

ORIGINAL ARTICLE

A taxonomy and framework for identifying and developing actionable statements in guidelines suggests avoiding informal recommendations

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Abbreviations: TB, Tuberculosis; COVID-19, Coronavirus Disease 2019; WHO-GTB, World Health Organization Global TB Programme; GRADE, Grading of Recommendations Assessment, Development and Evaluation; GDG, Guideline Development Group; GRC, Guideline Review Committee; NTP, National TB Programme; PICO, Population, Intervention, Comparator, Outcome; ASH, American Society of Haematology, PICO, Population Intervention Comparator Outcome(s); NA, Not Applicable.

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Abstract

Objective: To propose a taxonomy and framework that identifies and presents actionable statements in guidelines.

Study design and setting: We took an iterative approach reviewing case studies of guidelines produced by the World Health Organization and the American Society of Hematology to develop an initial conceptual framework. We then tested it using randomly selected recommendations from published guidelines addressing COVID-19 from different organizations, evaluated its results, and refined it before retesting. The urgency and availability of evidence for development of these recommendations varied. We consulted with experts in research methodology and guideline developers to improve the final framework.

Results: The resulting taxonomy and framework distinguishes five types of actionable statements: formal recommendations; research recommendations; good practice statements; implementation considerations, tools and tips; and informal recommendations. These statements should respond to *a priori* established criteria and require a clear structure and recognizable presentation in a guideline. Most importantly, this framework identifies informal recommendations that differ from formal recommendations by how they consider evidence and in their development process.

Conclusion: The identification, standardization and explicit labelling of actionable statements according to the framework may support guideline developers to create actionable statements with clear intent, avoid informal recommendations and improve their understanding and implementation by users. © 2021 Published by Elsevier Inc.

Key Words: Guidelines; Standards; Recommendations; GRADE; Practice statements; Policy

What is new?

Key findings

- Guidelines, policy guidance and similar standard setting documents can include different types of actionable statements. While formal recommendations are the key actionable statement, others are necessary: good practice statements, research only recommendations, remarks or implementation considerations, tools and tips. We used case studies from published guidelines by the American Society of Hematology, the World Health Organization, and a random sample of COVID-19 guidelines to explore and define the various kinds of statements appearing in guidelines.
- Our framework provides definitions and criteria for each type of statements (formal recommendations, remarks, good practice statements, implementation considerations, tools and tips, research only recommendations), and distinguishes an additional category, informal recommendations, that guideline developers can avoid by referring to the characteristics we showcased.

What this study adds to what was known

- The unifying framework we propose can be used to distinguish the different types of actionable statements in the text of a guide-

line, and to present statements when evaluating a guideline. Informal recommendations can appear ubiquitously in the text of a guideline or accompanying publications, and can be identified following the characteristics we provide.

What is the implication and what should change now?

- Prospectively, guideline developers can use the unifying framework to be clear and transparent about each actionable statements' role and purpose. Informal recommendations can also be more easily identified and avoided. Retrospectively, guidelines developers can identify potential gaps in guideline question development and ensure these can be addressed in future planning or iterations of their guidelines.

1. Introduction

Guideline recommendations are explicit actionable statements that suggest a choice from alternative options to optimize desirable consequences of these options and include elements of the population, interventions and comparators from the question they address [1-4]. Formal recommendations should be based on the best available evidence and developed according to trustworthy and transparent methods and standards [4-9]. These methods

include concepts such as the systematic and transparent consideration of the certainty of the evidence and determining the strength of the recommendation based on explicit judgments of a guideline development group with relevant expertise and managed conflicts of interest. We will refer to guidelines but include all products that include recommendations, such as guidance, policy documents, or standards.

Guidelines frequently include other types of statements, in addition to recommendations, that might take the form and actionability of recommendations but did not undergo a full development process [10]. Definitions for some types of those statements, such as good practice statements (GPS), and guidance for the development of formal recommendations exist [10,11]. Guideline panels issue GPS when they deem these statements as not being appropriate for formal ratings of certainty of evidence to develop recommendations. Issuing GPS can be due to various reasons including the process, priorities, timeline, resources or nature of the evidence being assessed but is rooted in the fact that answers are obvious [10,11].

Recommendations can be limited in providing the necessary nuances relevant to their implementation in clinical care, public health and health policy. For example, they may not specify a drug's dose, or the necessary technical details about how to carry out a laboratory test. Implementation considerations, tools and tips represent another type of actionable statements that a panel may issue (Box 1). Implementation considerations, tools and tips typically consist of narrative text providing additional information to support the use of formal recommendations in practice (Box 1). [12].

