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Study protocol

Project Protocol for AGREE II Extension for Guidelines in Surgery

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ABSTRACT

Introduction AGREE II is an instrument that informs development, reporting and assessment of clinical practice guidelines. Previous research has demonstrated the need for improvement in methodological and reporting quality of clinical practice guidelines specifically in surgery. We aim to develop an AGREE II extension document for application in surgical guidelines.

Methods and analysis We have performed a structured literature review and assessment of guidelines in surgery using the AGREE II instrument. In exploratory analyses, we have identified factors associated with guideline quality. We have performed reliability and factor analyses to inform the development of an extension document. We will summarize this information and present it to a Delphi panel of stakeholders. We will perform iterative Delphi rounds and we will summarize the final results to develop the extension instrument in a dedicated consensus conference.

Ethics and dissemination Funding bodies will not be involved in the development of the instrument. We will request board approval by Northern Care Alliance NHS Group, UK. Conflicts of interest, if any, will be addressed by re-assigning functions or replacing participants with relevant conflicts.

KEYWORDS

AGREE II; clinical practice guideline; reporting quality; development; methodology; EQUATOR Network

STRENGTHS AND LIMITATIONS

- This is the first project to address guideline development and reporting in surgery.
- It will combine statistical considerations, conceptual parameters to be derived from qualitative synthesis and a formal Delphi process.
- It will involve a panel of stakeholders from a variety of scientific, cultural and geographical backgrounds.
- The project will not address specific disciplines of surgery.

INTRODUCTION

Research evidence is the primary source to inform medical practice forming the cornerstone of evidence-based medicine.[1] An average of 5,639 new articles were indexed per month under the subject heading 'Surgery' in the National Library of Medicine over the past decade.[2] Given this fact, keeping abreast of the latest evidence is a strenous task for healthcare practitioners. Clinical practice guidelines evaluate, summarize and contextualize research evidence into actionable recommendations.[3] As such, guidelines have a direct impact on delivery of healthcare and surgical services. It is therefore of paramount importance to ensure the highest quality standards in developing and reporting guidelines.

A great amount of scientific endeavor in the past few years has focused on the quality of scholarly work, including clinical practice guidelines.[4] Reporting standards have been developed for virtually all study designs and have been summarized by the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) Network.[5] AGREE II (Appraisal of Guidelines for Research and Evaluation) constitutes a framework for developing, appraising and reporting clinical practice guidelines.[6] It is endorsed by major international and national agencies, including the World Health Organization and the National Institute for Health and Care Excellence (NICE) in the United Kingdom.[7,8] AGREE II is a generic tool that applies to all disciplines of medicine and no modification or extension of the framework has been proposed, described or developed for specific clinical branches such as surgery.

The tool is comprized of 23 items organized in 7 thematic domains: Scope and purpose, Stakeholder involvement, Rigor of development, Clarity of presentation, Applicability, and Editorial independence. It concludes with an overall

assessment and a statement of whether the guideline is considered of sufficient quality to be used or recommended in clinical practice **(Appendix)**.

The need for an AGREE II extension

Our research group has acted as methodological and content coordinators of landmark surgical guidelines and have served as members of surgical guideline development groups.[9,10,11,12,13,14] Even though members of our group, in their role as guideline developers, have made every effort to comply with the highest methodological standards, as indicated by adherance to GRADE (Grading of Recommendations Assessment, Development and Evaluation) and AGREE II methodologies,[15,16] we noticed that compliance with all aspects of several parameters of the AGREE II instrument was not possible. For example, the item "The potential resource implications of applying the recommendations have been considered" may be difficult to be universally addressed, because cost-effectiveness studies are scarce in the surgical literature and relevant evidence typically varies in different settings.[17] We have hypothesized that the original AGREE II document may not be applicable to clinical practice guidelines in surgery, which ofter represent complex and multifaceted interventions.

Objective

There are a few guideline reporting documents in other fields of medicine,[18,19] however a scoping literature review by our group has not identified any document to inform guideline development and reporting in the field of surgery. Our aim is to

develop an extension of the AGREE II instrument that is specific for surgery through an evidence-informed and consensus-based approach.

METHODS

We have formed an international multi- and inter-disciplinary collaborative research working group, that consists of surgeons, guideline developers, evidence synthesis experts, GRADE methodologists,[20] biostatisticians and a lead member of the AGREE collaboration. This is a tripartite project named *Guideline Assessment Project: Filling the GAP in Surgical Guidelines*. A summary of the project is outlined in **Fig. 1**.

This protocol complies with the Guidance for Developers of Health Research Reporting Guidelines.[21]

- *GAP I Project: Literature review and exploratory analyses*

We have previously performed a structured review to identify clinical practice guidelines in the field of surgery published over a 10-year period.[22] We have assessed the methodological and reporting quality of the selected guidelines using the original AGREE II criteria. Domain scores (calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain)[16] ranged between 0-56%, suggesting generally inadequate and highly variable guideline quality. The median overall score was 4 out of a maximum of 7, and 40% of guidelines were not considered suitable for use based on their quality as assessed using the AGREE II instrument.

In exploratory analyses, we have found guidelines produced by surgical organizations with a high (≥1 guideline per year) output (odds ratio 3.79, 95%

confidence interval, 1.01–12.66) and those produced by surgical organizations with a guideline committee (odds ratio 4.15, 95% confidence interval, 1.47–11.77) have higher odds of reaching sufficient quality and being recommended for use.[22]

- *GAP II: Statistically calibrating the AGREE II instrument*

The second part of this project was focused on statistical calibration of the AGREE II instrument. We employed a series of statistical methods to explore reliability, internal consistency and unidimensionality of the AGREE II instrument. We investigated the internal consistency that refers to the extent to which all items of the instrument measure the same hypothetical construct. We explored if and how test items are intercorrelated. Large intercorrelations among test items are indicative of the items measuring the same construct. Using reliability analysis, Kendall's tau statistics, factor analysis and the item response theory, we explored whether items of each AGREE II domain are intercorrelated and are, therefore, indicators of the same construct. We have finally drafted a modified AGREE II document for guidelines in surgery, on the basis of the outcomes of statistical models.

- *GAP III: AGREE II Extension for Surgical Guidelines*

The third part of the project aims to use the information from the previous GAP projects and other published information on the topic to develop the extension document using a structured Delphi process involving relevant stakeholders.

