Harmonizing Guidelines and other Clinical Practice Documents: A Joint Comprehensive Methodology Manual by AATS, EACTS, ESTS, and STS

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Introduction

Clinical practice guidelines (CPGs) are essential documents offering practical recommendations developed to enhance patient care and inform healthcare. Properly formulated through meticulous assessment of scientific evidence and medical expertise by multidisciplinary teams, they strive to ensure an optimal balance between care benefits and potential risks. With the dynamic nature of medicine, healthcare professionals often balance delicate decisions with significant uncertainties. They rely on scientific literature, personal skills and experience, patient preferences, and guidelines from different organisations. Yet, these sources can suggest different paths derived from the same evidence, leading to ambiguities and notable variations in care (1).

There is an absence of universally accepted standards for developing CPGs, even though multiple methodologies exist for evaluating and translating research evidence into treatment recommendations (2-5). The Institute of Medicine (IOM) provides an authoritative and comprehensive guide for CPG development, introducing several pivotal characteristics regarded essential for producing reliable documents: 1) transparency, 2) diversity in development, 3) COI management, 4) thorough systematic literature reviews, 5) synthesis of evidence and evidence strength ratings, 6) clear communication in recommendation and supporting text, 7) external validation, and 8) regular updates. While these criteria may seem straightforward, aligning with them can be challenging (6). Many organizations have hesitated to embrace IOM's criteria entirely, emphasizing the rise in expenses and publication delays without substantial added value (7).

In response to the critical demand for a standardized medical language with the exponential growth of medical knowledge and technology, leading organizations including the European Association for Cardio-Thoracic Surgery (EACTS), the American Association for Thoracic

Surgery (AATS), the Society of Thoracic Surgeons (STS), and the European Society of Thoracic Surgeons (ESTS) have taken significant steps. These bodies have embarked on initiatives to enhance awareness among healthcare professionals and patients about the vital role of evidence-based practices in improving outcomes. This is achieved by developing, distributing, and extensively discussing clinical guidelines and other pertinent materials that serve to direct clinical decision-making and practices.

While it is well recognized that a significant portion of guideline recommendations might extend beyond strictly empirical scientific arguments, as indicated by the minimal proportion of directives grounded in the most robust level of evidence (8), the rapid proliferation of medical knowledge, anticipated to double at least every 73 days (9), underscores the essential need for reliable practice guidelines in dynamic medical fields. Moreover, in the light of disparate reported outcomes emerging from recent industry-sponsored versus investigator-initiated studies (10, 11), alongside burgeoning demands for heightened transparency and standardization (12-14), these associations are actively working to re-establish trust in guideline recommendations. The objective is to produce guidelines and other practice documents with utmost clarity and rigour, ensuring that physicians, patients, and pertinent stakeholders have access to and can depend upon this information. By adopting this methodology in future endeavours, this medical community aims to foster an environment where decisions are evidence-based, transparent, unbiased, and focused on the safety and effectiveness of patient care.

Development Methods

A writing panel was chosen by the governing bodies of the AATS, EACTS, ESTS, and STS to establish a uniform methodology for joint societies' projects. This document integrates

existing methodologies into a singular collaborative methodology (15, 16), further enriched by adopting the basic standards for development proposed by the key stakeholders (2, 5) (**Table 1**). All chapters were drafted in close collaboration among the writing panel, and the comprehensive processes were established during several committee meetings. Every process phase mandated consensus over specific voting with applied voting thresholds.

Given the substantial variability in economic parameters and the absence of standardized cost-effectiveness and cost-benefit data on a global scale, economic evaluations were not incorporated into the core process for developing clinical practice guidelines. Instead, this document concentrates solely on the processes for formulation of best practice recommendations, aligning with what is undeniably the physician's primary role. The developed document underwent internal validation and was approved by all writing committee members before being submitted for external review. It was then presented to the Editors-in-Chief of The Journal of Thoracic and Cardiovascular Surgery, the European Journal of Cardio-Thoracic Surgery, the Annals of Thoracic Surgery, and anonymous peer reviewers appointed by them. After concluding that the document was suitable for publication, it was sent for approval to the governing bodies of the involved societies and concurrently published in the abovementioned journals.

Types of Clinical Practice Documents

The writing panel proposes the creation of an array of specialized documents, each designed to meet particular needs within the cardiothoracic community. Regardless of the document's specific category or anticipated impact on patient care, adherence to fundamental stages of development is required. This includes a systematic literature review, careful synthesis of evidence, and strict adherence to prescribed process and transparency. The documents are

methodically categorized into three primary categories, each representing unique characteristics as detailed in Table 2, with slight variations possible depending on the project's scope.

Clinical Practice Guidelines

Clinical practice guidelines are documents that comprehensively address a broad topic of interest with “statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options” (2). They must offer structured recommendations that are clearly articulated and justified, with the primary aim of improving care to patients. Such recommendations should be derived from a thorough evaluation of current evidence and accumulated clinical experience, balancing various treatment options' potential benefits and risks. The formulation of these comprehensive and methodologically sound clinical guidelines requires a joint effort from a specialized, multidisciplinary Writing Committee of experts. This Committee should include an evidence review team composed of clinical methodologists, biostatisticians, dedicated research fellows, and a medical informatics expert, each contributing to a more rigorous and thorough evidence appraisal process.

The key aspects of guideline primarily depend on findings from rigorous, well-conducted, randomized trials and large patient registries, ensuring a robust evidence base. Regardless of whether the primary data come from randomized or observational studies, the Writing Committee must meticulously assess the quality of the evidence, relevance, and internal and external validity, focusing on study design, conduct, and methodological rigour. Sometimes, robust evidence is missing or may be difficult to obtain, particularly for long-standing procedures where further research could present ethical issues. The availability of new,

replacement therapies enables an evaluation of the relative merits of existing treatment strategies providing the opportunity for incremental advancement.

