



American Association
for Respiratory Care

Guidance Document

A Process Manual for Clinical Practice Guidelines Development

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A Process Manual for Clinical Practice Guidelines Development

Introduction

This AARC Guidance Document is presented to provide an overview of the process used in developing Clinical Practice Guidelines (CPGs). CPGs are evidence-based statements that allow providers, patients, and other stakeholders to make informed decisions about appropriate health interventions. As part of the 2022 AARC Strategic Plan, CPGs are to support AARC members and others in clinical practice, and aim to create trustworthy guidelines that assist in decision-making and enhance patient outcomes. AARC CPGs beginning in 2022, follow the directions of the Guidelines International Network (GIN). These methods enhance the comprehensiveness and transparency of CPGs for the benefit of patients, the public, respiratory therapists, and other relevant stakeholders. As such, this manual serves as a blueprint for developing and publishing recommendations and updating CPGs when new evidence is found.

For more information, see Guidelines International Network (GIN) <https://inguide.org/>.

For more information see GIN-McMaster Checklist for Guideline Development at: <https://cebgrade.mcmaster.ca/guidelinechecklistonline.html>.

Trustworthy Guidelines

There are six principles that CPGs should fulfill to make them both trustworthy and of high quality.¹

1. CPGs should be based on the best available evidence, using a systematic review methodology.
2. CPGs should be developed by a knowledgeable, multidisciplinary panel of experts, and representatives from key affected groups.
3. CPGs should focus on what matters to people who will be affected by the CPGs by considering patient values and preferences.
4. CPGs should provide a clear explanation of valid relationships between alternative care options and health outcomes; and provide ratings of both the quality of evidence and the strength of the recommendations.
5. CPGs should be reconsidered and revised as appropriate when important new evidence warrants modifications of recommendations.
6. CPGs should be based on a transparent process to minimize misrepresentation, biases, and conflicts of interest.

Levels of Evidence Pyramid

Understanding and interpreting evidence is an important part of evidence-based practice in respiratory care. Figure 1 is a visualization of the levels of evidence. The lowest level of evidence includes animal and laboratory investigations as these studies may not be translatable to humans. The highest level of evidence is a meta-analysis or a statistical process of analyzing and combining results from several similar studies. This provides greater certainty that can help researchers better understand the magnitude of results or an effect. Therefore, systematic reviews attempt to gather all available empirical research by using clearly defined criteria to obtain answers to a specific question.

The Guidelines Process

Step 1: The AARC Director of CPG Development is responsible for the organization, budget, planning, and operation of CPG panels. One panel member will be asked to chair the CPG development process. Methodologists, consultants, and stakeholders are also part of CPG panels. A librarian conducts the literature review and serves as a technical expert as needed. Active participation is expected in determining CPG recommendations. In making decisions regarding outcomes and recommendations, team members, stakeholders, and consultants are allowed to provide input and vote as needed.

Topic Selection

Step 2: CPG topics are selected in several ways. Topics can be suggested by past CPG team members, the result of literature reviews, a request from AARC members or community stakeholders, and other professional organizations. Guideline topics should serve a need and add value beyond what is currently available. The topic must have the potential to be used in clinical practice and is feasible based on enough research evidence to develop a systematic review. Refinement of the topic can occur in consultation with content area experts, CPG team members, and according to available resources. The AARC commits to researching topics that are important to the respiratory care community and to the work of respiratory therapists.

