic reviews<sup>refs</sup> in the [specific] setting and X RCTs.<sup>refs</sup> X RCTs included patients with [summarize patient inclusion]. X others, included only patients with [summarize patient inclusion].

*Clinical interpretation.* The inpatient trials enrolled [patient population]. To date, no trials have evaluated [intervention] in a cancer-only population. These recommendations were formulated by extrapolating the best available data. All RCTs included [criteria] as an eligibility criterion, but the definitions of [criteria] were not explicit or consistent.

## **CLINICAL QUESTION 2**

[Insert Clinical Question 2]

### *Recommendation 2.1*

[Insert recommendation 2.1] (Type: evidence based; benefits outweigh harms; Evidence quality: high, intermediate or low; Strength of recommendation: strong, moderate, or weak)

### *Recommendation 2.2*

[Insert recommendation 2.2] (Type: evidence based; benefits outweigh harms; Evidence quality: high, intermediate or low; Strength of recommendation: strong, moderate, or weak)

### *Recommendation 2.3*

[Insert recommendation 2.3] (Type: evidence based; benefits outweigh harms; Evidence quality: high, intermediate or low; Strength of recommendation: strong, moderate, or weak)

*Literature review [update] and analysis.* The updated systematic review identified X systematic reviews<sup>refs</sup> in the [specific] setting and X RCTs.<sup>refs</sup> X RCTs included patients with [summarize patient inclusion]. X others, included only patients with [summarize patient inclusion].

*Clinical Interpretation.* The absolute differences in [outcome] event rates between treated and control patients were [percentage] in most trials. Among the X systematic reviews, the absolute risk differences in [outcome] were [percentages] with estimates of the number needed to treat (NNT) of [numbers], respectively, to prevent one [outcome] event across the included trials. Importantly, individual patient data were not evaluated, limiting the assessment of patients with [characteristic], often receiving different cancer therapies, and with varying degrees of risk.

## **DISCUSSION**

*[Insert if needed: a high level summary of the evidence, quality, clinical interpretation, and other discussion items but don't repeat information from the literature review and analysis – this is a good place to add supplementary literature that the authors feel is important, but is not included as part of the literature review]*

**Topic A** If subtopic use *zbvzxbzbzxcbzxbzxbzxb*. Header level

**Topic B** If subtopic use *zbvzxbzbzxcbzxbzxbzxb*. Header level

**Topic C** If subtopic use *zbvzxbzbzxcbzxbzxbzxb*. Header level

## **SPECIAL COMMENTARY**

*[Insert as appropriate]*

**Topic A** If subtopic use *zbvzxbzbzxcbzxbzxbzxb*. Header level

**Topic B** If subtopic use *zbvzxbzbzxcbzxbzxbzxb*. Header level

**Topic C** If subtopic use *zbvzxbzbzxcbzxbzxbzxb*. Header level

## PATIENT AND CLINICIAN COMMUNICATION

*[Insert a section with input from patient representatives and co-chairs from the Expert Panel]*

## HEALTH DISPARITIES

Although SIO clinical practice guidelines represent expert recommendations on the best practices in disease management to provide the highest level of cancer care, it is important to note that many patients have limited access to medical care or receive fragmented care. Factors such as race and ethnicity, age, socioeconomic status, sexual orientation and gender identity, geographic location, and insurance access are known to impact cancer care outcomes. [Patel et al 2020] Racial and ethnic disparities in health care contribute significantly to this problem in the United States. Systemic racism underlies the reason for many if not all of these health inequities and intersects with other structural health inequities. Patients with cancer who are members of racial/ethnic minorities suffer disproportionately from comorbidities, experience more substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving fragmented care or poor quality care than other Americans. *[Insert the 4 references for this paragraph included in the REFERENCE section]* Many other patients lack access to care because of their geographic location and distance from appropriate treatment facilities. Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations. Additionally, stakeholders should work towards achieving health equity by ensuring equitable access to both high-quality cancer care and research and addressing the structural barriers that preserve health inequities. [Patel et al 2020]

Paragraph 2 and others indented.

## MULTIPLE CHRONIC CONDITIONS

*[Insert specifics and reference the latest paper and correct tables from the American Geriatric society if applicable]*

Creating evidence-based recommendations to inform treatment of patients with additional chronic conditions, a situation in which the patient may have two or more such conditions—referred to as multiple chronic conditions (MCC)—is challenging. Patients with MCC are a complex and heterogeneous population, making it difficult to account for all of the possible permutations to develop specific recommendations for care. In addition, the best available evidence for treating index conditions, such as cancer, is often from clinical trials whose study selection criteria may exclude these patients in order to avoid potential interaction effects or confounding of results associated with MCC. As a result, the reliability of outcome data from these studies may be limited, thereby creating constraints for expert groups to make recommendations for care in this heterogeneous patient population.

As many patients for whom guideline recommendations apply present with MCC, any treatment plan needs to take into account the complexity and uncertainty created by the presence of MCC and highlights the importance of shared decision making regarding guideline use and implementation. Therefore, in consideration of recommended care for the target index condition, clinicians should review all other chronic conditions present in the patient and take those conditions into account when formulating the treatment and follow-up plan.