The multidisciplinary Delphi panel will include surgical specialists, journal editors, guideline development bodies, GRADE representatives, and patient

representatives. Under consideration of the evidence, stakeholders will be asked to provide their input through a Delphi process, which will inform the preparation of an AGREE II extension for surgical guidelines.

Funding

This third part of the project is funded by United European Gastroenterology and the European Association for Endoscopic Surgery. The funding bodies did not have any influence on the previous work and will not have influence on the upcoming process.

Participants

The executive group consists of surgeons (MLC, SRM, GS, GAA, NKF, SAA), members of surgical quality and research boards (MLC, NKF, SAA), guideline developers (MLC, IF, MB, GS, NKF, SAA), evidence synthesis experts (IF, GAA, DM, SAA), GRADE methodologists (MLC, SAA),[20] biostatisticians (DM, ST), and 2 leads of the AGREE Group (IF, MB). It is further divided into 4 working groups with distinct functions and responsibilities:

- The strategic steering group is responsible for overseeing the project.
- The methods group coordinates the methodology of the project.
- The evidence review group will review the literature for evidence on candidate new items to be included in the extension document.
- The evidence synopsis group will summarize evidence for presentation to Delphi participants.

The group attended a one-day meeting to discuss the findings of previous work, define the methodology and study design, and identify potential stakeholder groups to comprise the Delphi panel.

Delphi process

The Delphi panel will consist of key stakeholders, including; representatives from different surgical disciplines (general surgery, urology, thoracic surgery, vascular surgery, pediatric surgery), guideline developers from different continents and representatives of guideline development organizations. The public will be involved by participation of patient representatives from the European Patients Forum **(Table 1)**. We will develop a web-based survey tool to facilitate Delphi exercises. Findings of previous work (GAP I and GAP II) and further evidence that will be identified through a scoping literature review will be summarized and presented to Delphi participants. Summary information will also be available on the project website at https://gap-project.org. Online links to full documents for detailed review of the evidence will be provided.

The first round will include open-ended questions to identify candidate items for inclusion in the extension document. Responses will be grouped and summarized by the methods group before the second round is commenced.

The second round will include closed-ended questions in a numeric Likert scale to assess participants' opinions and level of agreement on including candidate items or excluding existing items from the extension document. Candidate items will have been identified through GAP I and GAP II, and the scoping literature review. We will discard low-scoring items and use the shortlisted items in a third Delphi round.

We will repeat the process until new information reaches saturation and consensus with an alpha level of 0.8.

The Delphi panel's contribution will be acknowledged by group authorship in subsequent publications of the extension document, the elaboration document and supporting tools.

Qualitative synthesis

We will perform qualitative evidence synthesis to identify factors of conceptual importance to the quality of evidence in surgery. Furthermore, we will survey users of social media to nominate parameters of importance in the development and reporting of guidelines in surgery, and will group and summarize their responses. Evidence identified from the above pathways, along with information from GAP I and GAP II will be summarized and taken into account when developing the extension document.

Consensus meeting

Following the Delphi process, the executive group will meet to discuss the findings and compose the first draft of the extension document. We will present new items that will be identified through the Delphi exercise and the qualitative synthesis, and discuss their plausibility and possible inclusion in the instrument. Similarly, items to be excluded with the respective rationale will be discussed. The group will finalize the extension document by ordering and allocating items into domains.

The executive group will hold a further meeting with the advisory group that is comprised of journal editors and representatives of surgical associations to discuss

dissemination and implementation processes of the developed extension instrument.

Pilot-testing and assessment of internal validity

The extension instrument will be pilot-tested by 2 members of the executive group. One member will apply the instrument on the surgical guidelines which were identified by the structured search process as described in GAP I[22] and on additional guidelines that will be identified by extending the search to the present date. A second member will independently follow the same process in a randomly selected sample of 15 guidelines. The biostatistical team will assess the internal validity by applying the statistical models of GAP II. Any difficulties encountered with the use of the instrument will be documented and addressed. Results of the statistical assessment will be appraised against statistical findings of the appraisal of the original AGREE II instrument (GAP II).

AGREE II Extension Statement

The extension statement along with an explanation and elaboration (E&E) document will be composed by the executive group. The E&E document will detail the use of the extension instrument in developing and reporting a new surgical guideline and appraising an existing surgical guideline.

AGREE II Extension Checklist

A checklist including the AGREE II Extension items will be developed with the aim of this checklist to be used by guideline developers (to summarize development and

reporting parameters), guideline users (to appraise quality), peer reviewers and journal editors (to assess adequacy of reporting parameters).[23]

Publication and dissemination strategy

We will submit the final paper with the extension document to be considered for publication in the UEG Journal and Surgical Endoscopy, as defined in the respective pre-development agreements. We will negotiate simultaneous publications in other surgical journals for widest dissemination as recommended by the Guidance for Developers of Health Research Reporting Guidelines.[21]

We will make the extension document available in a dedicated website with links to the original publications. We will encourage surgical organizations with guideline development activities to use the instrument. We will further pursue dissemination through the websites of the funding bodies and channels of social media of major stakeholers, such as the Guideline International Network, GRADE and EQUATOR.

Through direct contact, we will advise international surgical and guideline development organizations, and policymakers to endorse the extension instrument. Furthermore, editors of surgical journals will be advised to provide an extension instrument checklist that authors of clinical practice guidelines should submit along with the original manuscript.

Feedback and criticism

We will invite constructive feedback on the instrument through the dedicated website (https://gap-project.org) and we will consider comments in letters to the

editor and via the social media. An ad hoc team will collect and summarize the feedback received in 3-monthly intervals for the first year after publication, and the executive group will discuss and address this information in web-based meetings.

Monitoring, update and future steps

The executive group will monitor the use of the extension document and appraise its applicability in surgical guidelines for a reasonable period of time after dissemination and will publish their findings. Following consideration of the outcomes, feedback, criticism, suggestions and new evidence in the field, we will discuss the need for an update. The development of further extension instruments for national surgical guidelines and guidelines in distinct surgical or other interventional disciplines will be considered following discussions with key stakeholders.

DISCUSSION

Implications for practice and research

Clinical practice guidelines directly impact clinical practice and healthcare delivery and, as such, development must follow rigorous methodological and reporting standards. The AGREE II instrument has been designed as a generic tool for development and appraisal of clinical practice guidelines.[6] It is not intended to substitute established detailed guidance on guideline development principles, processes and procedures, such as the GRADE approach.[15] It has addressed a vital need to summarize and detail essential development steps and reporting parameters for high quality guidelines. Furthermore, as an appraisal instrument, it

may be used by healthcare practitioners, policymakers and other stakeholders to inform decisions regarding the use of an existing guideline.