Developing the CPG Team

Step 3: Panel members are selected based on many factors such as experience, content knowledge and availability. Each CPG panel consists of at least seven members, including consultants and patients. Patients and patient representatives who serve on CPG panels are important as their perspective can be very informative to the panel. Stakeholders, who are respiratory care or medical industry partners, payers, and other healthcare organization representatives that are not considered members of the CPG panel, but may provide guidance or opinions. The director provides information

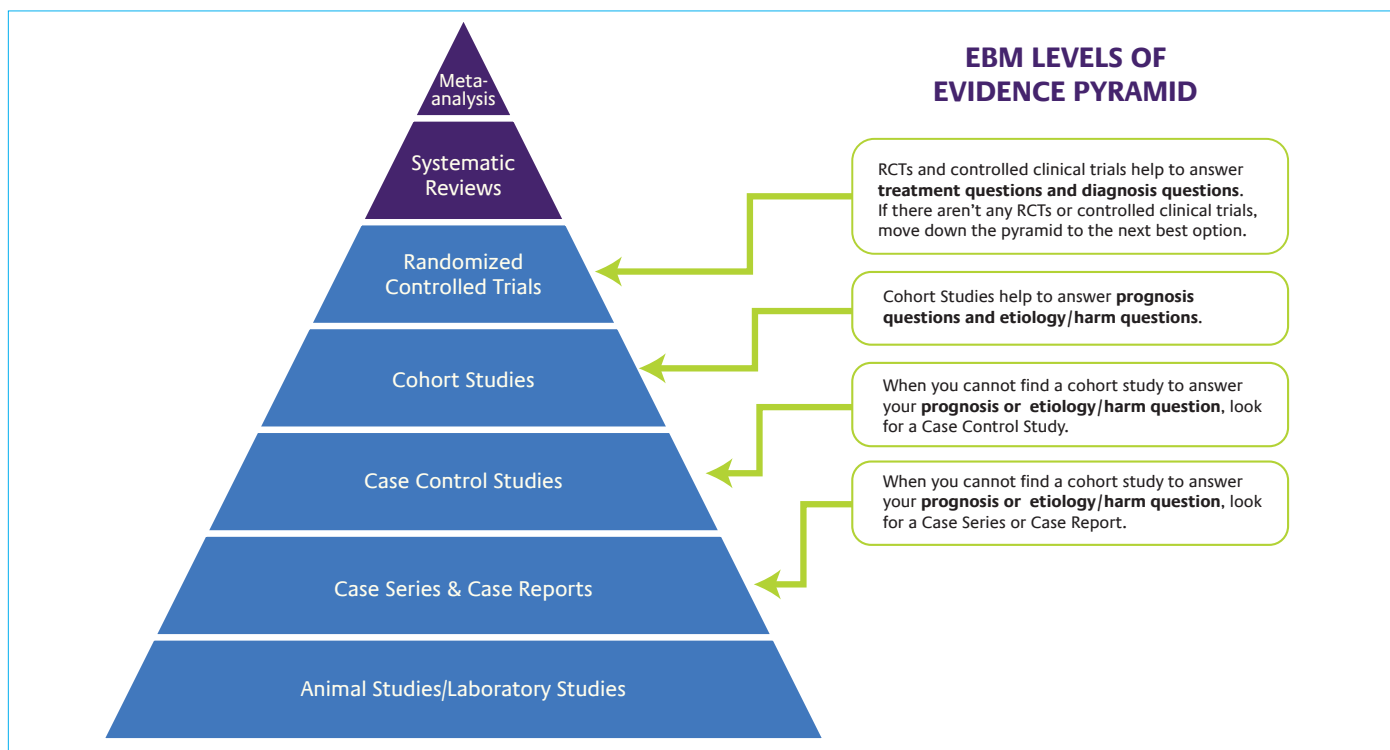


Figure 1. EBM Levels of Evidence Pyramid. From: guides.dml.georgetown.edu

regarding travel arrangements, panel members' duties, timelines, and follow-ups. The make-up of panel members include content experts (respiratory therapists, physicians, nurses, statisticians, etc.), practicing respiratory therapists, respiratory therapists in administrative roles, medical librarian(s), patients or consumer advocates (if appropriate for the topic), and advisory or consultant members. Diversity of age, gender, ethnicity, experience, and thought is expected. Respiratory therapists are required to be members of the AARC.

