Universitat Autònoma de Barcelona

ADAPTATION OF CLINICAL GUIDELINES: ADVANCES ON METHODS AND REPORTING

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PhD programme in Methodology of Biomedical Research and Public Health

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DOCTORAL THESIS

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ABSTRACT

ABSTRACT

Title

Adaptation of clinical guidelines: advances on methods and reporting.

Introduction

Clinical guidelines (CGs) aim to assist stakeholders in healthcare decision-making. However, most organisations do not have enough resources for developing high-quality CGs. Adapting existing CGs becomes an efficient way. Given that published adapted CGs are generally of low quality, poorly reported, and not based on CG adaptation frameworks, there is a pressing need to optimise the reporting and methodology used for CG adaptation.

Objectives

1) To investigate the CG methods used in one middle-income country regarding development, adaptation, and updating, 2) to explore the current practice and challenges of CG adaptation practice, and 3) to develop a checklist for the reporting of adapted CGs in healthcare.

Methods

For study I, we conducted a national survey on the methods used by Chinese CG organisations using a piloted questionnaire. We identified potential participating organisations from published Chinese CGs, Chinese CG developers, and Chinese clinical experts.

For study II, we conducted semi-structured interviews with CG adaptation experts. We applied a framework analysis for the CG adaptation process and thematic analysis for participants' views and experiences, regarding adaptation practice and challenge.

For study III, we followed a multi-step process: 1) establishing a Working Group (WG), 2) generating an initial checklist, 3) optimising the checklist (through an initial assessment of adapted CGs, semi-structured interviews, a Delphi consensus survey, an external review, and a final assessment of adapted CGs), and 4) approval of the checklist by the WG.

Results

In study I, we surveyed 48 Chinese CG development organisations. CGs development process in China still lacks specific CG development division, stakeholder engagement, formal updating process, monitoring, conflict of interest (COI) management, and funding. The methods used are variable and often informal. Only a few Chinese CG organisations use published adaptation or formal updating methods.

In study II, we interviewed ten CG adaptation experts and identified nine adaptation methodologies. The main steps of the adaptation practice include: scope selection, source materials assessment, formulation of recommendations, external review, and follow-up activities. Challenges on CG adaptation include: poor quality or reporting of source CG, lack of resources or skills, process intensity and complexity, and implementation barriers.

In study III, we developed the RIGHT-Ad@pt checklist (Reporting Tool for the Adapted Guidelines in Health Care), containing 34 items, grouped into seven sections: basic information, scope, rigour of development, recommendations, external review and quality assurance, funding, declaration, management of COI, and other information. We also developed a user guide, containing explanations and real-world examples for each item.

Conclusions

Current methods for adapting CGs remain variable and suboptimal. RIGHT-Ad@pt provides comprehensive guidance on the reporting of adapted CGs, including reporting of the methodological process and adapted recommendations, contributing to the improvement of the transparency and credibility of adapted CGs. RIGHT-Ad@pt can be used to inform the reporting of the adaptation process, assess the completeness of reporting in adapted CGs, and in combination with adaptation frameworks, to inform adaptation processes.

RESUMEN

Título

Adaptación de guías clínicas: avances en los métodos y la presentación.

Introducción

Las guías clínicas (GC) tienen como objetivo ayudar a las partes interesadas a tomar de decisiones de salud. Sin embargo, la mayoría de las organizaciones no tienen suficientes recursos para desarrollar GC de alta calidad. Adaptar las GC existentes se convierte en una forma eficiente. Dado que las GC adaptadas publicadas son generalmente de baja calidad, están mal informadas y no se basan en marcos de adaptación de GC, existe una necesidad apremiante de optimizar el informe y la metodología utilizados para la adaptación de GC.

Objetivos

1) Investigar los métodos de GC utilizados en un país de ingresos medios con respecto al desarrollo, la adaptación y la actualización; 2) explorar la práctica actual y los desafíos de la práctica de adaptación de GC, y 3) desarrollar una lista de verificación para informar sobre la adaptación de las GC en salud.

Métodos

Para el estudio I, realizamos una encuesta nacional sobre los métodos utilizados por las organizaciones chinas de GC, mediante un cuestionario piloto. Identificamos posibles organizaciones participantes a partir de CG chinas publicadas, desarrolladores de CG chinos y expertos clínicos chinos.

Para el estudio II, realizamos entrevistas semiestructuradas con expertos en adaptación de GC. Aplicamos un análisis marco para el proceso de adaptación del GC y un análisis temático para las opiniones y experiencias de los participantes con respecto a la práctica y el desafío de la adaptación.

Para el estudio III, seguimos un proceso de varios pasos: 1) establecer un grupo de trabajo (GT), 2) generar una lista de verificación inicial, 3) optimizar la lista de verificación (a través de una evaluación inicial de GC adaptados, entrevistas semiestructuradas, una encuesta de consenso de Delphi, una revisión externa y una evaluación final de las GC adaptadas), y 4) aprobación de la lista de verificación por parte del GT.

Resultados

En el estudio I, encuestamos a 48 organizaciones chinas de desarrollo de GC. El proceso de desarrollo de GC en China todavía carece de una división específica de desarrollo de GC, participación de las partes interesadas, proceso de actualización formal, monitoreo, gestión de conflictos de intereses (COI), y financiación. Los métodos utilizados son variables y, a menudo, informales. Solo algunas organizaciones de GC chinas utilizan métodos de adaptación publicados o de actualización formal.

En el estudio II, entrevistamos a diez expertos en adaptación de GC e identificamos nueve metodologías de adaptación. Los pasos principales de la práctica de adaptación incluyen: selección del alcance, evaluación de los materiales de origen, formulación de recomendaciones, revisión externa y actividades de seguimiento. Los desafíos en la adaptación de GC incluyen: mala calidad o informes de GC de origen, falta de recursos o habilidades, intensidad y complejidad del proceso y barreras de implementación.