In addition, AGREE II has been shown to be a valuable tool for assessment of guideline quality in several clinical disciplines and evidence fields.[22,24,25,26,27,28,29,30,31,32] Such summaries alert the scientific community to the need for improving specific aspects of clinical practice guidelines (corresponding to the instrument domains) or the overall quality of guidelines. Our previous research has highlighted the need for improvement of the quality of surgical guidelines.[22] An AGREE II extension for surgical guidelines is expected to meet this need.

The outcome of this project will be the first AGREE II extension document. RIGHT (Reporting Tool for Practice Guidelines in Health Care) is another reporting instrument for clinical practice guidelines.[33] We are aware of a planned RIGHT extension for public versions of guidelines and a RIGHT extension for adapted practice guidelines.[34,35] An extension document of RIGHT for surgical guidelines would be justified as well. However, in view of the evidenced gap in methodological quality of surgical guidelines,[22] we considered more appropriate to elaborate on AGREE II, as it addresses guideline development, reporting and appraisal.

Strengths and limitations

This tripartite project is the first to employ statistical models to inform the validity of an extension, modification or update document on guidelines reporting. We will correlate statistical findings with conceptual considerations of the need for adjustments/extension of the AGREE II instrument. The project methods group has adopted recommendations on developing research reporting guidelines, proposed

by a collaborative team who have developed a significant number of such guidelines.[21] The holistic approach to developing an extension document for clinical practice guidelines in surgery is reflected in the diverse scientific, cultural and geographical background of experts in the field involved in the project. Similarly, the Delphi panel will include stakeholders and members from a variety of backgrounds including clinicians/surgeons, methodologists, guideline developers, policy makers and the public (patient representatives).

A face-to-face meeting of Delphi participants, instead of a full web-based Delphi process, might be more efficacious in developing the extension document allowing direct exchange of opinions, information and ideas. We will encourage a full participation and exchange of information by developing a user-friendly and interaction-allowing web-based platform. Furthermore, we will incentivize participation and engagement of potential Delphi members by proposing group authorship and participation in future associated projects.

Research ethics

The executive group will seek Institutional Review Board approval by Northern Care Alliance NHS Group, UK We will request electronic informed consent from Delphi participants and the responses of the Delphi members will be anonymized.

We have obtained conflict of interest forms of all executive group members and will request electronic and/or written informed consent by Delphi participants and members of the advisory group. We will deal with potential conflicts of interest by re-assigning functions or replacing participants who pose interest conflict.

CONCLUSION

The GAP III study aims to address the need for improvement of the methodology, reporting and appraisal of surgical guidelines. An extension document specifically designed for clinical practice guidelines in surgery will further improve the value, use and applicability of the AGREE II instrument in the surgical field with the ultimate goal of enhancing patient care, experience and outcomes.

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FIGURE LEGEND

Fig. 1: Development steps of the Guideline Assessment Project with the ultimate objective to develop an AGREE II extension document for surgical guidelines

549 **Table 1.** Stakeholders to participate in a web-based Delphi process

550

Function
General Surgeon
Urologist
Thoracic Surgeon
Vascular Surgeon
Pediatric Surgeon
Journal Editor
National authority representative
NICE representative
Guideline developer/Representative from Europe
Guideline developer/Representative from North America
Guideline developer/Representative from Asia
Guideline developer/Representative from middle-income country
Healthcare provider representative
Representative from GRADE
Guideline implementer
Patient representative
WHO representative
European Commission representative
GIN representative
EQUATOR representative
NICE: National Institute of Health and Care Excellence GRADE: Grading of Recommendation Assessment, Development and Evaluation WHO: World Health Organization GIN: Guidelines International Network EQUATOR: Enhancing the QUAlity and Transparency Of health Research

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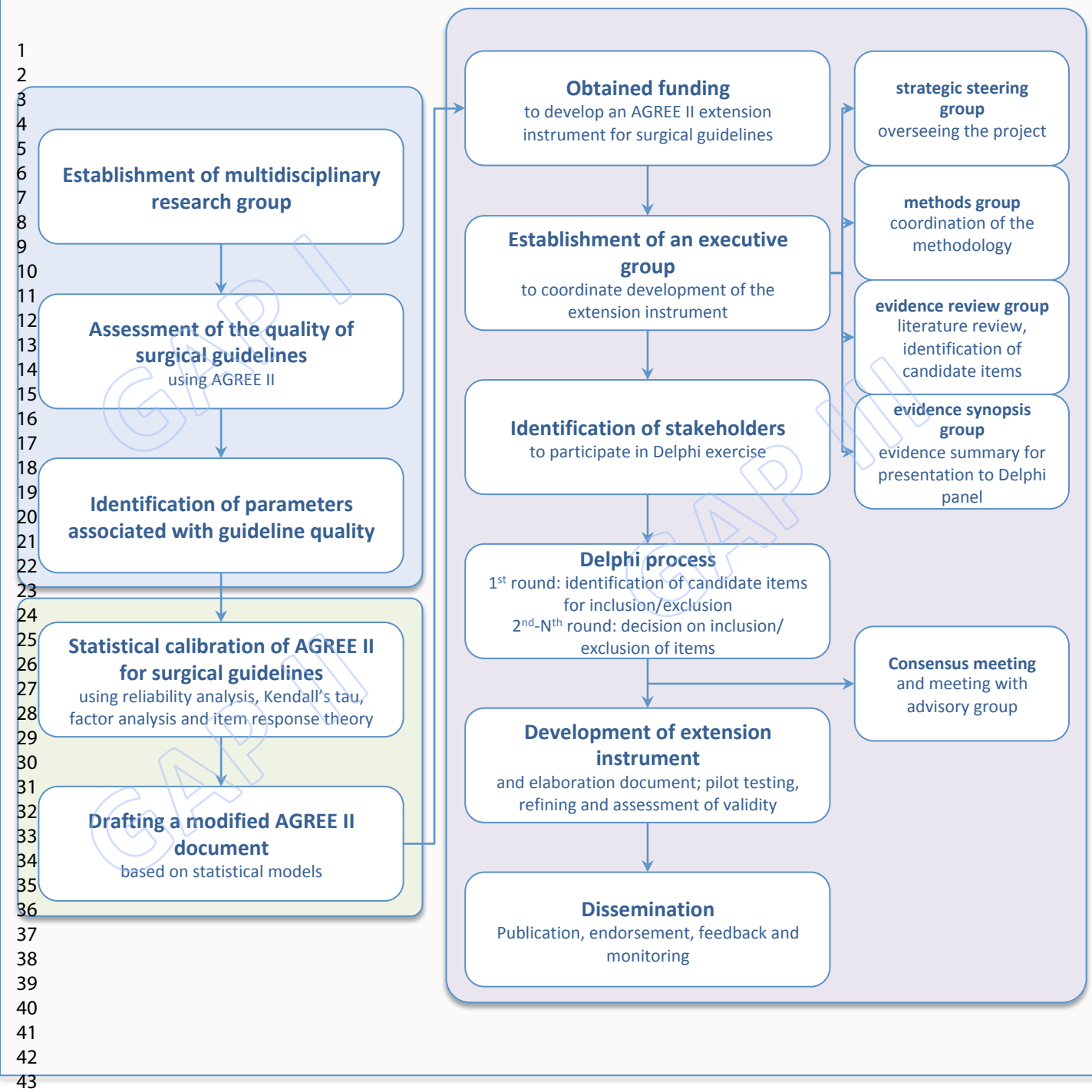
Establishment of multidisciplinary research group
Assessment of the quality of surgical guidelines
using AGREE II
Identification of parameters associated with guideline quality
Statistical calibration of AGREE II for surgical guidelines
using reliability analysis, Kendall's tau, factor analysis and item response theory
Drafting a modified AGREE II document
based on statistical models
Obtained funding
to develop an AGREE II extension instrument for surgical guidelines
Establishment of an executive group
to coordinate development of the extension instrument
Identification of stakeholders
to participate in Delphi exercise
Delphi process
1st round: identification of candidate items for inclusion/exclusion
2nd-Nth round: decision on inclusion/ exclusion of items
Development of extension instrument
and elaboration document; pilot testing, refining and assessment of validity
Dissemination
Publication, endorsement, feedback and monitoring
strategic steering group
overseeing the project
methods group
coordination of the methodology
evidence review group
literature review, identification of candidate items
evidence synopsis group
evidence summary for presentation to Delphi panel
Consensus meeting
and meeting with advisory group