Box 1 Examples of recommendations, good practice statements, implementation considerations, tools and tips

Recommendation: In adults and children with signs and symptoms of extrapulmonary TB, Xpert MTB/RIF or Xpert Ultra should be used for rifampicin-resistance detection rather than culture and phenotypic DST (Strong recommendation, high certainty in the evidence) [13].

Good practice statement: “Treatment of opioid dependence should be provided within the health-care system” [14].

Implementation considerations, tools and tips: “The minimum diagnostic capacity to appropriately implement the Isoniazid resistant-TB recommendations requires rapid molecular testing for rifampicin before the start of treatment with the Isoniazid resistant-TB regimen” [15].

In addition, recommendations may be further supported by statements that are often called remarks and deemed necessary to explain the recommendation and describe conditions necessary for their understanding. [16]. Implementation considerations, tools and tips can provide additional details that facilitate the appropriate use of a recommendation. Other statements in guidelines, sometimes explicitly or implicitly actionable, are research recommendations that specify the use of an intervention in the context of research. However, authoritative documents, such as the WHO Handbook on Guideline Development, do not yet include comprehensive descriptions of what types of actionable statements exist or are to be made by guideline development groups [17].

Our objective was to propose a taxonomy, along with a conceptual framework, to identify and present actionable statements in guidelines, and to support guideline developers in optimally presenting recommendations and other essential statements in guidelines.

2. Methods

2.1. General methods

We used case-studies of WHO Global TB Programme (GTB) guidelines American Society of Hematology (ASH) guidelines (February 2020), and COVID-19 recommendations (October 2020) to develop, refine, and apply this framework [16,18–24]. We drew the COVID-19 recommendations from the eCOVID19 Living Recommendations Map and Gateway to Contextualization (<https://covid19.recmap.org>).[25] Following these case studies, we used an iterative consensus approach to: 1) agree on operational definitions of formal recommendations and accompanying recommendation statements, which include good practice statements, research recommendations, remarks, and implementation considerations, tools and tips; 2) develop a framework that would provide clarity to guideline developers and users about how to classify guideline statements; 3) devise a list of examples to support the classification; and 4) provide guidance to guideline developers to identify the need for developing formal recommendations.

2.2. Participants

We invited a group of individuals with expertise in guideline development from different settings and countries with firsthand experience in WHO and other guideline development approaches. Initially, 11 health research methodologists, clinical researchers, and WHO officers were invited and six participated in discussing the framework. We reviewed existing guidelines from WHO and the American Society of Hematology and then refined the framework in the second phase of the project focusing on COVID-19 recommendations with the additional collaborators.

2.3. Approach to development of definitions and framework

A core group of investigators developed a draft conceptual framework based on examples and a review of previous work on types of statements contained within guidelines [2,26]. The initial framework proposed the addition of one additional category (informal recommendations) of statements that did not fit previously identified classifications. We also provided questions to guide the inquiry about the type of statement and presented examples of statements from WHO-GTB publications that collaborators considered and classified (Appendix A). We then aggregated these contributions and narratively assessed them to conceptualize the taxonomy and framework proposed.

2.4. Case studies

2.4.1. WHO tuberculosis recommendations

We began by reviewing WHO-GTB publications to identify statements that followed the taxonomy developed, as a proof of concept, by drawing 15 examples to support each category.

These statements were reviewed in duplicate to inform the refinement of definitions. Following this, we randomly selected five PICO questions from an additional five guidelines to undergo a systematic application of the framework in duplicate (Appendix C). These recommendations are available on the WHO TB map for recommendations (<https://who.tuberculosis.recmapp.org/>) [25].

2.4.2. American Society of Hematology guidelines

We chose four actionable statements from two ASH guidelines for review because they had followed rigorous and harmonized processes across different guideline panels [16,18,19,27,28]. We focused on challenging questions in pediatric hematology where evidence was usually indirect and often of very low certainty. In an iterative fashion, one author applied the framework to these recommendations and another author validated the judgements [27].

2.4.3. COVID-19 guidelines

A working group of the COVID19 living recommendation map and gateway to contextualization (<https://covid19.recmapp.org>) systematically extracted information from a random sample of actionable statements [25]. These recommendations came from three guidelines. We iteratively classified these statements according to the taxonomy. We discussed these examples and refined our framework using the outcomes of these discussions, particularly focusing on statements presenting challenges in their classification.

2.5. Agreement on taxonomy and framework

We presented the resulting framework during investigator meetings of the eCOVID19RecMap project for review and asked other authors of this manuscript for critical

input. We then reached agreement on the taxonomy and framework, including for how to identify informal recommendations and consider if their use was appropriate.