Addressing these challenges, observational and case studies, combined with the accumulated clinical knowledge, can also play a crucial role in tackling prevalent clinical questions. These insights form the basis for consensus-driven recommendations that aim to enhance patient outcomes. The responsibility of a Writing Committee is to harness this collective expertise, developing guidelines that not only aim to mitigate adverse outcomes but also to elevate the standard of patient care. This consensus is especially critical in fields where comparative data are scarce and treatment practices vary widely. By striving to minimize complications and bolster patient care, the committee also highlights areas in need of further research, thereby paving the way for continuous improvement in healthcare delivery and research efforts.

Before its official release, each guideline undergoes a thorough review process involving relevant experts and entities, coordinated by the editorial offices of the affiliated societies and Guideline Committees. Concurrently, the guideline is made available online for public commentary, necessitating that the Writing Committee diligently reviews and considers all feedback received. This review phase concludes only after the authors have satisfactorily addressed feedback from anonymous reviewers and secured final approval from the lead reviewers and editors-in-chief. Subsequently, upon validation and endorsement by the Governing Bodies, the guideline is officially finalized and prepared for publication.

Expert Consensus Statements

Expert Consensus Documents offer collective insights on specialized, potentially contentious topics where substantial evidence is insufficient to inform critical clinical questions. These documents discuss areas characterized by significant variations in practice patterns and

where uncertainty about the best treatment strategies precludes the development of a more definitive guideline document. Instead of delivering firm recommendations, Expert Consensus Documents provide clinical suggestions through statements not supported by a designated level of evidence or class of recommendation and are explicitly identified as such. The process starts with identifying the central clinical issues and associated questions. An expert Writing Committee conducts an extensive literature review and synthesizes the evidence. These documents typically include an introduction that sets the context for the issue, a critical appraisal of the evidence obtained, and expert statements while highlighting the respective knowledge gaps to encourage further research. Prior to consideration for publication, they undergo a comprehensive review and approval process similar to the clinical practice guidelines. The only notable exception is that, unlike guidelines, these documents are not mandated to be posted for public comment, streamlining their path to publication.

Clinical Statements/White Papers

A clinical statement or white paper is a meticulously drafted, concise document authored by leading experts or authoritative figures within medical associations. It tackles subjects such as novel procedures and technologies, recent research, or newly proposed health policy documents where conclusive findings may be limited, deemed inappropriate, and subject to interpretation. These papers aim to assess the existing literature thoroughly, highlight divergent opinions, and explore potential treatment implications, offering direction for further clinical practice and research. The main objective is to clarify societies' positions on critical clinical issues while emphasizing areas of ongoing uncertainty or concern for patient safety.

Development Process for Clinical Practice Guidelines

The formulation of clinical practice guidelines is a comprehensive process organized into three critical interconnected phases. The initiation or preparatory phase lays the foundation by establishing goals, delineating the scope, and selecting the Writing Committee to ensure the soundness of the document and preserve scientific integrity. This is followed by the writing phase, where evidence is meticulously gathered, synthesized, and formulated into preliminary recommendations. The concluding phase, validation, involves thorough peer review, public comment when appropriate and adjustments to ensure accuracy, relevance, and consensus before the guidelines are finalized and disseminated to the healthcare community. Each phase is crucial, building upon the previous one to develop authoritative and practical guidelines.

It is expected that the collaboration on most documents will involve multiple surgical associations, reflecting a unified approach to addressing clinical topics. This cooperative effort may vary, however, depending on the specific subject matter and the importance of regional insights, which could necessitate a more localized perspective. Despite this variability, a consistent level of coordination among the associations is anticipated, ensuring adherence to established structures, processes, and procedures as detailed in this document. Additionally, a list of ongoing and future projects should be made publicly available to ensure transparency and encourage wider participation.

Initiation phase

The initiation phase for clinical guidelines is the foundational step that involves selecting a relevant topic, establishing clear objectives, and assembling a dedicated Writing Committee while managing practical considerations such as timelines, budgets, and conflicts of interest.

Topic selection

A successful clinical practice guideline document begins with an explicit and well-defined purpose, focused on the diagnosis, treatment, or follow-up of a disease or condition. The selected topic and associated clinical question(s) must be both timely and relevant to contemporary medical practice, typically addressing areas with significant variation in clinical approaches and associated outcomes, indicating a clear need for standardized guidance. Crucially, the development of such a document is warranted only when there is a substantial body of evidence to support its creation, thus ensuring that the guidance is scientifically valid and clinically applicable.

In this context, the working groups led by societal guideline committees carefully select topics, crafting critical clinical questions and proposing them to the society's governing bodies for approval. Recognizing the constraints of finite resources and the duty of care to patients and clinicians to provide robust and defensible recommendations, the associations make strategic decisions, including provisional publication timelines. Individual members from each association are also invited to suggest topics and put forward proposals using the form provided in the supplementary appendix. These proposals undergo an initial evaluation by the guideline committee of the member's primary association. Based on the proposal's merits, a decision is made on whether to proceed to the next steps. Proposals that pass this initial vetting phase are forwarded together with preliminary acceptance to the other associations guideline committees for further appraisal and collectively deciding whether it should be developed into a clinical practice guideline, an expert consensus document, or a clinical statement while determining urgency and priority. They communicate conclusions with the proposer to convey if the project is declined, deferred due to insufficient priority or

lack of immediate resources, or advanced to the governing bodies of all associations for final ratification. The process is finalized with the agreement of all involved parties and the execution of a memorandum of understanding, which outlines the roadmap for developing any clinical practice document.