All CPGs require a chair and a methodologist. The chair should be an individual who has experience in leading groups. The ideal chair is pragmatic, diplomatic, can mediate disagreements, and facilitate compromise, efficient, and persuasive to coax individuals to get the work done in a timely manner. The methodologist should have experience in leading both systematic reviews and projects that have applied the Grading, Recommendations, Assessment, Development, and Evaluation (GRADE) approach to formulating recommendations. The methodologist must have good communication skills, as he/she must work closely with the chair and is frequently called upon to explain the rationale for various steps in the guideline development process. The methodologist is expected to be listed as the middle co-author on the final guideline, and the first author on any systematic reviews that are published as independent byproducts.

Panel members are expected to commit to attending all conference calls and completing assignments (review of the literature, writing recommendations, etc.). If not able to attend meetings, notify the chair of the CPG panel and the Director of CPG Development. All meetings during the guideline development process are recorded, with a note-taker present for in-person meetings. Minutes are accessible via a Microsoft Teams shared folder. Participation in the guidelines team may be made public as part of guideline transparency.

Conflict of Interest

Step 4: Disclosure and management of potential conflicts of interest (COI) are important aspects of guideline development. Conflicts of interest can be direct, such as financial interests, and indirect, such as academic, intellectual, and personal conflicts. All team members are asked to disclose any potential conflicts of interest using the **AARC Disclosure of Conflict-of-Interest Statement**. Divulging a financial or non-financial relationship does NOT prevent participation. However, serving on a speaker's bureau is commonly a disqualifying factor for CPG participation but this will be determined on an individual basis. The AARC Director of Clinical Practice Guidelines Development reviews and signs the returned COIs. Any disclosures are active for two years and should be updated if any conflicts or relationships change.

Relevant and disclosable financial relationships may include:

- Being an employee of, or a paid consultant to, a medical equipment manufacturer or pharmaceutical company
- Serving on a speaker's bureau and/or having been paid honoraria/expenses as a speaker by a medical equipment manufacturer, or pharmaceutical company (See comment above)
- Receiving grant funds for a research project from a medical equipment manufacturer or pharmaceutical company
- Receiving royalties from the sale of a book
- Patent holder
- Ownership interest (stocks, stock options, or other ownership interests)

Examples of relevant and disclosable non-financial relationships may include:

- Serving in a formal capacity on a review panel or advisory board for a medical equipment manufacturer, or pharmaceutical company
- Serving as a Trustee or on the Board of Directors for an Association, Foundation, medical equipment manufacturer, or pharmaceutical company

Work Plan

Step 5: A CPG is different from a narrative review in that it consists of answering diagnostic and/or treatment questions via a review of the known evidence and providing evidence-based recommendations. Therefore, no review of clinical manifestations, indications, contraindications, etc. is required except in very few cases. Once the topic and overview of the process are discussed, panel members whose skills are best suited to generating and prioritizing clinical questions, lead the team through a scoping exercise.

Clinical Questions

In developing CPGs, good questions lead to good recommendations. For instance, is the question common in practice? Is there uncertainty in practice? Has this question been raised before? Is there new evidence to consider? Are there variations in practice, and why or why not? Are there consequences for resources or cost? Another way of thinking is to consider if Treatment A or Treatment B be used in a specific patient population with condition X? The question does not address the purpose of the testing, but the purpose of administering a suggested form of treatment.

First, the CPG team will generate potential PICO questions (**P**opulation, **I**ntervention, **C**omparators, **O**utcomes), which is a framework that can assist in forming recommendations based on evidence (See Figure 2. PICO).

Population – helps to describe the population in as much detail as necessary for the recommendations. This can include age, hospitalization, ambulatory, mechanical ventilation, etc. The evidence can be applied narrowly or broadly to ensure the question can be informed by evidence.

Intervention – describes the practices with as much detail as possible. Or, which treatment, which program, which method, when to test, how to test, etc.

Comparators – needed to describe the alternative to the intervention. This can be no treatment, another treatment, a different test, or an alternative program.