APPENDIX

The AGREE II instrument

Adapted from: Brouwers MC, Kerkvliet K, Spithoff K. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. *BMJ*. 2016:i1152.

Domains	Items	Assessment*
I. Scope and purpose	1. The overall objective(s) of the guideline is (are) specifically described.	1 to 7
	2. The health question(s) covered by the guideline is (are) specifically described.	1 to 7
	3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	1 to 7
II. Stakeholder involvement	4. The guideline development group includes individuals from all relevant professional groups.	1 to 7
	5. The views and preferences of the target population (patients, public, etc.) have been sought.	1 to 7
	6. The target users of the guideline are clearly defined.	1 to 7
III. Rigor of development	7. Systematic methods were used to search for evidence.	1 to 7
	8. The criteria for selecting the evidence are clearly described.	1 to 7
	9. The strengths and limitations of the body of evidence are clearly described.	1 to 7
	10. The methods for formulating the recommendations are clearly described.	1 to 7
	11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	1 to 7
	12. There is an explicit link between the recommendations and the supporting evidence.	1 to 7
	13. The guideline has been externally reviewed by experts prior to its publication.	1 to 7
	14. A procedure for updating the guideline is provided.	1 to 7

IV. Clarity of presentation	15. The recommendations are specific and unambiguous.	1 to 7
	16. The different options for management of the condition or health issue are clearly presented.	1 to 7
	17. Key recommendations are easily identifiable.	1 to 7
V. Applicability	18. The guideline describes facilitators and barriers to its application.	1 to 7
	19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	1 to 7
	20. The potential resource implications of applying the recommendations have been considered.	1 to 7
	21. The guideline presents monitoring and/or auditing criteria.	1 to 7
VI. Editorial independence	22. The views of the funding body have not influenced the content of the guideline.	1 to 7
	23. Competing interests of guideline development group members have been recorded and addressed.	1 to 7
Overall guideline assessment	24. Rate the overall quality of this guideline.	1 to 7
	25. I would recommend this guideline for use.	• Yes • Yes, with modifications • No
** 7 corresponds to the highest possible quality.*		

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Protocol of an Interdisciplinary Consensus Project Aiming to Develop an AGREE II Extension for Guidelines in Surgery

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Study protocol

Protocol of an Interdisciplinary Consensus Project Aiming to Develop an AGREE II Extension for Guidelines in Surgery

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ABSTRACT

Introduction AGREE II is an instrument that informs development, reporting and assessment of clinical practice guidelines. Previous research has demonstrated the need for improvement in methodological and reporting quality of clinical practice guidelines specifically in surgery. We aim to develop an AGREE II extension document for application in surgical guidelines.

Methods and analysis We have performed a structured literature review and assessment of guidelines in surgery using the AGREE II instrument. In exploratory analyses, we have identified factors associated with guideline quality. We have performed reliability and factor analyses to inform the development of an extension document. We will summarize this information and present it to a Delphi panel of stakeholders. We will perform iterative Delphi rounds and we will summarize the final results to develop the extension instrument in a dedicated consensus conference.

Ethics and dissemination Funding bodies will not be involved in the development of the instrument. Research Ethics Committee and Health Research Authority approval was waived, since this is a professional staff study only and no duty of care lies with the NHS (National Health Service) to any of the participants. Conflicts of interest, if any, will be addressed by re-assigning functions or replacing participants with relevant conflicts. The results will be disseminated through publication in peer reviewed journals, the funders' websites, social media, and direct contact with guideline development organizations and peer-reviewed journals that publish guidelines.

KEYWORDS

AGREE II; clinical practice guideline; reporting quality; development; methodology; EQUATOR Network

STRENGTHS AND LIMITATIONS

- This is the first project to address guideline development and reporting in surgery.
- It will combine statistical considerations, conceptual parameters to be derived from qualitative synthesis and a formal Delphi process.
- It will involve a panel of stakeholders from a variety of scientific, cultural and geographical backgrounds.
- The project will not address specific disciplines of surgery.

INTRODUCTION

Research evidence is the primary source to inform medical practice forming the cornerstone of evidence-based medicine.[1] An average of 5,639 new articles were indexed per month under the subject heading 'Surgery' in the National Library of Medicine over the past decade.[2] Given this fact, keeping abreast of the latest evidence is a strenous task for healthcare practitioners. Clinical practice guidelines evaluate, summarize and contextualize research evidence into actionable recommendations.[3] As such, guidelines have a direct impact on delivery of healthcare and surgical services. It is therefore of paramount importance to ensure the highest quality standards in developing and reporting guidelines.