Determining scope and objectives

Defining the scope and objectives is pivotal in developing clinical practice guidelines. Although surgical management is a central theme, the guidelines often cover critical associated aspects of care, such as diagnosis and treatment selection through multidisciplinary decision-making, as well as the necessary post-intervention care to ensure adherence to guideline-proposed therapies and clinical follow-up. It is essential to recognize that the purpose of any guideline is to provide direct, evidence-supported guidance rather than an all-encompassing, textbook-style overview. To ensure they are comprehensive yet focused and practically applicable for clinicians, the guidelines should adhere to a maximum of 30,000 words and 500 references and provide an executive summary, regardless of the subject matter, thus providing a concise and clinically relevant set of recommendations.

Selection of Co-Chairs and Writing Committee members

The next step in creating clinical practice guideline requires assembling a Writing Committee composed not only of published experts in the relevant clinical field but also, depending on the type of the document, of professionals proficient in various aspects of guideline development, such as systematic reviews, research methodologies, statistics, epidemiology, and quality improvement initiatives. To ensure a comprehensive perspective, the committee's composition must reflect participating association membership, a broad range

of specialties, practice settings, and geographic, generation and gender distributions. Additionally, the involvement of patient representatives from relevant organizations is encouraged to enrich the dialogue and decision-making process.

The number of Writing Committee members should not exceed 20, including Co-Chairs, Methodologists, Research Fellows, and other Committee Members, to ensure an efficient workflow (2). All members are obligated to provide substantial input into the development of the document. This input can take various forms, including formulating clinical questions, synthesizing and evaluating evidence rigorously, drafting guideline sections, revising drafts, and engaging actively in group discussions and document revisions.

Typically, each association involved in the guideline production process appoint its Co-Chair. In the complex guideline production process, Co-Chairs play a pivotal role, leading the committee’s efforts and functioning as a dedicated facilitator available to the Writing Committee, Project Manager and governing bodies of the involved associations. The Co-Chairs have several critical tasks: they assist in the selection of Writing Committee members in conjunction with the Guideline Committees, prepare the initial table of contents according to the assigned scope of the project, delegate research and writing assignments, manage potential conflicts of interest, schedule and lead Writing Committee meetings, oversee the document's drafting, and meticulously review and revise the document drafts before submitting the final version for external validation. Additionally, the Co-Chairs supervise the review process, liaise between reviewers and the Writing Committee, and coordinate the creation of executive summaries when needed. The Co-Chairs are responsible for defining the clinical guidelines' work plan, establishing a completion timeline, and consistently updating the Guideline Committee on progress.

In the selection of other Writing Committee members, it is critical to prioritize candidates recognized for their expertise, substantial contributions to the field, and proven substantive involvement in relevant research work. The ideal members should be esteemed for their academic achievements, positive team dynamics and productive work habits, which are essential for collaborative success. To uphold the integrity of the selection process, the associations shall implement an open call for applications, ensuring that all interested parties are afforded an opportunity to participate. This call shall be widely disseminated through relevant channels to reach a diverse pool of potential candidates. Subsequently, applications should be evaluated carefully by the societies' selected committees in partnership with the Co-Chairs, who will oversee the assessment process per the previously established criteria (Supplementary Appendix). This process guarantees transparency and promotes diversity, reflecting a commitment to inclusive excellence. At the project's conclusion, the committee members' work will be assessed to ensure that those who have maximally contributed to the project's development are recognized and considered for participation in future endeavours. This evaluation will reinforce the merit-based selection of contributors and encourage ongoing dedication to the highest standards of collaborative academic work.

The structured approach ensures that the CPGs are developed by experts and carefully managed to produce a clinically relevant, evidence-based document that will stand the test of practical application in diverse healthcare settings.

Dealing with conflict of interest

Transparency in declaring and managing potential conflicts of interest (COI) is critical for developing trustworthy guidelines. A COI refers to any relationship that could bias or appear to bias an individual’s opinion or work, including financial relationships and intellectual biases.

Financial COIs include any relationship for which one receives remuneration or benefits in kind. These include holdings in individual investments (e.g. stocks, stock options, bonds, or any direct investment of pharmaceutical or device companies) and patents associated with licensing and/or financial or in-kind benefits. This applies to guideline participants, their spouses, domestic or life partners, dependents, and children. Intellectual COIs include any roles or activities that could influence an individual's position, opinion, and judgment.

Prior to appointment, candidates are required to submit declaration of interest forms that the selected members of a guidelines Committee will scrutinize. This review determines a candidate's eligibility, resulting in one of three types of decisions:

1. *Appointment*
2. *Appointment with management conditions, or*
3. *Disqualification*

Individuals appointed with management conditions will receive clear instructions regarding the limitations imposed on their participation. This may restrict their involvement in discussions, drafting sections of the text or recommendations, and voting on content related to specific conflicts.

Occasionally, a candidate may be considered for approval upon divesting from COI, provided there is substantial confidence that no further impact on the candidate's objectivity remains. Once approved, each candidate must sign a formal Writing Committee member agreement acknowledging the COI policies and, if applicable, the specific terms of their management.

To prevent any perception of bias, the initiation of new or additional relationships that could constitute a COI is discouraged during the development of the document and until its publication. Any Writing Committee member considering a new relationship must obtain written permission from the Chairs before engaging in the activity.

The final composition of the Writing Group should include Co-Chairs who have no relevant COIs and other members who have either no relevant COIs or those deemed manageable, as detailed in Table 4, which outlines a proposed disclosure process based on the refined standards of the American College of Chest Physicians (17). The Disclosure of Interest forms for each member should be made available online as a supplementary appendix.

[here]

Confidentiality agreement

Every member of the Writing Committee must sign a confidentiality agreement before the start of the project, which prohibits any communication of details related to the guideline's content and development before its official release. Until the document is published online, only the names of the Co-Chairs shall be disclosed to the public; the identities of other Writing Committee members and reviewers shall remain confidential until the official publication to diminish the potential influence of their decision during the development process. Any violation of confidentiality through unauthorized dissemination of information to external parties may result in the immediate exclusion of the involved Writing Committee member from all current and future activities pertaining to this area of work.