En el estudio III, desarrollamos la lista de verificación RIGHT-Ad@pt (*Reporting Tool for the Adapted Guidelines in Health Care*), que contiene 34 ítems, agrupados en siete secciones: información básica, alcance, rigor del desarrollo, recomendaciones, revisión externa y aseguramiento de la calidad, financiación, declaración, gestión de COI y otra información. También desarrollamos una guía de usuario, que contiene explicaciones y ejemplos del mundo real para cada elemento.

Conclusiones

Los métodos actuales para la adaptación de guías siguen siendo variables y subóptimos. El RIGHT-Ad@pt proporciona una guía para la presentación de GC adaptadas, incluido el informe sobre el proceso metodológico y las recomendaciones adaptadas, lo que contribuye a mejorar la transparencia y la credibilidad de las GC adaptadas. El RIGHT-Ad@pt puede utilizarse para informar sobre la presentación del proceso de adaptación, para evaluar su exhaustividad en las GC adaptadas y para que, en combinación con el uso de marcos para la adaptación, informe los procesos de adaptación.

RESUM

Títol

Adaptació de les guies clíniques: avenços en els mètodes i la presentació.

Introducció

Les guies clíniques (GC) tenen com a objectiu ajudar les parts interessades a prendre decisions sobre salut. No obstant això, la majoria de les organitzacions no tenen prou recursos per a desenvolupar GC d'alta qualitat. L'adaptació de les GC existents és una forma eficient. Atès que les GC adaptades que estan publicades tenen generalment una baixa qualitat, una informació deficient i no es basen en els marcs d'adaptació de les GC, hi ha una necessitat urgent d'optimitzar la informació i la metodologia utilitzada per a l'adaptació de les GC.

Objectius

1) Investigar les metodologies de les GC utilitzades en un país d'ingressos mitjans en relació amb l'elaboració, l'adaptació i l'actualització, 2) explorar la pràctica actual i els reptes de l'adaptació de les GC, i 3) desenvolupar una llista de verificació per a informar sobre l'adaptació de GC en salut.

Mètodes

Per a l'estudi I, vam dur a terme una enquesta nacional sobre les metodologies utilitzades per les organitzacions xineses de GC, utilitzant un qüestionari pilotat. Identificàrem les possibles organitzacions participants a partir de GC xineses publicades, elaboradors xinesos de GC i experts clínics xinesos.

Per a l'estudi II, vam dur a terme entrevistes semiestructurades amb experts en adaptació de GC. Aplicàrem una anàlisi del marc per al procés d'adaptació de les GC i una anàlisi temàtica per a les opinions i experiències dels participants respecte a la pràctica i dificultats de l'adaptació.

Per a l'estudi III, seguírem un procés de diversos passos: 1) establir un grup de treball (GT), 2) generar una llista de verificació inicial, 3) optimitzar la llista de verificació (a través d'una avaluació inicial de les GC adaptades, entrevistes semiestructurades, una enquesta de consens Delphi, una revisió externa i una avaluació final de les GC adaptades) i 4) aprovació de la llista de verificació per part del GT.

Resultats

A l'estudi I, vam estudiar 48 organitzacions xineses d'elaboració de GC. El procés d'elaboració de GC a la Xina encara no té una divisió específica d'elaboració de GC, una participació de les parts interessades, un procés d'actualització formal, una vigilància, una gestió de conflictes d'interessos (COI) ni un finançament. Els mètodes utilitzats són variables i sovint informals. Només unes poques organitzacions xineses de GC utilitzen marcs d'adaptació publicats o mètodes d'actualització formal.

En l'estudi II, entrevistàrem deu experts en adaptació de GC i identificàrem nou metodologies d'adaptació. Els principals passos de la pràctica d'adaptació són: selecció de l'abast, avaluació de fonts, formulació de recomanacions adaptades, revisió externa i seguiment d'activitats. Els reptes en l'adaptació de GC inclouen: mala qualitat o informació de la font de les GC, manca de recursos o habilitats, intensitat i complexitat del procés i barreres d'implementació.

En l'estudi III, desenvolupàrem la llista de verificació RIGHT-Ad@pt (*Reporting Tool for the Adapted Guidelines in Health Care*), que conté 34 elements, agrupats en set seccions: informació bàsica, abast, rigor en l'elaboració, recomanacions, revisió externa i control de qualitat, finançament, declaració i gestió de COI i altra informació. També desenvolupàrem una guia d'us, que contenia explicacions i exemples reals per a cada element.

Conclusions

Els mètodes actuals per adaptar les guies clíniques continuen sent variables i subòptims. El RIGHT-Ad@pt proporciona unes directrius detallades sobre la presentació de GC adaptades, incloent l'informe del procés metodològic i les recomanacions adaptades, fet que contribueix a millorar la transparència i la credibilitat de les GC adaptades. El RIGHT-Ad@pt es pot utilitzar per informar sobre la presentació del procés d'adaptació, per avaluar-ne l'exhaustivitat a les GC adaptades i perquè, en combinació amb l'ús de marcs per a l'adaptació, informi els processos d'adaptació.

LIST OF ALL ABBREVIATIONS

AAP	Alberta Ambassador program
ACA	Adopt–Contextualise–Adapt
ACP	American College of Physicians
ASCO	American Society of Clinical Oncology
CCO	Cancer Care Ontario's
ADAPTE	Resource Toolkit for Guideline Adaptation
AGREE	Appraisal of Guidelines for Research and Evaluation
AGREE-REX	Appraisal of Guidelines Research and Evaluation – Recommendations Excellence
CENTRAL	Cochrane Central Register of Controlled Trials
CheckUp	Checklist for the Reporting of Updated Guidelines
CAN-IMPLEMENT	A framework for guideline adaptation and implementation
DELBI	German Instrument for Methodological Guideline Appraisal
CG	Clinical guideline
COI	Conflict of Interest
EBM	Evidence-based medicine
EtD frameworks	Evidence to Decision frameworks
GIN	Guideline International Network
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
GRADE-ADOLOPMENT	GRADE Evidence to Decision frameworks for adoption, adaptation, and de novo development of trustworthy recommendations
GRIPP2	Guidance for Reporting Involvement of Patients and the Public
GUIDE-M	Guideline Implementability Decision Excellence Model
HIC	High-income country
IOM	Institute of Medicine
KTA	Knowledge-to-action
LMIC	Low- and middle-income country
MAGIC	Making GRADE the irresistible choice
MESH	Medical Subject Headings
NCCN	National Comprehensive Cancer Network
NEATs	NGC extent of the Adherence to Trustworthy Standards
NHMRC	National Health and Medical Research Council