Outcomes – Determines the direction or the strength of a recommendation in order to answer questions appropriately. The main outcomes should be described in terms of how decisions were determined about an intervention. Desirable outcomes are lower mortality, reduced hospital stays, reduced duration of oxygen use, or improvement in quality of life (QoL). Undesirable outcomes are higher mortality, adverse reactions, worsening of QoL, or symptoms. Note, not everything that is important is measured and not everything that is measured is important. Outcomes should be patient important.

The CPG team begins with a question such as, “What important clinical questions should be answered by this guideline?” A full list of potentially important questions are created using

the PICO framework. This scoping or brainstorming survey is structured by the objectives and deliverables of the guideline and will adhere to the methods endorsed by the AARC (e.g., GRADE⁴). Potential PICO questions will be drafted from this scoping exercise. Rating the relative importance of outcomes in the full list independently assists in determining which questions to reach a consensus on a final question list. Outcomes are prioritized by the CPG team by determining which outcomes are important. Median priority scores are 1 to 3 (low) are discarded, while median scores of 4 to 6 (moderate) are categorized as important, and high priority scores (7 to 9) are categorized as critical. Generally, 8 – 12 PICO questions are translated into recommendations. All meetings during the guideline development process are recorded, with a notetaker present for in-person meetings. The PICO questions are then ranked by priority from median scores, and the CPG team responses are recorded. The top-ranked questions are selected for inclusion based on the scope of the guideline.

Evidence Synthesis

Searching for evidence includes searching the literature, selecting relevant studies, extracting references, summarizing the body of evidence, and rating the quality of the evidence. Evidence synthesis is the most time-consuming part of guideline development. A medical librarian assists by designing a search strategy with keywords, determining study criteria, selecting relevant studies, and extracting studies from multiple reference databases, such as PubMed, EMBASE, CINAHL, and the Cochrane Database of Systematic