Timelines and milestones

Adhering to strict timelines is one of the most critical points. From the inception of the first meeting, the timing toward the publication of the document must not span beyond a period of 24 months, ensuring a timely delivery while maintaining the integrity and relevance of the information. A systematic literature review sets the foundation at the beginning of this period, providing a snapshot of existing evidence. It is acknowledged that delayed publications may yield outdated aspects of this review; thus, the urgency of progressing in a

timely manner through the development phases is critical. The writing phase, tasked with creating the submission draft, figures, and evidence tables, is allocated a strict one-year timeline to ensure meticulousness and efficiency in generating a robust draft. Subsequently, the focus shifts to the validation and publication phase, which is also subject to a maximum duration of one year. This final year ensures that the document undergoes rigorous scrutiny and adjustment before it reaches its readers, reflecting the latest point of view and expert insight in the field.

Support and Resource Allocation for Clinical Guidelines Development

Each Guideline project shall be managed by a single organization responsible for providing and funding the project manager and required technology. A project manager is essential for providing guidance and support to the Writing Committee, providing logistical support by organizing online and in-person meetings and delivering timely progress reports. The project manager collaborates closely with the delegated managers from involved associations and keeps them informed of significant developments.

The participating associations exclusively fund the development costs without permitting sponsorships or grants to contribute to the individual project. The leading association outlines the financial framework for guideline development and shares for approval to all involved parties, considering the expected number of Writing Committee members and the project's scope. This budget will typically include expenses for one in-person meeting, such as travel and venue arrangements. It is standard practice for the in-person meeting to take place during the final phase of the document's development when recommendations are being finalized, with online meetings previously employed intensively to maximize resource efficiency and minimise the carbon footprint. Furthermore, the budget will cover the

expenses for engaging an informatics medical specialist and a graphic designer, in addition to fees for publication costs, which include copyediting services and other expenditures that may arise during the project's development.

Writing phase

After completing all steps of the initiation phase, the writing phase of clinical practice guidelines begins. This most critical stage entails the comprehensive drafting of the guidelines, which includes creating submission drafts of the document and its supplementary material, detailed figures and evidence tables. It is a period characterized by intensive research, systematic information organization, extensive group discussions, and the meticulous articulation of recommendations. This ensures that the guidelines are both evidence-based and applicable in contemporary clinical settings. The phase commences with a mandatory introductory kick-off Writing Committee meeting and concludes with submitting the document for external validation.

Table of contents

The Table of Contents sets out a structured framework for the document’s composition, detailing the primary sections and their subdivisions following the project scope defined earlier. It lays the groundwork for formulating specific research questions and practice recommendations. The content encompasses the main text, central illustration and highlights, applied methodology, addresses critical knowledge gaps needing immediate medical community response, and distils key take-home messages with profound implications for clinical practice enhancements. The Co-Chairs prepare the preliminary outline, which is then refined based on the group's consensus during the initial meeting. Once

discussed and ratified, the Table of Contents is generally considered final; however, it may undergo modifications following external validation, with possible additions, adjustments, or omissions based on authoritative feedback from the lead reviewers. As an essential organizational tool, it facilitates a productive start to the literature review, drafting chapters and provides straightforward manuscript navigation post-publication, enabling scholars and practitioners to locate and consult relevant segments swiftly.

Standards for systematic literature review

A scoping literature review offers a swift and efficient alternative to systematic literature reviews for synthesizing research findings (18). This approach is crucial for developing recommendations or clinical statements in practice documents, balancing rigor with the need for rapid results. By making strategic trade-offs between scope and detail, it provides experts with an immediate grasp of the evidence's rigor, facilitating quicker decision-making in clinical guideline development. The Writing Committee members are tasked with conducting scoping reviews for each section that contains recommendations, adhering to the PICOT (Population, Intervention, Comparison, Outcome, and Time) questions framework:

- Population: Identifies the specific group of patients under consideration, typically those affected by the disease or condition of interest. The definition of the patient population should be precise.
- Intervention: Defines the treatment or diagnostic test, determining whether its application is beneficial. In the case of diagnostic assessments, the focus may be on the implications of positive versus negative test results.
- Comparison: Presents an alternative to the proposed intervention, often the current standard of care or control, which could include no treatment, a placebo, or an

alternative therapeutic approach. For screening questions, the comparison might involve opting not to screen.

- Outcome: Involves the determination of outcomes of clinical relevance to the patient population, establishing indirect measures in favour of those that directly impact patient care and indirectly the proposed recommendation. Therapeutic queries prioritize treatment effectiveness and safety, whereas diagnostic or prognostic inquiries concentrate on improving disease detection or forecasting outcomes.
- Time: Relates to the timeframe necessary for an intervention to show results or the duration of participant monitoring.

Using the developed set of PICOTs, medical informatics specialists can conduct focused searches for the established clinical questions, supplying chapter leaders with a narrowed literature review cleared of publication duplicates ready for subsequent title-abstract screening, possibly with a research fellow's assistance. The ultimate selection of articles for detailed review hinges on the scope and quality of the evidence in the field. Guidelines should be based on peer-reviewed studies published in English, with the understanding that the Writing Committee guide the evidence synthesis without additional analyses beyond those peer-reviewed and reported in the literature.

Evidence review

The literature search should be systematic, documented, and follow a reproducible methodology in line with PRISMA reporting standards (19), enabling potential replication by readers. In collaboration with the research fellow, chapter leaders will develop an evidence table containing comprehensive information on study design, population, interventions, and specific outcome data based on the formulated PICOT questions. Furthermore, additional

tables will be created to evaluate the individual quality of each paper and its risk of bias. The Writing Committee is responsible for preparing a final literature report. This report should encapsulate the search strategy, PRISMA flow diagram, evidence tables, risk of bias assessments, and a reference list, all of which will be included as supplementary material.