NICE	National Institute for Health and Care Excellence
NGC	National Guideline Clearinghouse
NIH	National Institutes of Health
PICO	Participants/patients, Interventions, Comparisons, and Outcomes
PGEAC	Practice Guideline Evaluation and Adaptation Cycle
RCT	Randomized controlled trial
RCN	Royal College of Nursing
RIGHT	Reporting Items for practice Guidelines in HealThcare
SGR	Systematic Guideline Review
SR	Systematic Review
WHO	World Health Organisation
WG	Working Group

1. INTRODUCTION

1 INTRODUCTION

1.1 Clinical guidelines

1.1.1 Definition and objectives

Clinical guidelines (CGs) are systematically developed evidence-based statements, including recommendations on how to diagnose, treat, or manage a health condition (1). CGs provide clinicians with a favourable way of using healthcare evidence to make decisions, ensuring optimal patient care. Rigorously developed CGs systematically synthesise existing evidence for specific clinical contexts and translate evidence into clinical practice recommendations by fully considering the effects of healthcare interventions and factors influencing healthcare decision-making.

CG definition has been gradually refined with the prevalent use in daily clinical practice (Table 01). Initially, CG definition refers to official statements or policies of clinical practice on specific healthcare interventions (2). Ten years later, the Institute of Medicine (IOM, now the National Academy of Medicine) of the United States specified the definition of CGs by combining the development basis of trustworthy CGs, as systematic statements informed by systematic reviews of healthcare interventions and assessing the benefits and harms (1). Nowadays, the World Health Organisation (WHO) includes the implementation goal in the CG definition, emphasising the necessity of the stakeholders' engagement during the CG development process (3).

Table 01. Definitions of clinical guidelines

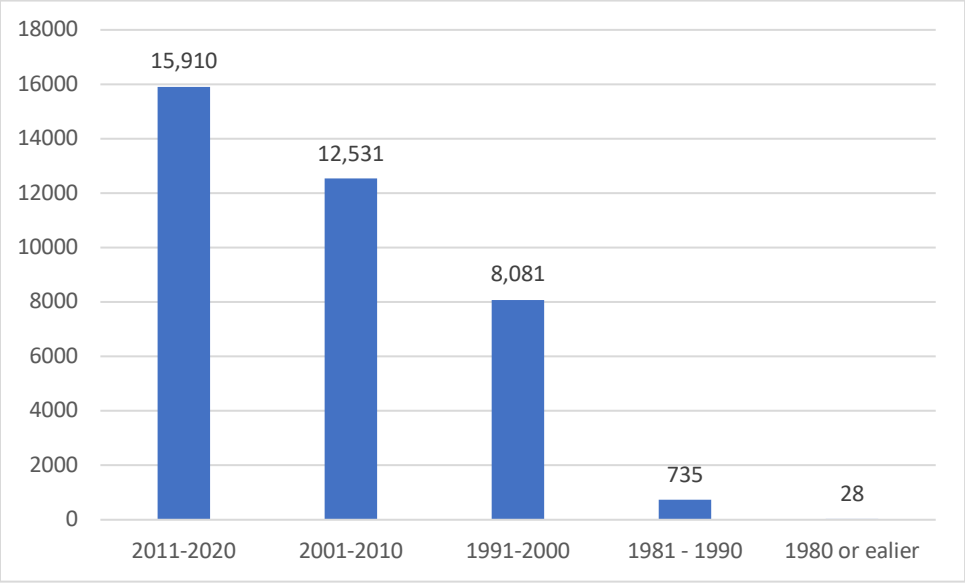
Year	Author/Institution	Definition
1990	Woolf et al (2)	*"Clinical guidelines are new reality in medicine, referring to the official statements or policies for performing a health care intervention or management for specific clinical problems"*
2011	Institute of Medicine (1)	*"Clinical guidelines we could trust are statements informed by a systematic review of evidence and an assessment of both the benefits and harms of alternative health care interventions"*
2014	World Health Organisations (3)	"*Clinical guidelines are recommendations that provide information to indicate the health care activities for policymakers, healthcare providers or patients"*

The objective of CGs is to improve clinical practice, minimise unjustified variations in clinical practice and unnecessary or ineffective services, and ensure effective use of healthcare resources (2). In addition, CG

recommendations aim to assist health providers, end users, and other stakeholders in making informed decisions and consequently optimise patient care (1, 3).

1.1.2 Increase of publications

Clinical guidelines (CGs) have been increasingly used to provide guidance for clinical practice, public health, or policy recommendations (3). Over the last two decades, the number of publications of CGs per year in PubMed increased from 8,081 to 15,910, and the total number reached 36,962 (Figure 01).



PubMed: searched by "Guideline" [Publication Type]

Figure 01: Number of published clinical guidelines

1.1.3 Methodology for developing clinical guidelines

Over the last three decades, CG development has gradually become more rigorous, including advances in the methods for their CG development, quality assessment, as well as reporting tools (Figure 02).