In light of these considerations, practice guidelines should provide information on how to apply the recommendations for patients with MCC, perhaps as a qualifying statement for recommended care. This may mean that some or all of the recommended care options are modified or not applied, as determined by best practice in consideration of any MCC.

### **COST IMPLICATIONS**

Increasingly, individuals with cancer are required to pay a larger proportion of their treatment costs through deductibles and co-insurance. [Schnipper et al 2015; Schnipper et al 2016] Higher



patient out-of-pocket costs have been shown to be a barrier to initiating and adhering to recommended cancer treatments. [Streeter et al 2011; Dusetzina et al 2014]

Discussion of cost can be an important part of shared decision-making. [Meropol et al 2009] Clinicians should discuss with patients the use of less expensive alternatives when it is practical and feasible for treatment of the patient's disease and there are two or more treatment options that are comparable in terms of benefits and harms. [Meropol et al 2009]

Table X shows estimated prices for the available treatment options addressed in this guideline. Of note, medication prices may vary markedly, depending on negotiated discounts and rebates.

Patient out of pocket costs may vary depending on insurance coverage. Coverage may originate in the medical or pharmacy benefit, which may have different cost-sharing arrangements. Patients should be aware that different products may be preferred or covered by their particular insurance plan. Even with the same insurance plan, the price may vary between different pharmacies. When discussing financial issues and concerns, patients should be made aware of any financial counseling services available to address this complex and heterogeneous landscape. [Meropol et al 2009]

As part of the guideline development process, SIO may opt to search the literature for published cost effectiveness analyses that might inform the relative value of available treatment options. Excluded from consideration are cost effective analyses that lack contemporary cost data; agents that are not currently available in either the United States or Canada; or are industry-sponsored. [Option 1] No cost effectiveness analyses were identified to inform the topic. [Option 2] The following cost effectiveness analysis was identified to inform the topic [list citation]. [Add a commentary about the published cost-effectiveness analyses relative to the clinical question and include a review with or without a commentary on the strength of the analyses.]

## **EXTERNAL REVIEW AND OPEN COMMENT**

*[Insert a very high level overview of the external review process and mention any major revisions made to the draft as a result]*

The draft recommendations were released to the public for open comment from [DATE] through [DATE], 2021. Response categories of “Agree as written”, “Agree with suggested modifications” and “Disagree. See comments” were captured for every proposed recommendation with # written comments received. A total of % of the # respondents either agreed or agreed with slight modifications to the recommendations and % of the respondents disagreed. Expert Panel members reviewed comments from all sources and determined whether to maintain original draft recommendations, revise with minor language changes, or consider major recommendation revisions. All changes were incorporated prior to CPGC review and approval.

The draft was submitted to X external reviewers with content expertise [in a joint guideline add information about reviewers from the other organization(s)]. It was rated as high quality, and it was agreed it would be useful in practice. Review comments such as xxxxxxxxxxxx were reviewed by the Expert Panel and integrated into the final manuscript before approval by the CPGC.

### **GUIDELINE IMPLEMENTATION**

SIO guidelines are developed for implementation across health settings. The additional role of this PGIN representative on the guideline panel is to assess the suitability of the recommendations to implementation in the community setting, but also to identify any other barrier to implementation a reader should be aware of. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers, and also to provide adequate services in the face of limited resources. The guideline Bottom Line Box was designed to facilitate implementation of recommendations. This guideline will be distributed widely through the xxxxxxxx

### **PROVIDER TRAINING/ LICENSING/CREDENTIALING (if applicable)**

Paragraph one flush left. xxxxxxxx

Subsequent paragraphs indented.

### **QUALITY ASSURANCE ON NATURAL PRODUCTS (if applicable)**

Paragraph one flush left. xxxxxxxxx

Subsequent paragraphs indented.

### **LIMITATION OF THE RESEARCH AND FUTURE RESEARCH**

Paragraph one flush left. xxxxxxxxx

Subsequent paragraphs indented.

***SIO believes that cancer clinical trials are vital to inform clinical decisions and improve cancer care, and that all patients should have the opportunity to participate.***

### **ADDITIONAL RESOURCES**

More information, including a supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at <https://integrativeonc.org/practice-guidelines/guidelines>.

Patient information is available at [www.cancer.net](http://www.cancer.net) and <https://integrativeonc.org/knowledge-center/patients>.

Related SIO Guidelines (text box to appear on last page of content)

- Add shortened title of guidelines that are related to the content, add to reference list, Keep list to 5-8 related guidelines.

### **AUTHORS DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

SIO/target journal(s) re-checks prior to final submission

### **AUTHOR CONTRIBUTIONS**

Target journal(s) finalizes prior to final submission

### **ACKNOWLEDGMENT**

The Expert Panel wishes to thank [Insert all external reviewers, CPGC reviewers] [Note consensus panel when applicable] and the SIO Clinical Practice Guideline Committee for their thoughtful reviews and insightful comments on this guideline.