Evidence grading system

The rigorous assessment of methodological quality is an indispensable step in appraising clinical research that informs practice guidelines. Every study selected for inclusion in recommendation tables requires a thorough evaluation of potential biases and methodological robustness. The Risk Of Bias 2 (ROB2) tool shall be utilized for randomized controlled trials to identify biases that might systematically influence outcomes (20). Observational studies shall be examined through the Risk Of Bias In Nonrandomized Studies - of Interventions (ROBINS-I) framework to gauge the likelihood of bias in the absence of randomization (21). When appraising when considering bias from missing outcomes in systematic reviews with meta-analysis, the Cochrane Collaboration's tool (ROB-ME) serves as a guideline to ascertain the synthesis's robustness and reliability (22). Each tool contributes to a rigorous analysis. However, they should be used as aids and not simple checklists, as their application alone may not reveal instances of research misconduct, such as incomplete reporting (23). This underscores the importance of diligently reviewing source materials, including trial protocols and statistical analysis plans, to ensure all relevant and significant results are accounted for.

Formulation of recommendations

Recommendations are the foundational elements of guidelines, serving as focal points that must stand alone and be understandable without reading the supporting text. Using clear, unambiguous language and precisely defined terms is crucial for accurately describing the patient group, the specific medical indication, and the target audience for the recommendation. The language used should vary only according to the 'Class of Recommendation' and must include the appropriate verb, as detailed in Table 3. The main text provides context, clarification, and a detailed explanation, documenting how these elements contribute to the formation of the recommendations.

A fundamental principle of Evidence-Based Medicine is the hierarchical system of classifying evidence, known as the levels of evidence. While adequately designed and conducted RCTs are usually assigned the highest Level of Evidence, not all RCTs are designed and executed equally, and therefore, their results must be scrutinized carefully. The grading system that provides the strength of evidence-based recommendations has evolved to prevent the automatic assignment of the highest Level of Evidence in cases where there is an increased risk of bias in the cited RCTs or when there is conflicting evidence between them. In such instances, the Level of Evidence shall be downgraded from A to B, which is only on par with observational data. The same principle applies to meta-analyses of RCTs when observed high risk of bias or significant heterogeneity exists. Finally, the universally accepted grading system indicates whether recommendations are based solely on consensus or supported by substantial evidence to improve academic rigour and stimulate further research.

Consensus achievement (discussion, voting, and dealing with conflict of interest)

The Writing Committee’s role in developing clinical guidelines is a dynamic and iterative process that occurs through all phases of guideline formulation. This process includes

continuous dialogue and consensus-building through multiple modes of communication, including online meetings, email correspondence, and in-person meetings.

The drafting of potential recommendations begins with the Chapter Leaders' evaluations of the available evidence. The Chapter Leaders are primarily responsible for presenting draft recommendations, which are then subject to collective deliberation and refinement during full group meetings. The Co-Chairs play a critical role in facilitating discussions among authors, resolving any differences in evidence classification, and refining the precise wording of each recommendation. The Writing Committee members with relevant conflicts of interest must recuse themselves from discussing and voting on any recommendations their interests could potentially influence. Once a provisional agreement of at least 75% of the present members is reached, the draft recommendation moves to the next phase. Subsequently, an anonymous electronic survey provides multiple-choice options (Agree, Disagree, Abstain) for voting on each recommendation, accompanied by the corresponding Class of Recommendation and Level of Evidence. Achieving an 80% response rate and a minimum of 75% agreement among those voting Agree is perceived as a reaching consensus. Authors who Disagree with a recommendation or choose to Abstain from voting are required to provide a rationale that will lay the groundwork for further discussion and refinement of the recommendation in preparation for another round of voting, if necessary. This iterative process is repeated until all recommendations receive a positive endorsement. The same applies to all proposed treatment algorithms, other illustrations or any table that provides different forms of clinical guidance.

Finally, the Writing Committee should refrain from finalizing recommendations when there is a significant divergence in expert opinion or when recommendations consistently fail to receive positive affirmation by members of the Writing Committee despite numerous

attempts. Such scenarios raise the risk of disseminating flawed guidance. Under these circumstances, describing the different inferences being drawn and proposing areas for future research to bridge the gaps in evidence and clinical experience is recommended. Instances of non-consensus among the Writing Committee shall be transparently indicated in the accompanying commentary of the voted recommendations. In addition, even when consensus is achieved regarding a given recommendation, an opportunity is afforded to members of the Writing Committee who voted in disagreement to explain the rationale for their dissenting opinion that should be presented in the supplementary material.

Final draft document

After securing affirmative votes on the recommendations, illustrations and tables, the next step involves revising the associated text to align with these decisions and finalizing master copy for additional commentary. The recommendations that have achieved consensus are now fixed; however, all authors are expected to review the draft text critically and collaborate to achieve enhanced clarity and consistency throughout the document. The Co-Chairs are responsible for preparing the final draft, which is then circulated among the authors for their conclusive feedback and endorsement. The document is ready for external validation only after it is supported by unanimous collective responsibility and the supplementary material, including the voting summary, is completed.

Validation phase

A robust validation phase is essential in practice guideline development. During this phase, preliminary document draft become finalized after the content undergoes a rigorous examination to ensure it aligns with established clinical standards and goals. The process

involves a thorough review, which is instrumental in establishing the quality and trustworthiness of the guidelines, culminating in their publication. Central to this process is the involvement of subject matter experts whose impartial evaluations and thoughtful assessments are critical to the integrity of the guidelines. This review is characterized by meticulous attention to detail and a stringent observance of established evaluation benchmarks to create a uniform and comprehensive inspection of the guidelines' facets.