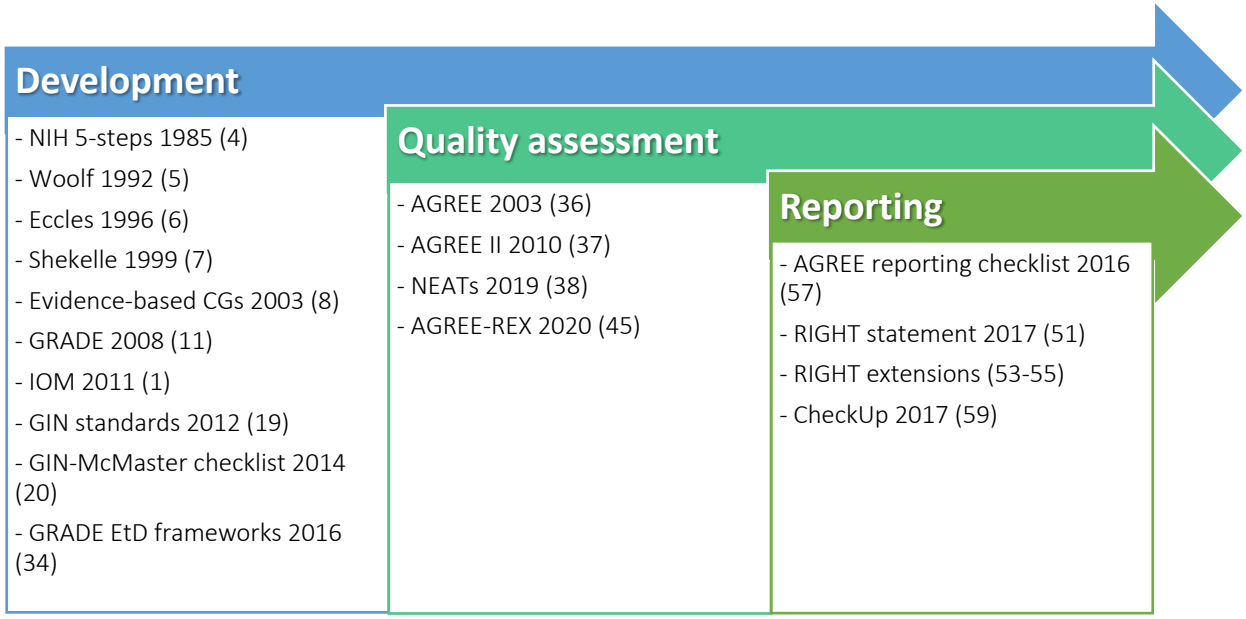


Figure 02. Methodological advances in clinical guidelines

AGREE: Appraisal of Guidelines, Research and Evaluation; AGREE-REX: Appraisal of Guidelines Research and Evaluation–Recommendations Excellence; CG: Clinical Guideline; CheckUp: Checklist for the Reporting of Updated Guidelines; EBM: Evidence-based Medicine; EtD frameworks: Evidence to Decision frameworks; GIN: Guideline International Network; GRADE: Grading of Recommendations, Assessment, Development and Evaluations; IOM: Institute of Medicine; NEATs: National Guideline Clearinghouse Extent of Adherence to Trustworthy Standards; NIH: National Institutes of Health; RIGHT: Reporting Tool for Practice Guidelines in Health Care; WHO: World Health Organisation.

1.1.3.1 Methodological history

Initially, the Office of American Medical Applications of Research of the National Institutes of Health (NIH) established a five-step (NIH 5-steps) process to guide the formulation of recommendations in consensus conferences (4). The five steps are: 1) establishing an independent panel, comprised of experts outside the NIH to balance objectives and knowledge on the topic, 2) panel meetings to present and discuss all data, and prepare the consensus statements, 3) answering previously posed questions by the conference participants, 4) drafting consensus statement, and 5) dissemination of the consensus statement (4).

In 1992, Woolf et al. standardised steps of the CG development based on a review of the CG methods development process, including: 1) introductory decisions on topic selection, group establishment, and

purpose clarifications, 2) assessments of clinical appropriateness regarding clinical benefits and harms, scientific evidence, expert opinion, and other determinations, 3) assessment of public policy issues, such as resource limitations or feasibility, and 4) CG documentation, dissemination, and monitoring (5).

In 1996, Eccles et al. proposed methods for CG development, based on an evidence-based CG development project in England, in primary care settings for the management of asthma and stable angina (6). The methods covered five topics: 1) form guideline development groups composed of healthcare professionals and patients, clinical experts, coordinators, and methods team, 2) evidence review and synthesis (search strategy; literature assessment; evidence synthesis), 3) external review of guidelines, 4) scheduled review of guidelines (updating), and 5) implications for practice (6).

In 1999, Shekelle et al. proposed a similar five-step process, combining the literature on CG development and their experience in CG development in North America and Britain. Their proposal includes: 1) identifying and refining the subject area, 2) establishing CG development groups, 3) identifying and assessing the evidence, 4) translating evidence into a clinical practice guideline, and 5) reviewing and updating (7).

1.1.3.2 Methodological advances

Along with the emergence of evidence-based medicine (EBM), research started exploring the development of CGs based on the systematic and analytical evaluation of evidence (8). EBM stimulates the use of clinical research in clinical decision-making, including assessing and synthesising evidence (9). Subsequently, evidence based CGs were promoted to assist healthcare providers' decision-making as systematic statements. To ensure their trustworthiness and benefits to end users, the development process of evidence-based CGs should be rigorous, combining stakeholders' considerations and including an implementation strategy (8).

Since 2000, CGs have been gradually more used by clinicians (10). CGs were initially used to respond to rising health costs or proposed by clinicians to avoid administrative pressure and preserve their professional independence. Subsequently, CGs have also been used to improve clinical practice (10).

A systematic review of evidence provides healthcare decision-makers with the synthesised results from previously published clinical research and the evaluation of the certainty of the evidence. Rating the

certainty of the evidence (sometimes referred to as the quality of the evidence) is essential for healthcare decision-makers to understand to what extent they should be confident in the estimated effects of healthcare interventions (11). Different organisations have proposed and used multiple rating approaches to rate the certainty of the evidence and the strength of recommendations (12, 13). In 2002, the American Agency for Healthcare Research and Quality systematically reviewed assessment methods of healthcare research results and identified seven existing rating systems for the certainty of the body of evidence, covering domains of quality, quantity, and consistency (13). In 2004, a review critically appraised the six existing rating systems for the body of evidence and strength of recommendations, including the American College of Chest Physicians (ACCP), Australian National Health and Medical Research Council (ANHMRC), Oxford Centre for Evidence-Based Medicine (OCEBM), Scottish Intercollegiate Guidelines Network (SIGN), US Preventive Services Task Force (USPSTF), US Task Force on Community Preventive Services (USTFCPS). However, no existing rating systems inclusively addressed the rating of the certainty of the evidence for different types of healthcare questions (effectiveness, diagnosis, prognosis, etc.), which may lead to difficulties for clinicians in understanding the evidence rating results (12).