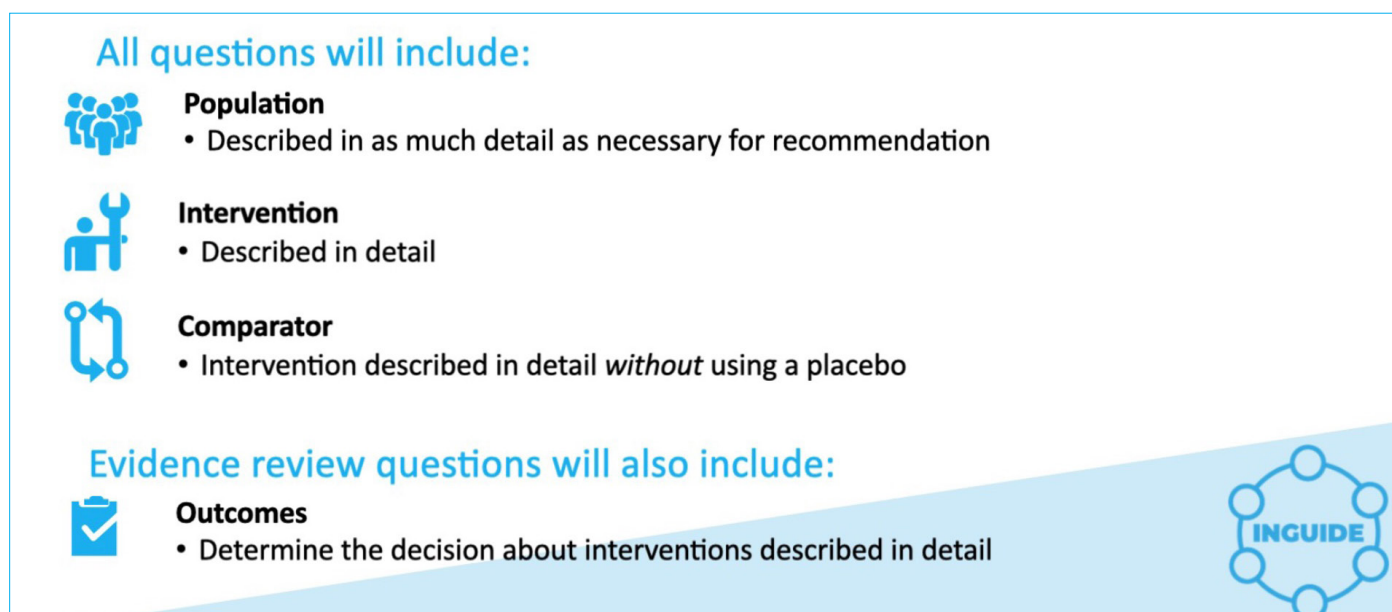


Figure 2. PICO. Reproduced with permission from the INGUIDE Program © 2022

Reviews. Referring to Figure 1, evidence is in a hierarchy of relevant, recently published systematic reviews, randomized controlled trials (RCTs), and observational studies. When little evidence is found, options moving forward are to state that further research is needed, search for lower quality evidence via case studies and case reports, acknowledging that poor evidence was found upon which the recommendation is based, or expanding the population or intervention in the search with intending to use indirect evidence (opinions) as the basis of judgments. Once the literature review is complete, recommendations can be summarized for each PICO question.

The next step is to evaluate the evidence using objective tools provided to the CPG panel (e.g., EndNote, Rayyan). A process of screening titles and abstracts with at least two reviewers is best practice. References that do not meet the study selection criteria are discarded or excluded. Those that meet the criteria are moved to a new file for further examination. Full texts articles meeting inclusion criteria are then reviewed and judged to be included or excluded in the final selection stage.

Outcomes

Evidence to support recommendations are best found by reviewing published high-quality (RCTs) systematic reviews and, if none exist, look at practical evidence synthesis for each clinical question. In determining the best range of outcomes, be sure to address benefits and harms. Base the choice of outcomes on what is important, and not on what outcomes are measured and for which evidence is available. If evidence is lacking for an important outcome, acknowledge, rather than ignore the outcome. Classify potential outcomes as critical or important for decision-making, important but not critical for decision-making, and limited or not important to decision-making. (See Figure 3, Rating Importance of Outcomes).

rating scale:								
1	2	3	4	5	6	7	8	9
of least importance						of most importance		
of limited importance for making a decision (not included in evidence profile)			important, but not critical for making a decision (included in evidence profile)			Critical for making a decision (included in evidence profile)		

Figure 3. Rating Importance of Outcomes. Reproduced with permission from the INGUIDE Program © 2022

Recommendations – Where to Begin?

Based on the studies reviewed for final inclusion for evidence synthesis, specific studies are used in determining what, if any, recommendations are drafted. Reviews of a single study contribute to a certain number of subjects in the intervention and control groups. Each study can also contribute a certain

number of outcomes or events. For example, study XX has five events in 23 subjects receiving mechanical ventilation. There were nine events in 23 subjects in the control group not receiving mechanical ventilation. Studies vary in size and number of events that lead to an overall effect. Each study receives a weight so that it adds up to 100%. A confidence interval is calculated to express precision of the estimate. Some studies have no events but are still included for completeness and transparency in forest plots. At the bottom of the plot is a scale indicating the magnitude of the Effect. By convention, effect estimates on the left-hand side of the forest plot typically indicate that the intervention is favored, and effect estimates on the right-hand side that the control is not favored. Finally, forest plots express the overall effect across studies by using diamond shapes to indicate the confidence intervals for the overall effects. See Figure 4 Forest Plot.