A great amount of scientific endeavor in the past few years has focused on the quality of scholarly work, including clinical practice guidelines.[4] Reporting standards have been developed for virtually all study designs and have been summarized by the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) Network.[5] AGREE II (Appraisal of Guidelines for Research and Evaluation) constitutes a framework for developing, appraising and reporting clinical practice guidelines.[6] It is endorsed by major international and national agencies, including the World Health Organization and the National Institute for Health and Care Excellence (NICE) in the United Kingdom.[7,8] AGREE II is a generic tool that applies to all disciplines of medicine and no modification or extension of the framework has been proposed, described or developed for specific clinical branches such as surgery.

The tool is comprized of 23 items organized in 7 thematic domains: Scope and purpose, Stakeholder involvement, Rigor of development, Clarity of presentation, Applicability, and Editorial independence. It concludes with an overall assessment and a statement of whether the guideline is considered of sufficient quality to be used or recommended in clinical practice **(Appendix)**.

The need for an AGREE II extension

Our research group has acted as methodological and content coordinators of landmark surgical guidelines and have served as members of surgical guideline development groups.[9,10,11,12,13,14] Even though members of our group, in their role as guideline developers, have made every effort to comply with the highest methodological standards, as indicated by adherance to GRADE (Grading of Recommendations Assessment, Development and Evaluation) and AGREE II methodologies,[15,16] we noticed that compliance with all aspects of several parameters of the AGREE II instrument was not possible.

For example, the item "The potential resource implications of applying the recommendations have been considered" may be difficult to be universally addressed. Cost-effectiveness studies are scarce in the surgical literature and relevant evidence typically varies in different settings.[17] Since surgical expertise varies across countries and institutions, there is a need for the instrument to consistently apply to different healthcare settings. Surgical interventions are complex and details on the interventions/comparators are imperative for the target users to be able to assess the external validity of the guidelines. Specialists from different specialties and allied health professionals with a wide range of expertise

are involved in the treatment of surgical patients, which makes their involvement in guideline development paramount. We have hypothesized that the original AGREE II document may not be applicable to clinical practice guidelines in surgery, which ofter represent complex and multifaceted interventions.

Objective

There are a few guideline reporting documents in other fields of medicine,[18,19] however a scoping literature review by our group has not identified any document to inform guideline development and reporting in the field of surgery. Our aim is to develop an extension of the AGREE II instrument that is specific for surgery through an evidence-informed and consensus-based approach.

METHODS AND ANALYSIS

We have formed an international multi- and inter-disciplinary collaborative research working group, that consists of surgeons, guideline developers, evidence synthesis experts, GRADE methodologists,[20] biostatisticians and a lead member of the AGREE collaboration. This is a tripartite project named *Guideline Assessment Project: Filling the GAP in Surgical Guidelines*. A summary of the project is outlined in **Fig. 1**. The project is a result of a partnership between an international team of surgical research experts and two of the AGREE research team leads (IF and MB). The AGREE research team is currently under a membership renovation process, and, therefore, neither of the authors can speak on behalf of the entire AGREE group. However, both AGREE research team leads state that AGREE has supported the project from its inception. Furthermore, they have agreed to support dissemination

activities by making this new tool available in the AGREE website (https://agreetrust.org).

This protocol complies with the Guidance for Developers of Health Research Reporting Guidelines.[21]

- *Patient and public involvement*

No patients were involved in the development of this protocol.

- *GAP I Project: Literature review and exploratory analyses*

We have previously performed a structured review to identify clinical practice guidelines in the field of surgery published over a 10-year period.[22] We have assessed the methodological and reporting quality of the selected guidelines using the original AGREE II criteria. Domain scores (calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain)[16] ranged between 0-56%, suggesting generally inadequate and highly variable guideline quality. The median overall score was 4 out of a maximum of 7, and 40% of guidelines were not considered suitable for use based on their quality as assessed using the AGREE II instrument.

In exploratory analyses, we have found guidelines produced by surgical organizations with a high (≥1 guideline per year) output (odds ratio 3.79, 95% confidence interval, 1.01–12.66) and those produced by surgical organizations with a guideline committee (odds ratio 4.15, 95% confidence interval, 1.47–11.77) have higher odds of reaching sufficient quality and being recommended for use.[22]

- *GAP II: Statistically calibrating the AGREE II instrument*

The second part of this project was focused on statistical calibration of the AGREE II instrument. We have used quality appraisal data from GAP I and employed a series of statistical methods to explore reliability, internal consistency and unidimensionality of the AGREE II instrument when it is applied in surgical guidelines. We investigated the internal consistency that refers to the extent to which all items of the instrument measure the same hypothetical construct. We explored if and how test items are intercorrelated. Large intercorrelations among test items are indicative of the items measuring the same construct. Using reliability analysis, Kendall's tau statistics, factor analysis and the item response theory, we explored whether items of each AGREE II domain are intercorrelated and are, therefore, indicators of the same construct. Statistical modeling showed that excluding 5 items from the original tool (items 1, 2, 5, 7 and 8) and re-arranging the remaining items into 4 domains instead of 6 would enhance the instrument.. We have finally drafted a modified AGREE II document for guidelines in surgery, on the basis of the outcomes of statistical models.

- *GAP III: AGREE II Extension for Surgical Guidelines*

The third part of the project aims to use the information from the previous GAP projects and other published information on the topic to develop the extension document using a structured Delphi process involving relevant stakeholders.

The multidisciplinary Delphi panel will include surgical specialists, journal editors, guideline development bodies, GRADE representatives, and patient

representatives. Under consideration of the evidence, stakeholders will be asked to provide their input through a Delphi process, which will inform the preparation of an AGREE II extension for surgical guidelines.

Funding

This third part of the project is funded by United European Gastroenterology and the European Association for Endoscopic Surgery. The funding bodies did not have any influence on the previous work and will not have influence on the upcoming process.

Participants

The executive group consists of surgeons (MLC, SRM, GS, GAA, NKF, SAA), members of surgical quality and research boards (MLC, NKF, SAA), guideline developers (MLC, IF, MB, GS, NKF, SAA), evidence synthesis experts (IF, GAA, DM, SAA), GRADE methodologists (MLC, SAA),[20] biostatisticians (DM, ST), and 2 leads of the AGREE Group (IF, MB). It is further divided into 4 working groups with distinct functions and responsibilities:

- The strategic steering group is responsible for overseeing the project.
- The methods group coordinates the methodology of the project.
- The evidence review group will review the literature for evidence on candidate new items to be included in the extension document.
- The evidence synopsis group will summarize evidence for presentation to Delphi participants.