3. Results

3.1. Taxonomy and Conceptual Framework

Our review of WHO GTB recommendations found that actionable statements were prevalent and dispersed among guidelines and accompanying publications. In addition to formal recommendations, remarks, research only recommendations, good practice statements, implementation considerations, tools and tips (Box 2), we identified *informal recommendations*. These informal recommendations are characterized by a lack of a clear link between supporting evidence and a formal description of the process for development of the recommendation. Appendix B lists examples of research only recommendations, good practice statements, implementation considerations, tools and tips, and informal recommendations.

Box 2 Definitions of types of statements used within a guideline

Formal recommendations

Definition: A formal recommendation is an actionable statement about the choice between two or more management or policy options (interventions) in a specific population and, if relevant, in a specific setting. Alternative option(s) (i.e. comparator(s)) should be specified in the recommendation if they are not self-evident. These statements are the results of a formal deliberation process and contain an explicit and direct link to the bodies of evidence resulting from a systematic literature search and appraisal process.

Explanation and notes: The statement should have a clear direction (for or against the options) and strength (e.g., strong or conditional) to support the options. Ideally, the strength of recommendation and the certainty of supporting evidence are explicitly stated for all factors that were considered when making the recommendation (e.g. intervention effects, test accuracy, values or cost, etc). A formal recommendation should be supported by a deliberative, structured and transparent development process. An explicit and direct link to the evidence is provided, preferably in the form of an evidence profile. In particular, it should be supported by systematic reviews or health technology assessments for the factors that determine its direction and strength.

What it is: It is an actionable statement about the choice between two or more management or policy options (interventions) in a specific population and, if relevant, in a specific setting. It was formally

deliberated upon, and it has an explicit and direct link to the related bodies of evidence.

What it is not: A complete guideline, policy statement or other standard setting document.

What it is for: It can be directly used for evidence-based decision making or implemented by practitioners

Remarks

Definition: A remark supports the interpretation of either the PICO subdomains (e.g., population characteristics) and/or the conditions framing one or more specific recommendation(s) or good practice statement (e.g. guiding the user on the intervention options when the recommendation is conditional). They are not actionable in isolation.

Explanation and notes: Remarks should not include actionable suggestions, although there is confusion about this. The recommendation or good practice statement and the actual accompanying remark should be seen as an inseparable unit.

What it is: It is an inseparable unit belonging to a formal recommendation or good practice statement that provides additional clarification.

What it is not: An actionable statement that can stand alone.

What it is for: It supports the framing of the recommendation and guides users

Research only recommendations

Definition: A research only recommendation is a recommendation that confines the use of intervention options in a specific population, to research setting.

Explanation and notes: Research only recommendations are appropriate when one or more of the following three conditions are met: 1) the certainty of the available evidence does not allow the guideline panel to issue a formal recommendation; and further 2) feasible; and 3) acceptable research has a potential for reducing uncertainty about the desirable or undesirable consequences of the intervention. These recommendations should describe the population or setting in which the intervention may be used (in the context of research). Research only recommendations should contain sufficient detail to inform future investigation. Research only recommendations may be accompanied by an explicit [strong] recommendation not to use the intervention outside of the research context. [2,26].

Formal recommendations also have implications for research but do not restrict the use of an intervention to within a research setting [29]. Research only recommendations are usually not appropriate when certainty in the evidence is high: a formal, sometimes strong recommendation would be more appropriate in such a situation [2,26].

What it is: It is an actionable statement that was developed explicitly using evidence

What it is not: A formal recommendation for clinical practice, public health or health policy

What it is for: Use in the context of formal research

Good Practice Statements

Definition: Good practice statements are necessary actionable and clear guideline statements. They describe the population and intervention options and, if appropriate, comparator components of the recommendation.

Explanation and notes: Good practice statements are not appropriate for formal ratings of certainty of evidence or strength of the recommendation. Development of good practice statements should adhere to five principles and pass the following question for evaluation (updated from [10], Dewidar et al, manuscript in preparation):

1. Is collecting and summarizing the evidence a poor use of a guideline panel's limited time and energy (opportunity cost is large)?
 - Would the evaluation of the evidence of the intervention effects result only in indirect evidence?
 - Is the alternative of the intervention highly unlikely to be chosen due to ethical and human right issues?
2. Is the message really necessary about actual health care practice?
 - Does the guideline group provide a rationale in the text of the guideline to why this message is necessary?
 - Is the statement relevant to clinical practice?
3. After consideration of all relevant outcomes and potential downstream consequences, does implementing the good practice statement result in a large net positive consequence?
 - Would the implementation of the good practice statement have a large net positive impact on health outcomes or other relevant Evidence to Decision (EtD) criteria without following the approach to developing formal recommendations?
4. Is there a well-documented clear and explicit rationale connecting the indirect evidence?
 - Is there a related description of the chain of linked evidence, used to infer the net desirable consequences (mainly large health benefits) after the implementation of the good practice statement?
5. Is the statement clear and actionable?
 - Does the statement specify what action is needed?