To overcome the limitation of previous rating systems and improve the communication of evidence rating results, the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach was developed in 2008 by the GRADE working group to comprehensively rate the certainty of the evidence and the strength of recommendations (14). The GRADE approach is the first rating system that combines all the advantages of other rating systems for the certainty of the evidence and strength of recommendations, regarding comprehensiveness, clarity, explicit rating methods, usefulness, transparency, and a clear, pragmatic interpretation of recommendations. The GRADE approach provides detailed guidance on rating the importance of outcomes, certainty for individual and all outcomes, distinguished the certainty of evidence from strength of recommendations, and a communication structure for CG developers and clinicians (14). As the GRADE approach has important implications for the decision-making in healthcare interventions, it has progressively become the most popular rating system used to assess the certainty of the evidence and move from evidence to decisions or recommendations (15). Many international organisations like the World Health Organisation (WHO), the National Institute for Health and Care Excellence (NICE), and the American College of Physicians (ACP) have adopted the GRADE approach during the CG development process (3, 16-18).

From 2010 to 2014, CG developments mainly focused on improving quality, credibility and standardisation. IOM proposed in 2011 a set of standards for the steps that informed the development process of a trustworthy CG (1) including 1) establishing transparency, 2) management of conflict of interest (COI), 3) CGs development group composition, 4) clinical practice guideline and systematic review intersection, 5) establishing evidence foundations and rating strength of recommendations, 6) presentation of recommendation, 7) external review, and 8) updating. The IOM emphasised the transparency of the CG development process, the engagement of relevant stakeholders, and COI management.

Subsequently, the Guideline International Network (GIN) in 2012 proposed key components of the CG development process to streamline the process (19). GIN standards include composition of the guideline development group, decision-making process, conflicts of interest, scope of guideline, methods, evidence reviews, guideline recommendations, rating of the evidence and recommendations, guideline expiration and updating, and financial support and sponsoring organisation (19).

Although previous CG development methods could ensure the credibility for CG development process, specific guidance on practical steps for developing guidelines is lacking. In 2014, the GIN-McMaster Guideline Development Checklist, containing a list of topics and items that outlined the practical steps to consider for developing CGs, came out to inform the CG development process (Table 02) (20). The authors systematically reviewed and summarised the CG development process based on multiple methodological data sources on CG developments, including institution CG manuals, scientific publications, and methodological reports. As a result, the GIN-McMaster Guideline development checklist was created as a comprehensive checklist to guide the CG development process. It contains 146 items attributed to 18 different topics, with promisingly valuable tools and relevant resources that CG developers could consider (20). In addition, many organisations worldwide have developed their CG development handbook, including WHO, NCCN (the National Comprehensive Cancer Network in the United States), NICE (the National Institute for Health and Care Excellence in the United Kingdom), and GuiaSalud (Ministry of Health in Spain) etc. (3, 17, 21, 22) (Table 02).

Table 02. Main steps on clinical guideline development

Main steps	Specific steps from GIN-McMaster Guideline Development Checklist, 2014 (20)
Planning	○ Organisation, Budget, Planning and Training ○ Priority Setting
	○ Membership of Guideline Group ○ Guideline Group Establishment ○ Define Target Audience and Topic Selection ○ Consumer and Stakeholder Involvement
	○ Conflict of Interest Considerations
Formulating clinical questions and prioritising the importance of outcomes	○ Question Generation (PICO) ○ Considering Importance of Outcomes and Interventions, Values, Preferences and Utilities
Systematically search and select evidence	○ Deciding what Evidence to Include and Searching for Evidence ○ Summarising Evidence and Considering Additional Information
Evidence synthesis and assessment	○ Judging Quality, Strength or Certainty of a Body of Evidence
Formulation of recommendations	○ Developing Recommendations and Determining their Strength ○ Wording of Recommendations and of Considerations of Implementation, Feasibility and Equity
External review	○ Reporting and Peer Review
Follow-up activities	○ Dissemination and Implementation
	○ Updating
	○ Evaluation and Use

1.1.3.3 Main development steps

The main steps in CG development process can be summarised into six main steps (Table 02, Figure 03) (3, 20):

1) Planning

The planning stage in the CG development process includes setting up the CG development group, training the group members on the required methodological expertise, identifying the target audience and topic selection, defining CG topic and scope, and declaration and management of COIs (3, 20). In addition, the panel composition should contain multiple and relevant stakeholders (e.g., methodologists, clinical experts, patients, policymakers, etc.) to collect stakeholders' considerations and improve the uptake of recommendations (23).

2) Formulating clinical questions, and prioritising the importance of health outcomes

A clearly formulated clinical question, using a structured format, facilitates the search and systematic review of relevant evidence (17). For example, the PICO format (Participants/patients, Interventions,

Comparisons, and Outcomes), specifying the population, intervention, comparison, and outcomes of interest (24). In addition, the CG development group may also prioritise the importance of outcomes based on patients' values and clinical relevance, both for desirable and undesirable effects, to inform the sequence of consideration when balancing benefits and harms during the decision-making process (20).

3) Systematically search and select evidence

For retrieving evidence, a systematic search for evidence and a rigorous eligibility process should be conducted (20). The systematic search is usually conducted based on electronic algorithms with a combination of controlled vocabulary (e.g., Medical Subject Headings (MESH) terms, or Emtree headings) and free text, in multiple databases (e.g., MEDLINE, EMBASE, or Cochrane Central Register of Controlled Trials (CENTRAL)) (25). The selected evidence is a set of studies that meet pre-specified eligible criteria, which need to be screened and selected independently by at least two reviewers to ensure rigour.