The group attended a one-day meeting to discuss the findings of previous work, define the methodology and study design, and identify potential stakeholder groups to comprise the Delphi panel.

Delphi process

The Delphi panel will consist of key stakeholders, including; representatives from different surgical disciplines (general surgery, urology, thoracic surgery, vascular surgery, pediatric surgery), guideline developers from different continents and representatives of guideline development organizations. The public will be involved by participation of patient representatives from the European Patients Forum **(Table 1)**. We will develop a web-based survey tool to facilitate Delphi exercises. Findings of previous work (GAP I and GAP II) and further evidence that will be identified through a scoping literature review will be summarized and presented to Delphi participants. Summary information will also be available on the project website at https://gap-project.org. Online links to full documents for detailed review of the evidence will be provided.

The first round will include open-ended questions to identify candidate items for inclusion in the extension document. Responses will be grouped and summarized by the methods group before the second round is commenced.

The second round will include closed-ended questions in a 5-point Likert scale to assess participants' opinions and level of agreement on including candidate items or excluding existing items from the extension document. As per protocol, 1/2 indicates strong/moderate disagreement, 3 indicates no opinion, and 4/5 indicates moderate/strong agreement. Candidate items will have been identified through GAP

I and GAP II, and the scoping literature review. We will discard low-scoring items (i.e. those with a median score of 1/2 on the Likert scale) and use the shortlisted items in a third Delphi round. We will repeat the process until an agreement of 80% (4/5 on the Likert scale) is reached among Delphi participants.

The Delphi panel's contribution will be acknowledged by group authorship in subsequent publications of the extension document, the elaboration document and supporting tools.

Qualitative research synthesis

We will perform qualitative evidence synthesis to identify factors of conceptual importance to the quality of evidence in surgery. The overarching question will be: How do clinical practice guidelines in surgery differ from non-surgical guidelines? Specific thematic questions will be addressed:

1. Which are the concepts that make surgical guidelines different from guidelines or summary evidence in other medical fields?
2. Which are potential items that may be of sufficient importance to be included in an AGREE II Extension for surgical guidelines?
3. Which are the items of the original AGREE II that might not be relevant to surgical guidelines?
4. How should items of the original AGREE II instrument be modified to be more relevant to an AGREE II Extension for surgical guidelines?

We will conduct a scoping search of PubMed, Embase and Google Scholar. In keeping with realist review guidelines,[23] there will be no restrictions on the types of study design eligible for inclusion. We will consider editorials, letters to the editor,

commentaries, opinions and any type of publication that captures the breadth discussions about development of surgical guidelines. Information will be used to identify characteristics that specifically apply to surgical guidelines.

The realist review will aim to develop an explanatory understanding of development and reporting of surgical guidelines, how surgical guidelines differ from non-surgical ones, and how AGREE II can be modified to reflect the specific aspects of surgical guidelines. According to the realist synthesis methodology, studies will be assessed based on criteria of relevance (whether they contribute to the development or testing of the initial theories)[24] and appropriateness for addressing the research questions.[25,26]

Studies will be entered into ATLAS.ti and coded to identify the specific features relevant to development and reporting of surgical guidelines. Themes will be discussed by the research team using an iterative and speculative process (Wong, Greenhalgh et al. 2010). Adjudication and triangulation will be applied to refine theories which can be used across the studies to understand findings.

Furthermore, we will invite users of social media through the project account on Twitter (@GAProject2) and through communication streams of the sponsoring bodies (Facebook, Twitter and email newsletters) to nominate parameters of importance in the development and reporting of guidelines in surgery, and will group and summarize their responses. Evidence identified from the above pathways, along with information from GAP I and GAP II will be summarized and taken into account when developing the extension document.

Consensus meeting

Following the Delphi process, the executive group will meet to discuss the findings and compose the first draft of the extension document. We will present new items that will be identified through the Delphi exercise and the qualitative synthesis, and discuss their plausibility and possible inclusion in the instrument. Similarly, items to be excluded with the respective rationale will be discussed. The group will finalize the extension document by ordering and allocating items into domains.

The executive group will hold a further meeting with the advisory group that is comprised of journal editors and representatives of surgical associations to discuss dissemination and implementation processes of the developed extension instrument.

Pilot-testing and assessment of internal validity

The extension instrument will be pilot-tested by 2 members of the executive group. One member will apply the instrument on the surgical guidelines which were identified by the structured search process as described in GAP I[22] and on additional guidelines that will be identified by extending the search to the present date. A second member will independently follow the same process in a randomly selected sample of 15 guidelines. The biostatistical team will assess the internal validity by applying the statistical models of GAP II. Any difficulties encountered with the use of the instrument will be documented and addressed. Results of the statistical assessment will be appraised against statistical findings of the appraisal of the original AGREE II instrument (GAP II).

AGREE II Extension Statement

The extension statement along with an explanation and elaboration (E&E) document will be composed by the executive group. The E&E document will detail the use of the extension instrument in developing and reporting a new surgical guideline and appraising an existing surgical guideline.

AGREE II Extension Checklist

A checklist including the AGREE II Extension items will be developed with the aim of this checklist to be used by guideline developers (to summarize development and reporting parameters), guideline users (to appraise quality), peer reviewers and journal editors (to assess adequacy of reporting parameters).[27]

Feedback and criticism

We will invite constructive feedback on the instrument through the dedicated website (https://gap-project.org) and we will consider comments in letters to the editor and via the social media. An ad hoc team will collect and summarize the feedback received in 3-monthly intervals for the first year after publication, and the executive group will discuss and address this information in web-based meetings.

Monitoring, update and future steps

The executive group will monitor the use of the extension document and appraise its applicability in surgical guidelines for a reasonable period of time after dissemination and will publish their findings. Following consideration of the outcomes, feedback, criticism, suggestions and new evidence in the field, we will discuss the need for an update. The development of further extension instruments for national surgical

guidelines and guidelines in distinct surgical or other interventional disciplines will be considered following discussions with key stakeholders.