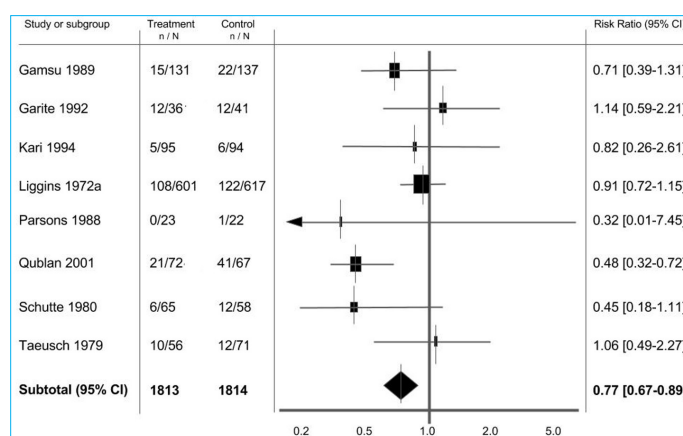


Figure 4. Forest Plot

Summary of Findings

Visual representations are helpful in explaining difficult concepts. A Summary of Findings table provides the number of studies, number of subjects in the intervention and control groups, number of events in the intervention and control groups, absolute effect, and relative effect for each outcome of an intervention. This provides certainty of the evidence. Assessment tables or Evidence Profiles, provide the number of studies, study design, assessment of the criteria for quality evidence, and quality of the evidence ratings for each outcome of an intervention. These tables serve to summarize the body of evidence and are helpful when the committee writes recommendations based on evidence. GradePro software is utilized which combines the summary of findings and quality assessment tables into a single table.

To determine the evidence for effects on health outcomes, recommendations are written to address the following criteria: the quality of the evidence, the balance of benefits

versus harm, patient preferences, economic costs, and available resources. An Evidence Profile provides certainty or quality or evidence for users to have a level of confidence to use the recommendations. The tool GRADE, (see gradepro.org) is used to show the certainty of evidence. This evidence profile provides detailed judgments per outcome. The strength of recommendations is strong or weak/conditional, and the quality of evidence is high, moderate, low, or very low. The strength of a recommendation indicates the degree of certainty that the desirable consequences outweigh the undesirable consequences. The quality of evidence indicates how confident the CPG panel is in the estimated effects used in informing their judgments. The CPG panel comes to a consensus and agrees that the recommendations are appropriate, but if this is not possible, a vote is taken to determine if the majority of the CPG team approves. If a majority vote fails, the recommendation is revised or deleted. GRADEpro software is used to guide the committee through decisions related to the strength of the recommendation.

Domain Limitations

Risk of Bias

Determining risk of bias is to ask "Are the research studies well done?" Limitations are factors that introduce bias into a study, including lack of concealment (blinding of the randomization process), lack of blinding (subject, caregiver, or assessor blinding), subjective outcomes, a large loss to follow-up, early termination of a trial due to benefit, failure to follow the intention-to-treat approach, baseline differences, and selection bias. If the body of evidence includes numerous studies with a risk of bias, the CPG panel may choose to downgrade the evidence one level from "no limitations" to "serious limitations." In contrast, if the risk for bias is extreme, the panel may elect to downgrade two levels to "very serious limitations." If included studies have design flaws, it is less certain that the evidence represents true effect.

Inconsistency

Determining inconsistency is to ask "Are the results consistent across studies?" Inconsistency is substantial variation in the direction or size of the effect across studies. For example, inconsistency is present if some studies found a benefit and others found harm, some studies demonstrated an effect and others did not, or some studies found a large effect and others found a small effect. For unexplained consistencies across studies, it is less certain that the evidence represents the true effect.

Indirectness³

Direct evidence allows for more confidence in the results. This means that your findings directly compare to the interventions being delivered to the populations and the important outcomes can be measured. Thus, indirectness can bring concerns when the population, intervention, or outcomes differ from those which are of interest. Additionally, indirectness of lower quality is observed when there are differences in the populations. Evidence is lower in quality when comparisons are indirect. Indirectness includes concepts such as applicability, generalizability, external validity, transferability, and translatability. Evidence is lower in quality when comparisons are indirect.

Imprecision

Is the effect estimate precise? There is variation due to random error or small sample size, which causes imprecision and is less certain than the evidence represents or the true effect. Imprecision is evaluated for the summary estimates not for the individual studies.