4) Evidence synthesis and assessment of certainty of evidence

Systematic reviews provide evidence synthesis on a specific healthcare condition for different types of clinical questions, including the effectiveness of a healthcare treatment or practice, the qualitative experience of clinical practice, the cost-effectiveness of the healthcare interventions, diagnostic test accuracy, or etiologic association of risk factors etc (26). During the review of the evidence, the risk of bias or limitations of individual studies should be assessed, the effects per outcome of interest should be synthesised or meta-analysed if possible, and the certainty of the body of evidence should be rated per outcome (27) (28).

GRADE provides a comprehensive and explicit rating method for assessing the certainty of the evidence, indicating to what extent the estimated effects supports a specific recommendation (29). The GRADE approach suggests rating the certainty of the evidence into four levels: high, moderate, low or very low. The criteria for rating down the certainty of the evidence are the risk of bias (30), imprecision (random error) (31), inconsistency (32), indirectness (33), and publication bias (34). On the other hand, the criteria for rating up the certainty of the evidence include the effect of association from observational studies is strong, dose-response relation exists, or confounding factors have decreased the estimated effect (14).

5) Formulation of recommendations

The formulation of the recommendations including rating the strength of recommendations require interpretation of the estimated effects of healthcare interventions, combining an overall rating of certainty of the evidence for all outcomes, the deliberation on the balance of benefits and harms, and other aspects like resources use, equity, acceptability, and feasibility, etc (11). The GRADE evidence to decision (EtD) frameworks is a practical tool to formulate recommendations and rate the strength of recommendations, providing structured and explicit guidance by addressing different considerations to inform the formulation of recommendations (35).

6) External review

The external review of the drafted recommendations by experts outside the CG development group, ensures the comprehensiveness of the CG recommendations. External reviewers should consist of relevant stakeholders including patients, policymakers, clinical experts on the CG topic, or clinical practitioners on healthcare recommendations (1).

7) Follow-up activities

Other activities include publishing the CG online or in scientific journals, disseminating the CG through healthcare organisations or government, creating an implementation strategy, monitoring the implementation, and planning for future updating.

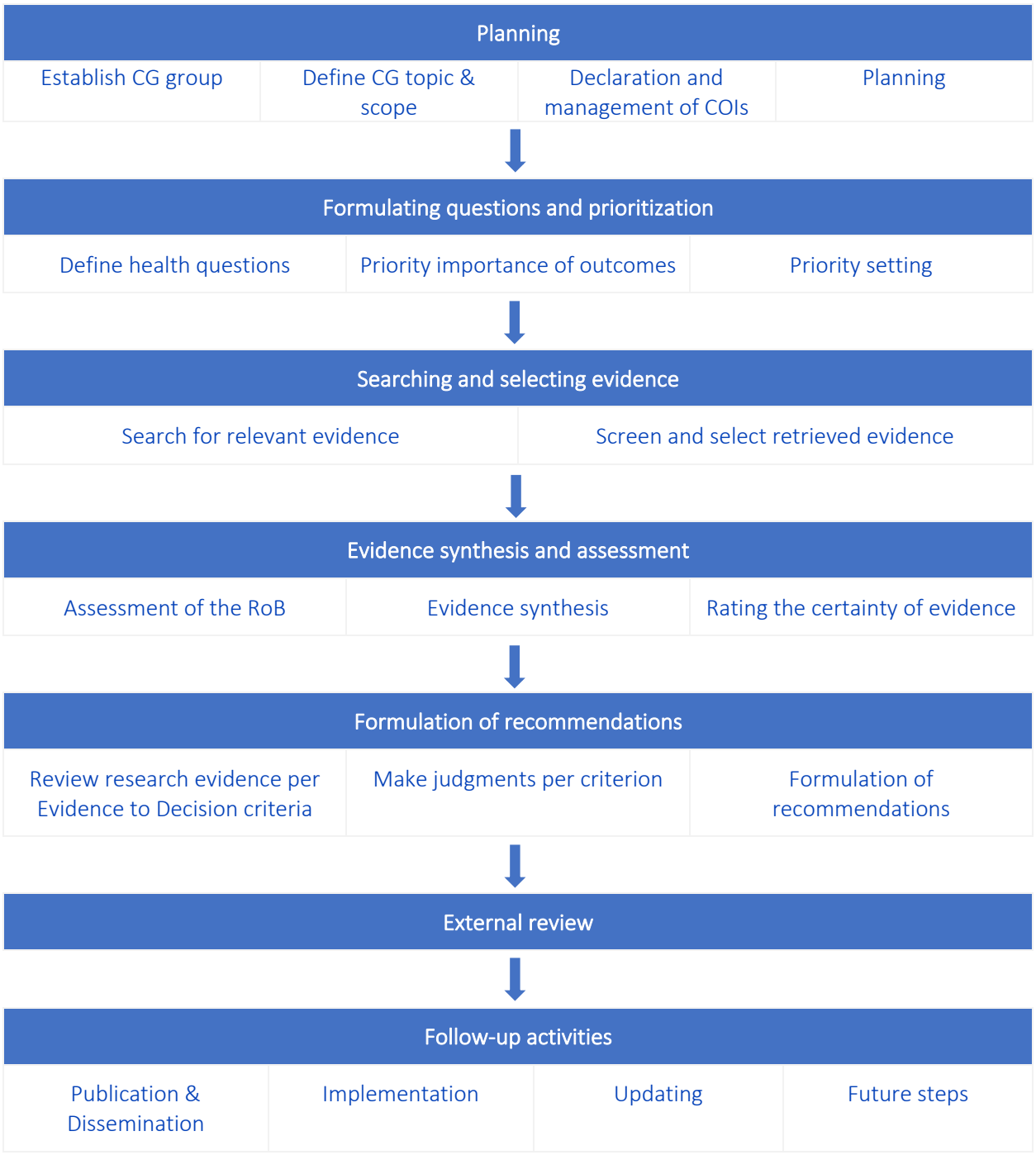


Figure 03. General steps in Clinical guideline development

CG: clinical guideline; COI: conflict of interest; RoB: risk of bias.