Implications for practice and research

Clinical practice guidelines directly impact clinical practice and healthcare delivery and, as such, development must follow rigorous methodological and reporting standards. The AGREE II instrument has been designed as a generic tool for development and appraisal of clinical practice guidelines.[6] It is not intended to substitute established detailed guidance on guideline development principles, processes and procedures, such as the GRADE approach.[15] It has addressed a vital need to summarize and detail essential development steps and reporting parameters for high quality guidelines. Furthermore, as an appraisal instrument, it may be used by healthcare practitioners, policymakers and other stakeholders to inform decisions regarding the use of an existing guideline.

In addition, AGREE II has been shown to be a valuable tool for assessment of guideline quality in several clinical disciplines and evidence fields.[22,28,29,30,31,32,33,34,35,36] Such summaries alert the scientific community to the need for improving specific aspects of clinical practice guidelines (corresponding to the instrument domains) or the overall quality of guidelines. Our previous research has highlighted the need for improvement of the quality of surgical guidelines.[22] An AGREE II extension for surgical guidelines is expected to meet this need.

The outcome of this project will be the first AGREE II extension document. RIGHT (Reporting Tool for Practice Guidelines in Health Care) is another reporting instrument for clinical practice guidelines.[37] We are aware of a planned RIGHT

extension for public versions of guidelines and a RIGHT extension for adapted practice guidelines.[38,39] An extension document of RIGHT for surgical guidelines would be justified as well. However, in view of the evidenced gap in methodological quality of surgical guidelines,[22] we considered more appropriate to elaborate on AGREE II, as it addresses guideline development, reporting and appraisal.

Strengths and limitations

This tripartite project is the first to employ statistical models to inform the validity of an extension, modification or update document on guidelines reporting. We will correlate statistical findings with conceptual considerations of the need for adjustments/extension of the AGREE II instrument. The project methods group has adopted recommendations on developing research reporting guidelines, proposed by a collaborative team who have developed a significant number of such guidelines.[21] The holistic approach to developing an extension document for clinical practice guidelines in surgery is reflected in the diverse scientific, cultural and geographical background of experts in the field involved in the project. Similarly, the Delphi panel will include stakeholders and members from a variety of backgrounds including clinicians/surgeons, methodologists, guideline developers, policy makers and the public (patient representatives).

A face-to-face meeting of Delphi participants, instead of a full web-based Delphi process, might be more efficacious in developing the extension document allowing direct exchange of opinions, information and ideas. We will encourage a full participation and exchange of information by developing a user-friendly and interaction-allowing web-based platform. Furthermore, we will incentivize

participation and engagement of potential Delphi members by proposing group authorship and participation in future associated projects.

ETHICS AND DISSEMINATION

Research Ethics Committee and Health Research Authority approval was waived, since this is a professional staff study only and no duty of care lies with the NHS (National Health Service) to any of the participants. We will request electronic informed consent from Delphi participants and the responses of the Delphi members will be anonymized.

We have obtained conflict of interest forms of all executive group members and will request electronic and/or written informed consent by Delphi participants and members of the advisory group. We will deal with potential conflicts of interest by re-assigning functions or replacing participants who pose interest conflict.

We will submit the final paper with the extension document to be considered for publication in the UEG Journal and Surgical Endoscopy, as defined in the respective pre-development agreements. We will negotiate simultaneous publications in other surgical journals for widest dissemination as recommended by the Guidance for Developers of Health Research Reporting Guidelines.[21]

We will make the extension document available in a dedicated website with links to the original publications. We will encourage surgical organizations with guideline development activities to use the instrument. We will further pursue dissemination through the websites of the funding bodies and channels of social media of major stakeholers, such as the Guideline International Network, GRADE and EQUATOR.

Through direct contact, we will advise international surgical and guideline development organizations, and policymakers to endorse the extension instrument. Furthermore, editors of surgical journals will be advised to provide an extension instrument checklist that authors of clinical practice guidelines should submit along with the original manuscript.

The GAP III study aims to address the need for improvement of the methodology, reporting and appraisal of surgical guidelines. An extension document specifically designed for clinical practice guidelines in surgery will further improve the value, use and applicability of the AGREE II instrument in the surgical field with the ultimate goal of enhancing patient care, experience and outcomes.

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AUTHOR CONTRIBUTION STATEMENT

George A. Antoniou: Conception and design, interpretation of data, drafting the work, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dimitris Mavridis: Conception and design, analysis of data, interpretation of data, drafting the work, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the

accuracy or integrity of any part of the work are appropriately investigated and resolved.

Sofia Tsokani: Analysis of data, interpretation of data, revising the work critically for important intellectual data, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Manuel López-Cano: Acquisition of data, analysis of data, interpretation of data, revising the work critically for important intellectual data, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Iván Flórez: Conception and design, interpretation of data, drafting the work, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Melissa Brouwers: Conception and design, interpretation of data, revising the work critically for important intellectual data, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Sheraz Markar: Interpretation of data, revising the work critically for important intellectual data, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the