- Is the population or setting (in case of health system statements) of interest specified in the statement?

What it is: It is a clear and necessary actionable statement

What it is not: A recommendation that has a defined strength or certainty of evidence attached to it

What it is for: Direct use for decision-making

Implementation considerations, tools and tips

Definition: Implementation considerations, tools and tips are statements that may be actionable and relevant to implementing one of the intervention options, once it has been chosen based on a recommendation. They may contain information supporting elements of formal recommendation such as the intervention (e.g., medication dosing or exact description of a complex intervention). They may include information about tools and tips that enhance implementation of the chosen intervention and/or its efficient utilization. They are not actionable without related recommendations.

Explanation and notes: These statements often describe the how, who, where, what, and when related to implementing a recommendation (e.g., including considerations about equity). Implementation considerations, tools and tips may not have a clear link to evidence. Further, an evidence review may be futile in some situations (e.g., only one dose of medication is available and that is described as part of the implementation consideration, tools and tips; modality of administration or use of the intervention; timing; precautions; how to use a test; technical requirements). Implementation considerations may be made available in separate documents or media and linked to formal recommendations in a guideline.

What it is: It supports implementation of formal recommendations.

What it is not: A separate formal recommendation on its own

What it is for: Provides setting specific information to enhance implementation

Informal recommendations

Definition: An informal recommendation is an actionable statement about the choice of one or more intervention options in a specific population and, if relevant, in a specific setting. These statements were not issued following a formal deliberative process, do not directly link to the bodies of evidence assembled for the guideline, and do not fulfill the rigorous set of logical rules identifying good practice statements.

Explanation and notes: Alternative option(s) (i.e. comparator(s)) may be specified in the recommendation if they are not self-evident. Informal

recommendations may be informed by evidence but lack a clear and transparent link to that evidence or are not the result of a structured or coordinated process, e.g. a systematic review, for developing recommendations. If the direct link between the evidence and the recommendation is missing, this type of recommendation can be mis-interpreted as having resulted from a deliberative, structured and transparent process when this was not so. Thus, they may assume the informative power of a formal recommendation which is not justified. Furthermore, to distinguish informal recommendations from good practice statements, the large net desirable consequences of the recommended options are either not obvious without completing a formal process (the opposite course of action is not considered inappropriate) or the indirect evidence supporting large net desirable consequences is not described. A question that can be answered with a formal recommendation should not be addressed with an informal one. Informal recommendations should not be regarded as evidence-based because they are typically not based on a trustworthy evidence synthesis (in which case they would be a formal recommendation). A highly credible evidence-based guidelines should be able to completely avoid informal recommendations

What it is: It is an actionable statement about the choice of one or more management or policy options (intervention) in a specific population and, if relevant, in a specific setting.

What it is not: It is not a proper recommendation because it was not formally deliberated upon and/or it has not an explicit and direct link to formally reviewed and appraised systematic bodies of evidence and it does not fulfill criteria for a good practice statement.

What it is for: It should not be used for decision making without additional scrutiny such as a review of the related systematically reviewed evidence.

3.2. Describing the relationship between the different types of statements in a guideline

Fig. 1 depicts the relationships between formal recommendations, good practice statements, research only recommendations, remarks, implementation considerations, tools and tips and informal recommendations. Beginning with any actionable guidance found in the text of a guideline, the degree of information included, the link to evidence and the degree to which the evidence was considered in a structured process by guideline developers (graded or not), it classifies the types of actionable statements and remarks. Along with the definitions, this framework helps to distinguish, classify and