The validation phase enhances the reliability and authority of the clinical practice guidelines, thereby increasing their utility to both practitioners and patients. The primary goal of this phase is to refine the guidelines into their most practical and relevant form, ensuring they are ready for distribution and application within clinical environments.

Selection and role of review coordinators and reviewers

At the outset of the writing process, the Governing Bodies assign a review coordinator and appoint up to five anonymous reviewers from each participating entity to contribute to the external validation process. Apart from commenting on the content, the coordinator's role is to summarize and relay concerns, liaise between the Writing Committee and the reviewers, and address ongoing issues. Typically, there are two review rounds: an initial review is conducted as individual chapters are completed and a second review when the entire document is completed. Each round of review takes no more than one month, matching the Writing Committee's timeframe for responding to comments. Upon the leading reviewer's request, the review duration may be extended until all issues are addressed. Changes in recommendations and algorithms necessitate a formal vote prior to resubmission. The process concludes when the review coordinators are satisfied with the responses to their critique and the Writing Committee members formally endorse the revised document. Finally,

the document is posted online for two weeks of public comment. Any feedback should be evaluated by the Co-Chairs and the review coordinators to determine whether any significant changes to the document are warranted. The latter would entail an additional cycle of approvals by the reviewers and the Writing Committee.

Reviewers' efforts are recognized by listing their names as contributors in the final document, although they can opt for anonymity in the publication.

When disagreements that cannot be overcome arise between the Writing Committee and the reviewers, the Societies activate a de-escalation process. This involves proposing up to three impartial experts with the requisite expertise to mediate the conflict. These experts work closely with the Co-Chairs and Co-Leading Reviewers to bridge gaps in understanding and interpretation, fostering a collaborative environment. Their goal is to steer both parties towards a mutually agreeable resolution, ensuring that the clinical guidelines are both evidence-based and consensually validated.

Governing approval process

Once the reviewer coordinators have given their final approval, the document is first sent to the language editor for final copyediting and subsequently for proofreading to the Co-Chairs. The document then proceeds to the association's executive committee or board for final approval, these bodies serving as the ultimate tier of review. The Writing Committee should address these final concerns with the same rigour as they would for earlier reviewers. The document is deemed acceptable for publication only when it has received the collective agreement of all parties involved, including the Writing Committee.

Publication process

The publication process signifies the completion of the clinical guidelines' development and often aligns with a scientific conference. This strategic timing ensures the guidelines are presented to a diverse audience, allowing authors to address questions and concerns directly in real-time. Once published, the guidelines should be freely accessible online to foster engagement from the broader medical community. In the case of joint publications across various journals, efforts are made to synchronize their release. Such coordination guarantees widespread and uniform distribution of the guidelines, facilitating a unified understanding and adoption of the recommendations within the medical community.

In the interest of transparency, all proceedings, including agendas, minutes, reviews, written comments, and correspondences relating to the document development process, should be archived and recoverable upon request, subject to joint leadership review and approval for at least 3 years.

Update process

As medical practices evolve, the regular reassessment and updating of clinical guidelines to include new therapeutic and diagnostic developments are crucial (24). A methodical process must ensure that clinical practice guidelines are revised at least every five years or when there are significant advances in the evidence base, aligning with current research and its effects on established advice and practices. Updates should be executed promptly when new critical evidence arises, entailing precise modifications or comprehensive evaluations as needed. The scope of these updates and the requirement for a Writing Committee are determined by the extent of the changes required. Notably, the current version should be regarded as authoritative until an updated or revised guideline or clinical statement prompting specific clinical action is published.

Distinguishing Features in the Development and Content of Clinical Guidelines Versus Other Clinical Practice Documents

The development of clinical guidelines is distinct from other clinical practice documents in several vital aspects: scope, evidence strength, nature of recommendations, review thoroughness, and updated schedules, as presented in Table 2. Clinical guidelines offer a broad and thorough perspective on patient care, underpinned by robust evidence from a multitude of prospective well designed and conducted studies, ensuring a solid foundation for recommendations. Other clinical documents, with a narrower focus, address specific patient care issues or clinical questions marked by variable practices, typically relying on observational studies. However, distinguishing document types solely on evidence strength can be complex.

Guidelines offer well-defined recommendations for healthcare providers and policymakers, detailed with classes of recommendations and levels of evidence, whereas other documents show clinical statements or suggestions to serve as consultative guidance. The scrutiny for guidelines is more comprehensive, demanding input from a broad array of reviewers and confirmation by prominent authoritative bodies. Other clinical documents are subject to a simplified review process, needing only the consensus of a select review panel and the approval of the journal's editorial board. Finally, the timing for updating guidelines is more rigorous, ensuring they consistently reflect the latest evidence. In contrast, revising other documents is more flexible, with timing that adjusts to new evidence and allows for deferral without significant findings.

Irrespective of the document type, it's crucial to recognize that all clinical documents must be developed through a systematic process that includes comprehensive literature reviews,

meticulous statement development, and achieving consensus via voting, with strict adherence to these procedures and transparency about the process being imperative.

Dissemination and implementation of clinical practice guidelines

The dissemination and implementation phase of international clinical practice guidelines is critical and can result in low adoption rates if not rigorously approached (25). Factors identified as major barriers to guideline adherence include the complexity of guideline documents and the high number of weak or conditional recommendations (26). Effective dissemination ensures the guidelines reach the intended audiences, including healthcare providers, policymakers, and patients. This may be achieved through multiple channels, including publication in scientific journals using layman's terms language, distribution via professional networks, social media, presentations at conferences presentations, and incorporation into educational materials and clinical decision support systems.