Publication Bias

Determining publication bias is to ask "Were all relevant studies found that have been conducted?" If other studies are not reviewed, for instance, negative studies, this leads to publication bias. If investigators do not publish negative results, there may be no overall effect.

Formulating Recommendations

GRADEPro will be used to formulate recommendations. The questions asked in the Evidence to Recommendations (EtR) framework include the following:

1. Is the clinical problem a high priority?
2. What is the overall quality of the evidence?
3. How much uncertainty is there about how much patients value the main outcome?
4. Are the desirable anticipated effects large?
5. Are the undesirable anticipated effects small?
6. Are the desirable effects, large relative to the undesirable effects?
7. Are the resources required small?
8. Is the incremental cost small relative to the net benefits?
9. What would be the impact on health inequities?
10. Is the option acceptable to key stakeholders?
11. Is the option feasible to implement?

Once these questions are considered, the CPG team decides whether the:

1. undesirable consequences clearly outweigh the desirable consequences
2. undesirable consequences probably outweigh the desirable consequences
3. desirable consequences clearly outweigh the undesirable consequences
4. desirable consequences probably outweigh the undesirable consequences
5. balance is uncertain

Based upon these determinations, the CPG panel can choose to recommend for or against the intervention. Recommendations should be supported by explanatory remarks, background information, subgroup considerations, and justifications that can be linked to other recommendations.

Strength of Recommendations

Once the recommendations are formulated, the strength of each recommendation is determined. The strength of the recommendation reflects the degree of certainty that the CPG panel has that the recommended intervention is correct. A strong recommendation indicates that the panel is certain that the recommended intervention is the right thing to do, while a conditional (weak) recommendation indicates uncertainty, usually because either the desirable and undesirable consequences are finely balanced, or the quality of the evidence provides little confidence in that balance. If the strength of the recommendation cannot be determined by consensus, voting may be required. Results of the votes are to be recorded and included in the guidelines. Other options for the strength of recommendation may be stated by indicating that this is the right thing to do for more than 95% of patients, while a conditional recommendation indicates that it is the right thing to do for more than 50% of patients but not as many as 95%.

Weak recommendations are likely to change as additional evidence is published. An example of an exception is an intervention that might prove a very important outcome, has few or only minor adverse effects, is inexpensive, and is without which a poor outcome is probable.

Grading Recommendations

GRADE is helpful in that every recommendation will concisely state the population action, intervention, and comparator. For recommendations, “we recommend” precedes strong recommendations, and “we suggest” is used for conditional (weak) recommendations. For instance, general formats in GRADE are:

- For patients with X, we recommend Y rather than Z
- For patients with X, we suggest Y rather than Z
- For patients with X, we suggest NOT doing Y
- For patients with X, we recommend NOT doing Y

Note: X is the population, Y is the intervention, and Z is the comparator.

Writing the Guideline Manuscript

AARC CPGs will be submitted for peer review and publication in *RESPIRATORY CARE* or other appropriate journals and posted to the AARC website. An executive summary with key recommendations and a brief rationale for those recommendations will accompany the full CPG.

The following format is recommended for AARC guidelines:

- Outline
- Abstract (Background, target audience, methods, recommendations, conclusions)
- Overview (An introductory paragraph followed by a bulleted list of key conclusions and recommendations)
- Introduction
- Methods
- How to use these guidelines
- Question 1
 - Description of the evidence and its quality
 - Desirable consequences and their magnitudes
 - Undesirable consequences and their magnitudes
 - Rationale for the recommendation
 - What others are saying
 - Recommendation
 - Values and preferences
 - Discussion
 - Repeat same sections for additional questions
- Repeat same sections for additional questions
- Conclusions
- References

In closing, using systematic reviews in developing CPGs is an effective and efficient way to assess a body of evidence. It can help explore differences between studies, and it's a reliable basis for decision-making. Figure 5 is a graphic overview of the development process and is a great visual guide to the entire process.