1.1.4 Quality of clinical guidelines

Apart from the advances in CG development methods, several tools and instruments have emerged to assess the quality of CGs, (Figure 02). In 2003, the Appraisal of Guidelines for Research and Evaluation (AGREE) collaboration developed and validated a quality assessment instrument for appraising the quality of CGs. The instrument was updated in 2010, as the AGREE II (36, 37). The AGREE II instrument consists of 23 items organised in six domains: 1) scope and purpose, 2) stakeholder involvement, 3) rigour of development, 4) clarity of presentation, 5) applicability, and 6) editorial independence (37). According to the authors, AGREE II aims to provide an innovative way for the development, reporting and evaluation of CGs (37).

In 2019, the ECRI Institute developed and tested the NGC (National Guideline Clearinghouse) extent of the Adherence to Trustworthy Standards (NEATs) instrument, based on the IOM standard for trustworthy CGs (1, 38). The NEATs instrument contains 15 items covering eight domains regarding funding source, management of COIs, CG development group composition, rigorous systematic review, recommendations formulation and strength of recommendations, presentation of recommendations, external review plans and updating (38). Since 2017, the NGC started displaying the adherence of NEATs instrument. However, due to shortage of funding, the NGC was out of service and it is unclear how has the NEATs tool been implemented (39).

With the advances in CG development methods and the implementation of the quality assessment instruments, CG developers paid more attention to rigour in CG development, and CG quality has improved gradually over the last two decades (40, 41). Two overviews of the quality assessment studies have showed an improvement in CG quality assessed with AGREE II instrument, mainly in the overall assessment (number of guidelines rated as recommended), and the domains of “Editorial independence” and “Rigour of development”(41). CG quality seems to still be improving. For example, a systematic assessment study of adult bronchiectasis CGs’ quality published in 2020 identified a progressive improvement in CG quality. The quality assessment rating of CG published after 2015 was significantly higher ($P<0.05$), improving from 27.7% to 58.3% (42). Another systematic assessment of fall prevention and management CGs published in 2021, found relatively good quality assessed with the AGREE II; mean total score is 80.1% (43).

Despite the improvement in CG quality with the implementation of the AGREE II instrument, some instrument domains keep scoring low (40, 41). For example, domain “Applicability” received a mean score

of 22% in SR published in 2010 (40), and 37.1% in SR in 2017 (41); domain "Editorial independence" showed similar suboptimal results, as the mean score was 30% in 2010, and 41.8% in 2017 (41). These results highlight the further necessity to improve recommendations' applicability and editorial independence. Furthermore, the quality of a CG does not guarantee that the recommendations are optimal. For example, Nuckols et al. assessed the clinical acceptability of recommendations of five high-quality CGs assessed with the AGREE II instrument (44) (36). Despite their apparent quality, the proportion of recommendations assessed as moderately comprehensive ranged from 50% to 69%, while the proportion assessed as valid ranged from 6% to 50%. Moreover, the recommendations of one high-quality CG were assessed as invalid overall (44).

In 2020, the AGREE collaboration developed and validated a new tool named AGREE-REX (Appraisal of Guidelines Research and Evaluation – Recommendations Excellence), to evaluate the quality of CG recommendations (45, 46). The AGREE-REX focuses on four domains, considered during the formulation of CG recommendations: 1) the evidence justification, 2) the clinical applicability, including clinical relevance, relevance to patients/populations, and implementation relevance, 3) the values justification, including guideline developer values, target user values, patient population values, policy values, and alignment of values, and 4) feasibility considerations, including local applicability, resources, capacity, and tools (45, 46).

1.1.5 Reporting clinical guidelines

1.1.5.1 Methodology for developing reporting guidance

Moher et al. in 2010 defined reporting guidance as *"a checklist, flow diagram, or explicit text to guide authors in reporting a specific type of research, developed using explicit methodology"* (47). Reporting checklists include a minimum set of criteria that indicates study design, process, analysis, to help readers interpret the study results and assess the validity of results (47, 48). Optimal reporting enhances health research accuracy, completeness, and transparency, ensuring its reproducibility reliability, avoiding potential ethical and moral issues, such as publication bias or selective bias (49, 50). Moreover, transparent and adequate reporting provides readers with a whole picture of health research, and helps interpret the research process and results, facilitating research uptake and benefiting healthcare services (47).

To provide a generic approach to how to develop guidance for health research reporting, Moher's et al. proposed a guide with 18 steps grouped in five phases, based on their development experience in over ten reporting checklists. The five phases include: 1) initial steps to identify the need for a CG, review and identify

information from literature, 2) pre-meeting activities to recruit participants, perform the Delphi exercise, generate a list of items, and prepare agenda with materials for a face-to-face meeting, 3) a face-to-face meeting to discuss relevant evidence and the inclusion rationale for each item, 4) post-meeting activities to develop the guidance statement with a publication strategy, and 5) post-publication activities, such as dissemination, updating and implementation (47).

1.1.5.2 Reporting checklist for clinical guidelines

The Reporting Items of Practice Guidelines in Healthcare (RIGHT) was developed to guide the reporting of *de novo* CGs, including essential items for the content of CG, recommendations, and supportive evidence (51). The RIGHT checklist was developed by an international multidisciplinary working group, adhering to methods for developing reporting checklist (49, 51). The RIGHT checklist contains a structured format following the order and format according to the CG developer's preferences, including seven sections, 21 specific reporting topics and 35 items. The sections are "Basic information", "Background", "Evidence", "Recommendations", "Review and quality assurance", "Funding and declaration and management of interests", and "Other information" (51). The RIGHT checklist has been translated into five languages, including simplified and traditional Chinese, German, Italian, and Japanese (52). It also gets endorsement by different peer-reviewed journals as reporting standards for publishing CGs (52).