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Gianfranco Silecchia: Interpretation of data, revising the work critically for important intellectual data, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Nader K Francis: Interpretation of data, revising the work critically for important intellectual data, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Stavros A. Antoniou: Conception and design, acquisition of data, analysis of data, interpretation of data, drafting the work, final approval for the work to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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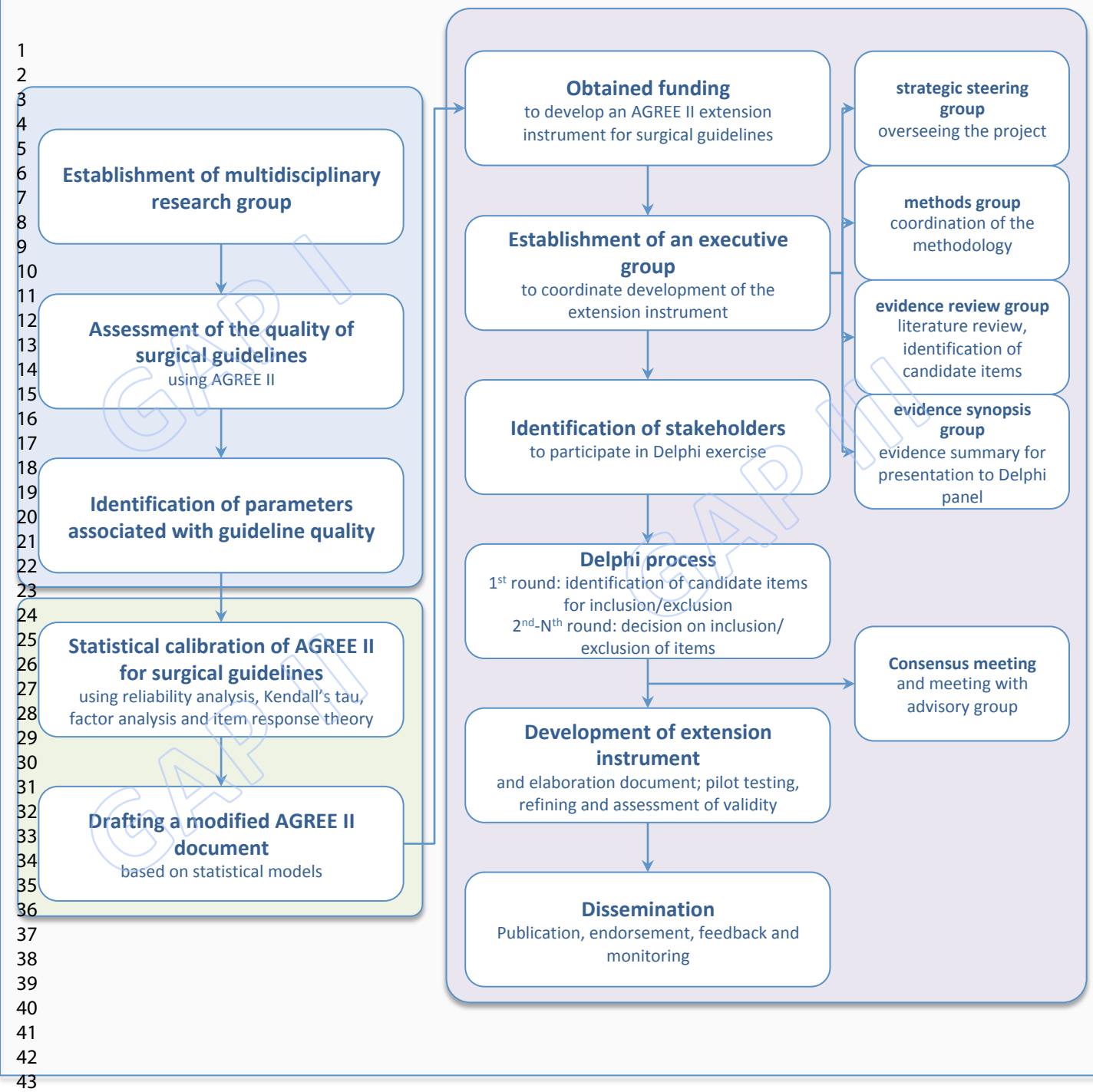
FIGURE LEGEND

Fig. 1: Development steps of the Guideline Assessment Project with the ultimate objective to develop an AGREE II extension document for surgical guidelines

Table 1. Stakeholders to participate in a web-based Delphi process

Function
General Surgeon
Urologist
Thoracic Surgeon
Vascular Surgeon
Pediatric Surgeon
Journal Editor
National authority representative
NICE representative
Guideline developer/Representative from Europe
Guideline developer/Representative from North America
Guideline developer/Representative from Asia
Guideline developer/Representative from middle-income country
Healthcare provider representative
Representative from GRADE
Guideline implementer
Patient representative
WHO representative
European Commission representative
GIN representative
EQUATOR representative
NICE: National Institute of Health and Care Excellence GRADE: Grading of Recommendation Assessment, Development and Evaluation WHO: World Health Organization GIN: Guidelines International Network EQUATOR: Enhancing the QUAlity and Transparency Of health Research


Establishment of multidisciplinary research group
Assessment of the quality of surgical guidelines
using AGREE II
Identification of parameters associated with guideline quality
Statistical calibration of AGREE II for surgical guidelines
using reliability analysis, Kendall's tau, factor analysis and item response theory
Drafting a modified AGREE II document
based on statistical models
Obtained funding
to develop an AGREE II extension instrument for surgical guidelines
Establishment of an executive group
to coordinate development of the extension instrument
Identification of stakeholders
to participate in Delphi exercise
Delphi process
1st round: identification of candidate items for inclusion/exclusion
2nd-Nth round: decision on inclusion/ exclusion of items
Development of extension instrument
and elaboration document; pilot testing, refining and assessment of validity
Dissemination
Publication, endorsement, feedback and monitoring
strategic steering group
overseeing the project
methods group
coordination of the methodology
evidence review group
literature review, identification of candidate items
evidence synopsis group
evidence summary for presentation to Delphi panel
Consensus meeting
and meeting with advisory group

APPENDIX

The AGREE II instrument

Adapted from: Brouwers MC, Kerkvliet K, Spithoff K. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. *BMJ*. 2016:i1152.

Domains	Items	Assessment*
I. Scope and purpose	1. The overall objective(s) of the guideline is (are) specifically described.	1 to 7
	2. The health question(s) covered by the guideline is (are) specifically described.	1 to 7
	3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	1 to 7
II. Stakeholder involvement	4. The guideline development group includes individuals from all relevant professional groups.	1 to 7
	5. The views and preferences of the target population (patients, public, etc.) have been sought.	1 to 7
	6. The target users of the guideline are clearly defined.	1 to 7
III. Rigor of development	7. Systematic methods were used to search for evidence.	1 to 7
	8. The criteria for selecting the evidence are clearly described.	1 to 7
	9. The strengths and limitations of the body of evidence are clearly described.	1 to 7
	10. The methods for formulating the recommendations are clearly described.	1 to 7
	11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	1 to 7
	12. There is an explicit link between the recommendations and the supporting evidence.	1 to 7
	13. The guideline has been externally reviewed by experts prior to its publication.	1 to 7
	14. A procedure for updating the guideline is provided.	1 to 7

IV. Clarity of presentation	15. The recommendations are specific and unambiguous.	1 to 7
	16. The different options for management of the condition or health issue are clearly presented.	1 to 7
	17. Key recommendations are easily identifiable.	1 to 7
V. Applicability	18. The guideline describes facilitators and barriers to its application.	1 to 7
	19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	1 to 7
	20. The potential resource implications of applying the recommendations have been considered.	1 to 7
	21. The guideline presents monitoring and/or auditing criteria.	1 to 7
VI. Editorial independence	22. The views of the funding body have not influenced the content of the guideline.	1 to 7
	23. Competing interests of guideline development group members have been recorded and addressed.	1 to 7
Overall guideline assessment	24. Rate the overall quality of this guideline.	1 to 7
	25. I would recommend this guideline for use.	• Yes • Yes, with modifications • No
** 7 corresponds to the highest possible quality.*		