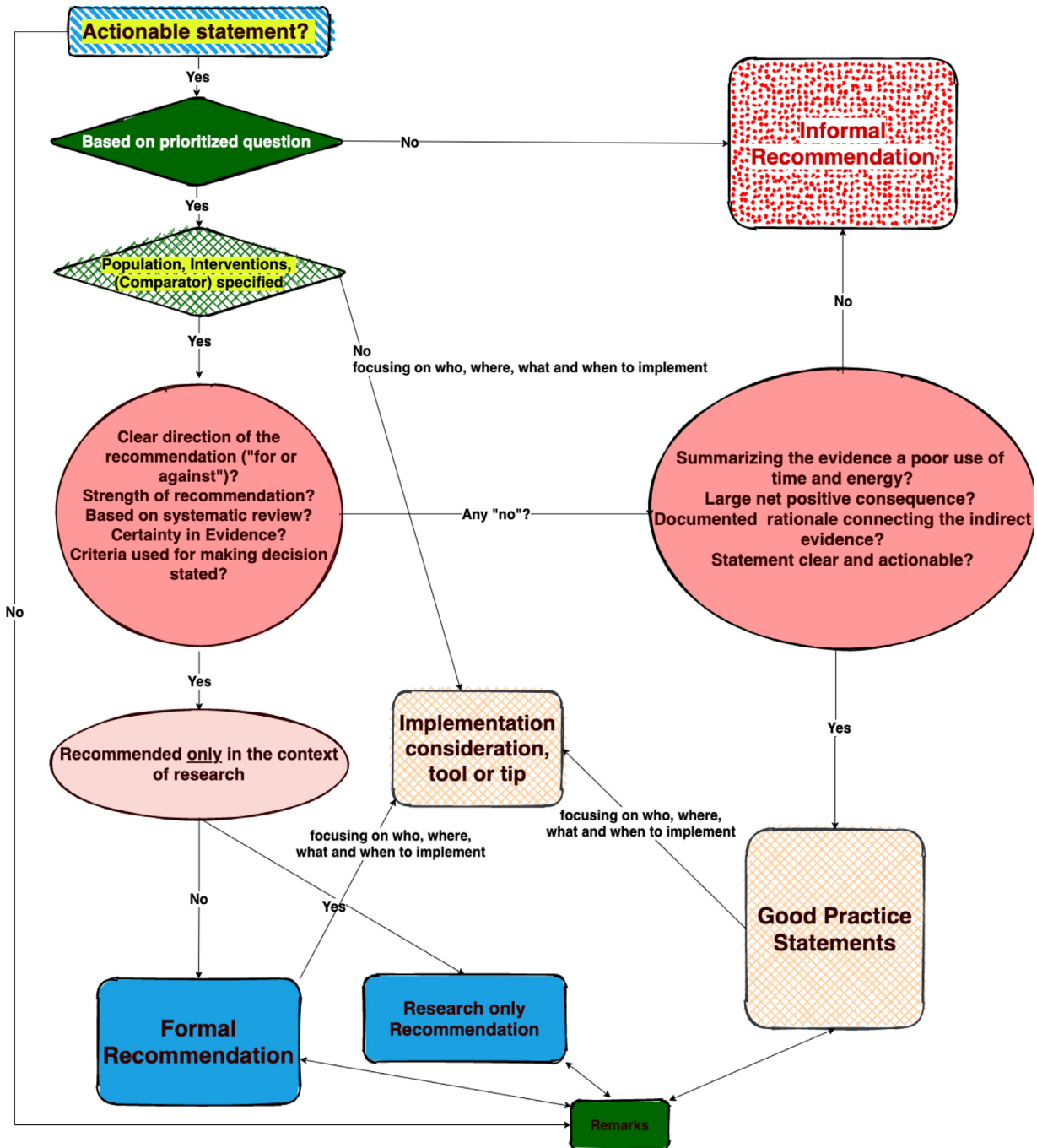


Fig. 1. Relationship between different types of actionable statements and remarks contained in guidelines.

present statements when developing, using or evaluating a guideline. Table 1 summarizes the components of the different types of actionable statements and remarks in guidelines.

3.3. Application of the Conceptual Framework

We present our analysis of the text surrounding these PICO questions and the related statements and extracted, classified, and justified judgments in Appendix C.

4. Discussion

4.1. Summary of findings

Formal recommendations are the key outputs of a guideline, and although they are the central aim of guideline development, additional types of statements about good practice, research only recommendations or implementation considerations, tools and tips are necessary to clarify, support or complement them. We describe a unifying framework for the identification

Table 1. Summary of components by statement

Type	Actionable	Population component	Intervention component	Comparator component***	Strength	Direction	Certainty in the evidence	Supported by SRs/HTAs
<i>Desirable statements</i>								
Formal recommendation	+	+	+	+	+	+	+	+
Remark*	-	±	±	±	-	-	-	-
Research only recommendations**	+	+	+	±	±	±	+	±
Good Practice Statement****	+	+	±	±	-	±	-	Possibly for linked evidence
Implementation considerations, tools and tips ***	+	±	±	-	-	-	-	±
<i>Undesirable statements</i>								
Informal recommendation	+	+	+	±	±	±	-	-

* should accompany recommendation, cannot be published alone

**Only applicable in research setting

***should be inseparable from recommendation as important for the recommendation's interpretation and implementation

****Refer to Box 2 for criteria

(+): present; (-): absentApplication of the Conceptual Framework

and presentation of statements that accompany formal recommendations: remarks, research recommendations, good practice statements, implementation considerations, tools and tips and informal recommendations. We have supported our findings with examples which were derived from randomly selected WHO TB guidelines, ASH and a random sample of global COVID-19 recommendations. The key contribution is the recognition of the existence of informal recommendations in typical guidelines and clear definitions of other actionable statements.