This project was funded by...to develop clinical practice guidelines.

**NOTE: Appendices:**

All Appendices and Acknowledgment material (including the table of Expert Panel members) are online-only.

**Appendix**

**Table A1. Title of Guideline Expert Panel Membership**

*[Insert author and institution information i.e. first name, middle initial, last name; Organization, City, State]*

Name (and designation - check with authors)	Affiliation	Role or Area of Expertise

**GLIDES Rating Definitions**

Term	Definitions
<b>Quality of Evidence</b>	
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (e.g., balance of benefits versus harms) and further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Intermediate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect, however it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change the magnitude and/or direction of this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. Reliance on consensus opinion of experts may be reasonable to provide guidance on the topic until better evidence is available.
<b>Strength of Recommendation</b>	
Strong	There is high confidence that the recommendation reflects best practice. This is based on: a) strong evidence for a true net effect (e.g., benefits exceed harms); b) consistent results, with no or minor exceptions; c) minor or no concerns about study quality; and/or d) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on: a) good evidence for a true net effect (e.g., benefits exceed harms); b) consistent results with minor and/or few exceptions; c) minor and/or few concerns about study quality; and/or

	<p>d) the extent of panelists' agreement.</p> <p>Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.</p>
Weak	<p>There is some confidence that the recommendation offers the best current guidance for practice. This is based on:</p> <ul style="list-style-type: none"> <li>a) limited evidence for a true net effect (e.g., benefits exceed harms);</li> <li>b) consistent results, but with important exceptions;</li> <li>c) concerns about study quality; and/or</li> <li>d) d) the extent of panelists' agreement.</li> </ul> <p>Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.</p>

## REFERENCES

### USE REFERENCE STYLE AS NOTED BY THE TARGET JOURNAL(S)

#### *Methods references*

1. Shiffman RN, Michel G, Rosenfeld RM, et al: Building better guidelines with BRIDGE-Wiz: development and evaluation of a software assistant to promote clarity, transparency, and implementability. *J Am Med Inform Assoc* 19:94-101, 2012
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1. Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). *SEER Cancer Statistics Review, 1975-2013*, National Cancer Institute. Bethesda, MD, [http://seer.cancer.gov/csr/1975\\_2013/](http://seer.cancer.gov/csr/1975_2013/), based on November 2015 SEER data submission, posted to the SEER web site, April 2016.
2. American Cancer Society: *Cancer Facts & Figures for African Americans 2016-2018*. Atlanta, GA, American Cancer Society, 2016. <http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-047403.pdf>
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#### *Cost considerations references*

1. Schnipper LE, Davidson NE, Wollins DS, et al: American Society of Clinical Oncology statement: A conceptual framework to assess the value of cancer treatment options. *J Clin Oncol* 33: 2563-2577, 2015
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3. Streeter SB, Schwartzberg L, Husain N, et al: Patient and plan characteristics affecting abandonment of oral oncolytic prescriptions. *J Oncol Pract* 7:46s-51s, 2011
4. Dusetzina SB, Winn AN, Abel GA, et al: Cost sharing and adherence to tyrosine kinase inhibitors for patients with chronic myeloid leukemia. *J Clin Oncol* 32:306-311, 2014
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## Appendix I



### Drafting the Recommendations and the Manuscript

#### Drafting the recommendations

- a. The CPG Panel will be divided into subgroups. Subgroups are determined by categories of modalities or interventions, and Panel members are assigned to a subgroup based on expertise.
- b. Subgroups are responsible for drafting the recommendations for the modalities or interventions in their group. The guideline methodologist will provide each subgroup with clear instructions and examples on the recommendation drafting structure.
  - i. Subgroups review the literature for their group to:
    - 1) Define an intervention: action and actors, population and circumstances, benefit vs. harm, cost(s)
    - 2) Rate the quality or strength of evidence for recommendations: high, intermediate, low, insufficient
    - 3) Determine the type of recommendation: evidence-based, formal consensus, informal consensus, no recommendation
    - 4) Determine the level of obligation: should, may
- c. The guideline methodologist will work with each subgroup individually to ensure maximum productivity and output.
- d. Once all drafts are complete, the CPG Panel Co-Chairs, along with the guideline methodologist, will review the drafts, edit as needed, and combine to develop the list of draft recommendations.

#### Drafting the manuscript

- a. The manuscript is drafted in accordance with the SIO manuscript template that can be modified to fit submission to targeted journals.
- b. The CPG Panel will again divide into subgroups. Subgroups are responsible for writing their group's section of the manuscript. The guideline methodologist will provide each subgroup with clear instructions and examples on the manuscript writing structure.
  - i. For each recommendation, a double-spaced, five hundred (500) word maximum summary will be written.
- e. The guideline methodologist will work with each subgroup individually to ensure maximum productivity and output.



- f. Once all drafts are complete, the CPG Panel Co-Chairs, along with the guideline methodologist, will review the drafts, edit as needed, and combine to develop the draft manuscript.