Implementation refers to the practical application of the guidelines in clinical settings. This often requires a strategy to encourage adoption by healthcare professionals in the clinical setting. Strategies include national society endorsement and the integration of guidelines into electronic health records. Monitoring of guideline implementation is critical at this phase, to provide feedback on the extent to which the guidelines are being followed and their impact on clinical practice. Data derived from regional and national databases and membership surveys can inform the extent and variation of penetration of the guidelines and identify hurdles and opportunities for enhanced adoption. Moreover, the implementation process considers the various barriers that may impede the integration of guidelines into routine practice, such as resistance to change, lack of resources, or contradictory guidelines. Addressing these challenges often involves tailored interventions to support healthcare

providers and organizations in making the necessary changes to align with the best practices recommended within the guidelines.

Ultimately, dissemination and implementation aim to ensure that clinical practice guidelines lead to improved health outcomes, enhanced quality of care, and greater patient safety by translating the best available evidence into everyday clinical practice.

Gaps in knowledge and future perspectives

Identifying and addressing knowledge gaps is a dynamic and ongoing process in the field of clinical practice documents. As medicine evolves with emerging research and new technologies, guidelines must be responsive, assimilating new findings and addressing current gaps. Future directions in guideline development increasingly focus on personalized medicine, shaping recommendations to fit individual patient's unique genetic, environmental, and lifestyle contexts.

Embracing a multidisciplinary approach is critical for the development of clinical guidelines, ensuring engagement with patient organizations, clinical methodologists, and consumer representatives to develop comprehensive, inclusive, and patient-oriented guidelines. Efforts are also underway to embed patient preferences and values into the heart of guideline development, fostering evidence-based, patient-centered care. Leveraging artificial intelligence and big data analytics offers exciting prospects for enhancing the precision of guidelines and more effectively tailoring interventions to specific patient groups.

As the sophistication of guidelines increases, so does the necessity for improved dissemination and implementation methods, ensuring seamless integration into clinical practice. The adherence to guidelines is not well studied and might be another topic of future perspectives. Overall, solid guidelines would be desirable to implement and integrate into

healthcare plans. This could include innovative educational resources, decision support systems, and policy measures that embed recommendations and quality metrics into daily practice.

Looking to the future, clinical practice guidelines are characterized by constant learning and flexibility, maintaining their pivotal role in informing clinical decisions and elevating patient care outcomes.

Conclusions

The credibility of clinical practice guidelines has come under scrutiny due to transparency issues, the lack of multidisciplinary input, potential biases, and conflicts of interest, all of which have led healthcare practitioners and patients to doubt their utility. In response, the AATS, EACTS, ESTS, and STS have thoroughly reviewed and discussed the critical methods for creating clinical practice documents, resulting in a detailed manual that outlines procedures for formulating joint guidelines with precise, stringent adherence to established principles. Emphasizing fundamental development principles, the necessity of systematic literature reviews, comprehensive evidence synthesis, precise evidence grading, and transparency are all integral steps to meeting high standards. The aim is to establish methodological norms for equitable, achievable, and unbiased guidelines and gain physicians' trust for crucial healthcare decisions. This collaborative effort enhances the methodological rigor and transparency in guideline creation, strengthens confidence in their recommendations, and sets the stage for future projects that will continue to advance patient care.

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Table 1. The fundamental principle proposed for the development of clinical practice guidelines.

Organizations	Writing Committee Composition	Standards for Initiating a Systematic Review	Evidence Review Committee	Evidence Appraisal System	Conflict of Interest (COI)	Recommendations	Economic Consideration
AATS, EACTS, ESTS, and STS	Multidisciplinary team of 10-20 balanced members, including clinicians, a variety of methodological experts (such as statisticians, epidemiologists, and/or public health specialists), and if needed, representatives from populations expected to benefit from the guideline.	The patient, intervention, comparison, outcome and time (PICOT) framework	Experts in clinical content, an expert in systematic review and an expert in searching relevant evidence	The Risk Of Bias 2 (ROB2) tool for randomized trials, the Risk of Bias due to Missing Evidence (ROB-ME) in a meta-analysis and the Risk Of Bias In Non-randomised Studies - of Interventions (ROBINS-I) frameworks	Individuals being considered for the writing committee should comprehensively declare interests and activities that may result in COI with development group activities through written disclosure before selection. The Chair or Co-Chairs should not have any COI, and other members should either have no relevant COIs or those deemed manageable.	Members with potential COI are excluded from related votes. A 75% provisional agreement of present members is required to advance a recommendation. The Delphi Method requires an 80% response rate and at least 75% agreement for approval of an individual recommendation. Voting continues based on anonymous feedback until consensus is reached.	No economic evaluation for treatment interventions; recommendations for best practice care should be provided.

AATS, American Association for Thoracic Surgery; EACTS, European Association for Cardio-Thoracic Surgery; ESTS, European Society of Thoracic Surgeons; STS, Society of Thoracic Surgeons.

Table 2. Types of Clinical Practice Documents

	Clinical Practice Guidelines	Expert Consensus Statements	Clinical Statements/White Papers
Definition	Evidence-based documents containing systematically developed recommendations with an explicit clinical scope and explicit consideration of benefits, harms, values, and preferences.	Expert position on a controversial or specific clinical topic, formulated as a statement of facts based on available evidence and expert consensus, in situations where high-level evidence is not available.	Extensive reports outlining positions on critical clinical issues while highlighting areas of ongoing uncertainty or concern for patient safety.
Source of Evidence	Randomized controlled trials (RCTs) are available and serve as the primary source of information; observational data are used if considered robust.	Robust observational data are available and serve as the primary source of information in conjunction with a limited number of RCTs.	Any research and healthcare regulations
Number of Writing Committee Members	Up to 20	Up to 20	Up to 10
Review	A review coordinator and up to five anonymous reviewers from each participating entity in collaboration with the governing bodies	A review coordinator and up to five anonymous reviewers from each participating entity in collaboration with the governing bodies	Up to 3 anonymous reviewers from each participating entity
Length	Up to 30,000 words and a total of 500 references	Up to 15,000 words and a total of 300 references	Up to 5,000 words and a total of 50 references
Time Frame	24 months	12 months	6 months
Meetings	Conference calls, email correspondence, and in-person meeting	Conference calls and email correspondence	Conference calls and email correspondence

Table 3. Definition of Classes of Recommendation and Levels of Evidence.