As many guidelines are produced by organizations that do not have to adhere to specific legislation or rules and often are the result of professional desire to offer advice, informal recommendations can appear ubiquitously throughout the text of guidelines and accompanying publications, as well as in supporting tables. Our framework invites guideline developers to recognize the differences between informal recommendations and other types of actionable statements. Their mere inclusion suggests that informal recommendations require prioritization for appropriate development or, in some circumstances, may be classified as good practice statements or implementation considerations, tools or tips. The setting in which the statements are developed might affect the rigorousness of development. For example, the COVID-19 pandemic required urgent guideline development. However, despite this urgency guiding principles for trustworthy guidelines should be adhered to [30–32].

While the different types of statements play a role in providing comprehensive guidance, the role and degree of methodological rigor behind their conception, the weight

they carry, and their standardized presentation in a guideline, differ and should thus be clearly differentiated. Our framework helps users identify and structure the various types of statements, and assists guideline developers in identifying and encouraging the use of formal recommendations or good practice statements wherever possible. This seeks to avoid the associated risks of injudicious use of informal recommendations by those who may not readily be able to distinguish between formal and informal recommendations.

Whilst the definitions of guideline statements proposed in our taxonomy use formal recommendations as the key actionable statement type, guideline writers may also wish to include additional explanatory information that contains pertinent population, intervention and comparison details. This information can be provided in remarks, footnotes or glossaries that elaborate on any of the PICO elements and should be considered as an extension or supplement of the formal recommendation rather than a separate type of statement such as implementation considerations, tools and tips.

4.2. Strengths and limitations

The strength of this work comes from the diversity of guidelines consulted, the range of topics and settings examined and the use of examples. Guidelines issued by the WHO TB programme, and ASH provide reliable, evidence-based, and transparently developed recommendations to provide pragmatic guidance for health systems, clinical and public health practice. This ensured a solid

base upon which to develop the draft taxonomy. Applying this draft framework to COVID-19 guidelines presents another strength, as these guidelines have been developed under considerable resource and time pressures and provide a particularly robust scenario in which to test the taxonomy. Further, the inclusion of a large group of methodologists and care providers with extensive experience in guideline development, research methods, and epidemiology adds relevance to this work. As with any narrative analysis, there is a risk of bias in the conclusions drawn, reflective of the notions held by participants. We believe the breadth of recommendations offered by the WHO TB department (prevention, treatment, policy, etc.), the ASH and the various COVID-19 recommendations considered, address some of the applicability concerns of our findings to other guidelines.

4.3. Context to other findings

Our work is relevant to how semantic material within a guideline is classified. For example, Shiffman et al developed the Guideline Elements Model (GEM) in 2000, as a framework for digitally organizing the heterogeneous material that can be found in guidelines [33]. They identified three high-level knowledge components in the hierarchy of elements used in GEM. These are recommendations, definitions, and algorithms. Based on our work, good practice statements, implementation considerations, remarks, and if present, informal recommendations are additional elements of guidelines that require explicit labelling and identification.

4.4. Implications for policy and practice

The proposed framework provides a way to identify the type and purpose of actionable statements that appears in a guideline so that users and implementers can better assess the credibility and evidence-base of the recommendations they relate to. Wherever possible, guideline developers should aim to produce formal recommendations with the accompanying supporting evidence and development process rigor clearly documented. Remarks, should, when appropriate, be published, alongside any formal recommendation(s), with a clear reference to direct or indirect linked evidence. Guideline developers can use the checklist in **Box 3** to identify informal recommendations they have potentially developed and thus seek to avoid their use in future guidelines whenever possible. “They should follow the approaches for developing the other, more acceptable, actionable statements, e.g. by following the five criteria for good practice statements and describing how they are fulfilled. If they describe an actionable statement as an implementation consideration, they should link it to a recommendation and generate it as accompanying information rather than a statement of its own.”