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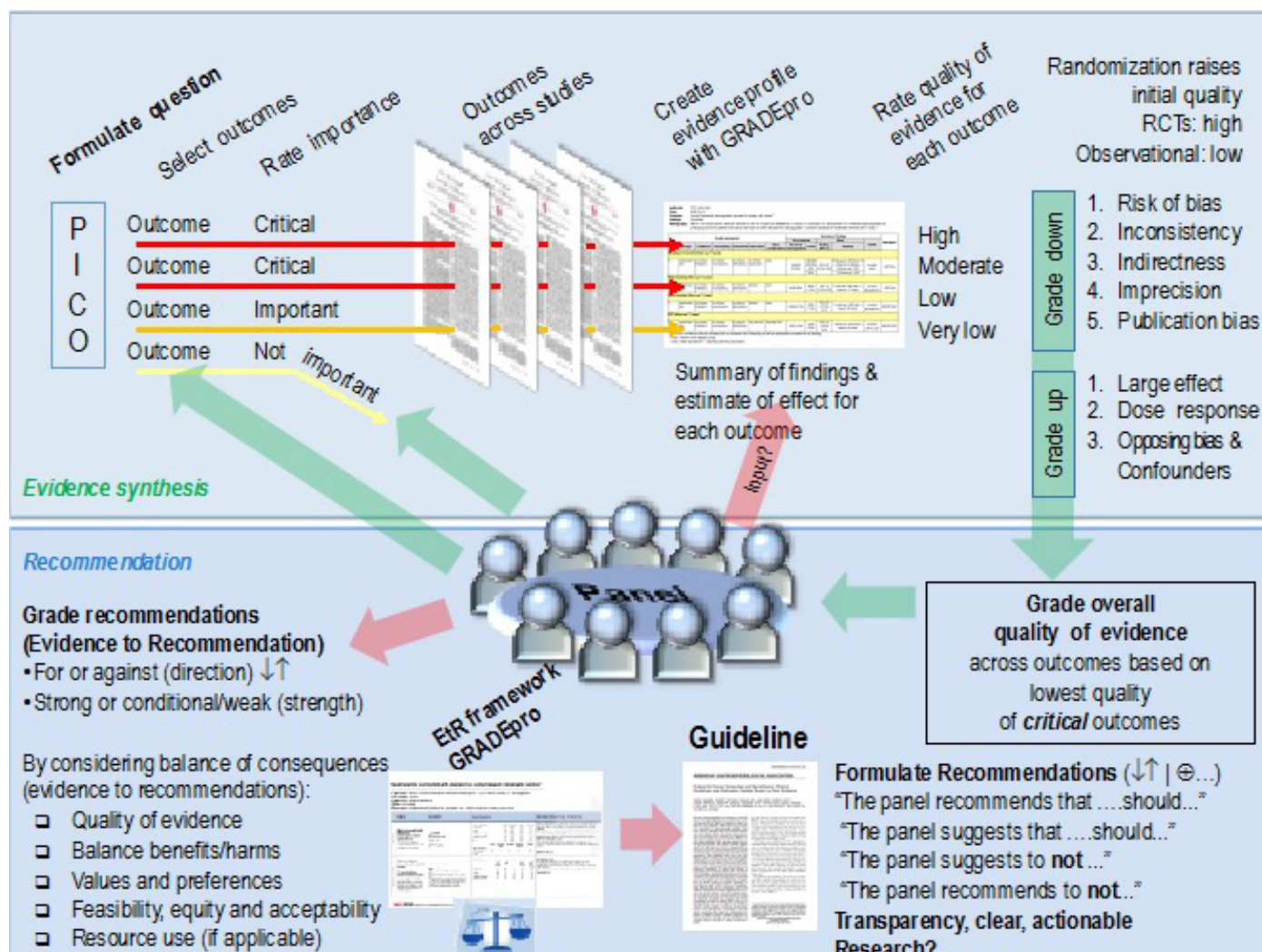


Figure 5. Grade Handbook