Class of Recommendation (Suggested phrases)	AATS/EACTS/ESTS/STS Definition
I	**Strong recommendation.** **Benefit >>> risk.** Suggested phrases for writing recommendations: • Is recommended • Is indicated
IIa	**Moderate recommendation.** **Benefit >> risk.** Suggested phrases for writing recommendations: • Should be considered • Should be reasonable • Can be useful/effective/beneficial
IIb	**Weak recommendation.** **Benefit ≥ risk.** Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered
III	**Strong recommendation.** **No benefit: risk = benefit.** **Harm: risk > benefit.**

	Suggested phrases for writing recommendations: • Is not recommended • Should not be performed/administrated/other
Level of Evidence	
A	High-quality evidence from more than one randomized controlled trial (RCT) with no concern of high risk of bias, or meta-analyses of high-quality RCTs with no significant treatment effects heterogeneity.
B	Randomized (B-R): Moderate-quality evidence from 1 or more RCT or meta-analysis of RCTs. Non-Randomized (B-NR): Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies or meta-analyses of such studies.
C	Limited data (C-LD): Studies with limitations of design or execution, meta-analyses of such studies, or physiological or mechanistic studies in human subjects. Expert opinion (C-EO): Consensus of expert opinion based on clinical experience.

AATS, American Association for Thoracic Surgery; EACTS, European Association for Cardio-Thoracic Surgery; ESTS, European Society of Thoracic Surgeons; STS, Society of Thoracic Surgeons.

Table 4. Type of relationship/activity, committee role, and decision about participation

Type of Relationship	Committee Role	
	Chair	**Other Members**
<u>Research and Scholarly Activity</u>		
• Authorship in scientific peer-reviewed and book chapters.	**A**	**A**
• Authorship of peer-reviewed publication in support of a commercial entity:		
○ With no product in the topic area	**A**	**A**
○ With a product in the topic area	**U**	**M**
• Investigator in grant-funded research on government-related topics, with funds directed to the institution.	**A**	**A**
• Investigator in grant-funded research on unrelated or related topics funded by a commercial entity with no product lines related to the topic:		
○ With funds directed to the institution	**A**	**A**
○ With funds directed to individual	**A**	**M**

• Investigator in grant-funded research topics funded by commercial entities with product lines related to the topic:
  ○ With funds directed to the institution
  ○ With funds directed to individual
	
	U
	U
		
		M
		M

<u>Educational Activities</u>
• Faculty in CME-/MOC accredited activity.
• Faculty in a commercially sponsored, nonaccredited activity where a not-for-profit organization fully controls speaker selection and content (e.g. AATS-run commercially sponsored symposia).
• Faculty in commercially sponsored nonaccredited activity in an unrelated area to the guideline topic:
  ○ With no product lines related to the topic
  ○ With product lines related to the topic
	
	A
	A
	
	A
	M
		
		A
		A
		
		A
		M

<u>Advisory/Consultancy</u> • Participation in a data safety monitoring board.	 **A**	 **A**

• Advisor/consultant to industry or industry-sponsored entity on study design, education, or focus group on an unrelated topic:		
○ With no product lines related to the topic	**A**	**A**
○ With product lines related to the topic	**M**	**M**
• Advisor/consultant to industry or industry-sponsored entity on study design, education, or focus group on a related topic.	**U**	**M**
• Participation in a speaker's bureau on any topic for a commercial entity, where the company controls the content:		
○ With no product lines related to the topic	**U**	**M**
○ With product lines related to the topic	**U**	**M**
<u>Public Statements</u>		
• Issuing statements on an unrelated topic on behalf of a commercial entity:		
○ With no product lines related to the topic	**U**	**M**
○ With product lines related to the topic	**U**	**U**
• Issuing statements on a related topic on behalf of a commercial entity.	**U**	**U**

• Providing paid expert testimony on an unrelated topic on behalf of a commercial entity:
  o With no product lines related to the topic
  o With product lines related to the topic
• Providing paid expert testimony on a related topic on behalf of a commercial entity.
• Providing paid expert testimony on a related or unrelated topic privately for a non-commercial entity (e.g. patient, private sector).
	
	U
	U
	U
	A
		
		M
		U
		U
		A

<u>Intellectual property and Investments</u>
• Patent holder or applicant:
  o Patent unrelated to the topic
  o Patent related to topic
• Investments (e.g. stock holdings, stock options, warrants, shares, bonds, or any other form of direct investment (not as part of mutual fund) in pharmaceutical companies or any other commercial entities (e.g. device manufacturers) that manufacture or sell products related to management of an individual with disorders addressed by cardiothoracic surgery:
	
	A
	U
		
		A
		M

○ With no product lines in the topic area	**A**	**A**
○ - With product lines in the topic area	**U**	**M**
<u>Employment</u> • Full-time/part-time employment arrangement with a commercial entity		
○ With no product lines related to the topic	**U**	**M**
○ With product lines related to the topic	**U**	**U**

Key: Acceptable: A**;** Manageable: M**;** Unacceptable: U

Definitions of Commercial Entity: ACCME definition of a commercial entity is any entity producing, marketing, reselling, or distributing health care goods or services. The ACCME does not consider clinical service providers directly to patients as commercial interests - unless the provider of clinical service is owned or controlled by an ACCME-defined commercial entity.