Box 3 Characteristics of actionable statement that constitute informal recommendations

- The actionable statement lacks a clear description of the population, intervention and comparison elements that are consistent with the guideline question.
- The actionable statement does not result from a deliberative, structured and transparent process for developing recommendations.
- The actionable statement does not have a clear relation to relevant systematically reviewed evidence (e.g. it may only cite selected or no evidence).
- The criteria that lead from the evidence, or lack thereof, to the recommendation are not clear.
- The statement would be more appropriate and informative as a good practice statement by following the five principles for good practice statements (should be checked against the five criteria for a good practice statement, and if it fits all of them, should be issued as such).

Our guidance also provides suggestions (in the “Implementation considerations, tools and tips” section) for guideline derivative products, such as operational guides and implementation manuals, which should always be linked to the original guideline they supplement. The GRADE Working Group suggests that these components of the guideline recommendation are integrated into the implementation considerations of an Evidence to Decision-making (EtD) framework to ensure they remain linked to the relevant recommendations even if these derivative products are developed after the formal recommendation is made and published [4]. As guidelines progress toward digital, computable, and living publications, a framework is needed to identify and classify additional actionable guidance that is published in these modes. .

4.5. Implications for research

We suggest that others test our framework in their work. Prospective application and evaluation of our guidance for developing actionable statements and avoiding informal recommendations may further refine this guidance. For example, our current work on the eCOVIDRecMap (<https://covid19.recmap.org>) has revealed that existing guidance for good practice statements within many organizations does not allow for their proper identification and/or that guideline developers do not follow the existing definitions or criteria for good practice statements. ((25) and Dewidar et al, in preparation) We will, therefore, work with the GRADE Working Group to provide guidance on how to further develop information pertaining to good practice statements. The framework and the classification of guideline state-

ments will be applied within the forthcoming European Commission Initiative on Colorectal Cancer (ECICC) for the development of evidence-based guidelines on colorectal cancer prevention, screening and diagnosis, this will be a good opportunity for testing and refinement. This may reveal further insights and assist to validate the framework.

6. Conclusion

The occurrence of statements that accompany recommendations in guidelines and related publications can impact the issued guidance by presenting additional actionable information that has not been properly developed or do not belong to one of the described categories. The identification of these statements is a prerequisite to their management. This framework provides guidance for clear, transparent and practical presentation and use of high-quality actionable statements. Further, the classification of guideline statements, and an understanding of what elements constitutes each, paves the way for standardization of how they are written and presented. The application of this framework should inform and improve future guideline development, usage and uptake.

Author contributions

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.jclinepi.2021.09.028](https://doi.org/10.1016/j.jclinepi.2021.09.028).

References

- [1] Cochrane Collaboration. PICO Ontology. Cochrane Collaboration Linked Data 2021 <https://linkedata.cochrane.org/pico-ontology>, [Accessed 30 May 2021].
- [2] Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol.* 2013;66(7):719–25.
- [3] Alonso-Coello P, Oxman AD, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. *BMJ* 2016;353:i2089.
- [4] Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach

- to making well informed healthcare choices. 1: Introduction. *BMJ* 2016;353:i2016.
- [5] Qaseem A FF, Macbeth Fergus, Ollenschläger Phillips, S P vdW. Guidelines international network: toward international standards for clinical practice guidelines. *Ann Intern Med.* 2011;156:525–31.
 - [6] Shekelle P, Woolf S, Grimshaw JM, Schunemann HJ, Eccles MP. Developing clinical practice guidelines: reviewing, reporting, and publishing guidelines; updating guidelines; and the emerging issues of enhancing guideline implementability and accounting for comorbid conditions in guideline development. *Implement Sci.: IS* 2012;7:62.
 - [7] Schunemann HJ, Wiercioch W, Etzeandia I, Falavigna M, Santesso N, Mustafa R, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. *Can Med Assoc J.* 2014;186(3):E123–42.
 - [8] Schunemann HJ, Best D, Vist G, Oxman AD, Group GW. Letters, numbers, symbols and words: how to communicate grades of evidence and recommendations. *Can Med Assoc J.* 2003;169(7):677–80. *CMAJ.*
 - [9] Oxman AD, Fretheim A, Schunemann HJ. Improving the use of research evidence in guideline development: introduction. *Health Res Policy Syst* 2006;4:12.
 - [10] Guyatt GH, Alonso-Coello P, Schunemann HJ, Djulbegovic B, Nothacker M, Lange S, et al. Guideline panels should seldom make good practice statements: guidance from the GRADE Working Group. *J Clin Epidemiol.* 2016;80:3–7.
 - [11] Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011;64(4):383–94.
 - [12] Schunemann HJ, Wiercioch W, Brozek J, Etzeandia-Ikobaltzeta I, Mustafa RA, Manja V, et al. GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: Grade-Adolopment. *J Clin Epidemiol.* 2017;81:101–10.
 - [13] World Health Organization. Available from: https://tuberculosis.evidenceprime.com/recommendation/WHO_CDS_TB_2020_72_9.
 - [14] World Health Organization. Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. 2009. Accessed on 30 May 2021.
 - [15] World Health Organization. WHO treatment guidelines for isoniazid-resistant tuberculosis: supplement to the WHO treatment guidelines for drug-resistant tuberculosis. 2018. Accessed on 30 May 2021.
 - [16] Wiercioch W, Nieuwlaat R, Akl EA, Kunkle R, Alexander KE, Cuker A, et al. Methodology for the American society of hematology VTE guidelines: current best practice, innovations, and experiences. *Blood Adv* 2020;4(10):2351–65.
 - [17] World Health Organization. WHO Handbook for guideline development: World Health Organization 2014.
 - [18] Izcovich A, Cuker A, Kunkle R, Neumann I, Panepinto J, Pai M, et al. A user guide to the American society of hematology clinical practice guidelines. *Blood Adv* 2020;4(9):2095–110.
 - [19] Monagle P, Cuello CA, Augustine C, Bonduel M, Brandao LR, Capman T, et al. American Society of hematology 2018 guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism. *Blood Adv* 2018;2(22):3292–316.
 - [20] Christof C, Nussbaumer-Streit B, Gartlehner G. WHO Guidelines on Tuberculosis Infection Prevention and Control. *Gesundheitswesen (Bundesverband der Ärzte des Öffentlichen Gesundheitsdienstes (Germany))* 2020.
 - [21] World Health Organization Management of physical Health conditions in Adults with Severe mental disorders: WHO guidelines. World Health Organization. 2018. <https://apps.who.int/iris/bitstream/handle/10665/275718/9789241550383-eng.pdf>, [Accessed 30 May 2021].
 - [22] World Health Organization WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders. World Health Organization. 2012. https://apps.who.int/iris/bitstream/handle/10665/44789/9789241503006_eng.pdf?sequence=1, [Accessed 30 May 2021].
 - [23] World Health Organization. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB. World Health Organization 2013. Report No.: 9241506334. https://apps.who.int/iris/bitstream/handle/10665/112472/9789241506335_eng.pdf?sequence=1&isAllowed=y, [Accessed 30 May 2021].
 - [24] World Health Organization Treatment of tuberculosis: guidelines: World Health Organization. World Health Organization 2010. https://apps.who.int/iris/bitstream/handle/10665/44165/9789241547833_eng.pdf?sequence=1, [Accessed 30 May 2021].
 - [25] Lotfi T, Stevens A, Akl EA, Falavigna M, Kredo T, Mathew JL, et al. Getting trustworthy guidelines into the hands of decision-makers and supporting their consideration of contextual factors for implementation globally: recommendation mapping of COVID-19 guidelines. *J Clin Epidemiol.* 2021.
 - [26] Andrews JC, Schunemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol.* 2013;66(7):726–35.
 - [27] Witt DM, Nieuwlaat R, Clark NP, Ansell J, Holbrook A, Skov J, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Adv.* 2018;2(22):3257–91.
 - [28] Witt DM, Nieuwlaat R, Clark NP, Ansell J, Holbrook A, Skov J, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Adv.* 2018;2(22):3257–91.
 - [29] Schunemann HJ, Cushman M, Burnett AE, Kahn SR, Beyer-Westendorf J, Spencer FA, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. *Blood Adv* 2018;2(22):3198–225.
 - [30] Akl EA, Morgan RL, Rooney AA, Beverly B, Katikireddi SV, Agarwal A, et al. Developing trustworthy recommendations as part of an urgent response (1-2 weeks): a GRADE concept paper. *J Clin Epidemiol.* 2021;129:1–11.
 - [31] Munn Z, Twaddle S, Service D, Harrow E, Okwen PM, Schunemann H, et al. Developing guidelines before, during, and after the COVID-19 pandemic. *Ann Intern Med* 2020;173(12):1012–14.
 - [32] Schunemann HJ, Santesso N, Vist GE, Cuello C, Lotfi T, Flottorp S, et al. Using GRADE in situations of emergencies and urgencies: certainty in evidence and recommendations matters during the COVID-19 pandemic, now more than ever and no matter what. *J Clin Epidemiol.* 2020;127:202–7. doi:10.1016/j.jclinepi.2020.05.030.
 - [33] Shiffman RN, Karras BT, Agrawal A, Chen R, Marengo L, Nath S. GEM: a proposal for a more comprehensive guideline document model using XML. *J Am Med Inform Assoc* 2000;7(5):488–98.