The RIGHT checklist has produced extensions for different fields of clinical disciplines, and methodological research. Currently, published RIGHT extensions are the reporting checklist for acupuncture, traditional Chinese medicine, and public or patient versions of guidelines (51, 53, 54). Those checklists specify the reporting on relevant contexts; for example, in the extension for acupuncture and traditional Chinese medicine, the authors emphasised the reporting on the detailed manner of acupuncture and traditional Chinese medicine in the "Background", and "Evidence" sections (53, 55), while in the extension for public or patient versions of guidelines, the authors improved the reporting on the recommendations for patients, and provided alternative options when undesirable outcomes are available (54). Other extensions of the RIGHT statement are under development (56).

The AGREE Reporting Checklist is a reporting checklist for *de novo* CGs, developed by the AGREE Next Steps Consortium based on the AGREE II instrument, to improve the comprehensiveness, completeness, and transparency of reporting in practice guidelines (57). The AGREE reporting checklist retained the domains of AGREE II (Scope and Purpose, Stakeholder involvement, Rigour of development, Clarity of presentation,

Applicability, and Editorial independence), while indicating how to report specific contents (57). For example, item 7 in domain 3 of AGREE II instrument was modified from *"Systematic methods were used to search for evidence"* into *"Search methods: report details of the strategy used to search for evidence".*

The AGREE-REX reporting checklist was adapted from the AGREE-REX assessment tool, to guide the reporting of CG recommendations (45) (58). According to the authors, lower assessment scores using AGREE-REX may reflect suboptimal reporting. This tool, therefore, may guide the reporting of CG recommendations to ensure their clinical credibility and implementability (45, 46).

The Checklist for the Reporting of Updated Guidelines (CheckUp) is a reporting tool for updated CGs (59). CheckUp was developed by an international expert panel, following Moher's guidance, with several additional steps, to optimise the checklist content. The checklist contains 16 items, covering the presentation of updated CGs, editorial independence, and methodology of the updating process (59). CheckUp has been used to assess the completeness of reporting of updated CGs, and to inform the CG updating process (60, 61).

1.1.5.3 Completeness of reporting in clinical guidelines

The completeness of reporting in CGs assessed by the RIGHT checklist is suboptimal across different clinical disciplines (62-64). Three systematic assessments of the reporting in published CGs about colorectal cancer, lung cancer, and paediatric CGs, showed that the proportion of CGs that reported the sections of "Evidence" is lower than 50% (62-64). In addition, the proportion of CGs that reported the "Review and quality assurance" section, ranged from 12.2% to 29.9%, and the proportion reporting the "Funding and declaration and management of interests" section ranged from 24.1% to 42.9% (62-64). In addition, other studies found that optimal reporting in CGs is closely related with better quality CGs (64, 65).

Similarly, the completeness of reporting in updated CGs varies significantly among different organisations, and there is significant room for improvement (60). The assessment study on the reporting in updated CGs using CheckUp showed that the reporting for the presentation of updated CGs, and the updating methodology is suboptimal, scoring 5.7-5.8 out of a maximum score of 10 (59, 60). The reporting of the justification of updated recommendations, external review methods, and updating implementation strategy is specifically poor, lower than 40% of included CGs reported on those aspects (60).

1.1.6 Developing clinical guidelines in low- and middle-income countries

CG development process requires resources, including expert personnel, and it is often complex and time-consuming (3, 20). However, resources like methodologists or funding are often limited (66). Most low- and middle-income countries (LMICs) still do not have formal organisations, technical capacity, expertise or collaborations to develop evidence-based guidelines (67). Several studies have shown that LMICs lack appropriately developed CGs to assist healthcare professionals in their daily work. Consequently, healthcare providers in those settings tend to adapt CGs developed in high-income countries (HICs) (67, 68). Other CG organisations also start developing *de novo* CGs by retrieving existing CGs first to avoid duplication of effort (69).

Although CG adaptation has been used in LMICs for CG development, the quality of CGs developed in LMICs is generally suboptimal (70-72). For example, one quality assessment study on the CGs of the Southern African Ministries of Health using AGREE II observed that all identified CGs scored lower than 25% for the domains of 'Applicability', 'rigour of development' and 'editorial independence' (71). Another systematic assessment in Brazil showed that none of the assessed CGs was rated as high quality (72).

1.1.6.1 China as a case study

Since the 90s, CGs have been developed and used to inform clinical practice in the Chinese context, with an increasing number of published CGs (73, 74). Most Chinese CGs have been developed by the Chinese Medical Association, its branches or clinical expert committees (73-75).

During the last decade, from 2010 to 2020, the quality of Chinese CGs was suboptimal assessed with the AGREE II instrument and showed lower scores than western countries (73, 74, 76-79). Quality assessment studies on Chinese CGs using AGREE II found a 30% mean score for domains "stakeholder involvement", "rigour of development", "applicability", and "editorial Independence". A review on Chinese CGs also concluded that the general quality of Chinese CGs is lower than those of western countries and urgently needs to improve (74). Similarly, another comprehensive assessment study found that around 93% (186/200) of Chinese CGs for cardiovascular disease were developed based on only consensus statements, without any formal approach or systematically evidence synthesis (80). Few Chinese CGs were developed based on research evidence (16; 14.7%), while even fewer assessed the certainty of evidence (13; 11.9%) (76). Most Chinese CGs failed to consider essential factors (e.g., resources use, equity, acceptability, and

feasibility) when formulating recommendations. Consequently, the adherence to Chinese CGs among clinicians in China is also suboptimal and varies widely (81-83).

The CG adaptation process has been seldomly performed adequately and transparently in China (73, 75). Previous systematic assessment studies of Chinese CGs found that most CGs were developed based on source CGs from HICs, for example, CGs from the National Comprehensive Cancer Network (NCCN) in United States or the National Institute for Health and Care Excellence (NICE) in the United Kingdom (76). However, the process, including how existing CGs were assessed and adapted, is generally poorly reported, which may lead to lower ratings of the quality of Chinese CGs (75, 84, 85).

1.2 Adapted clinical guidelines

1.2.1 Definition and objectives

Adapted CGs are those CGs developed based on existing trustworthy CGs, with (adapt), without (adopt) modifications, or including *de novo* recommendations, to provide local, regional or national guidance (86, 87). CG adaptation can be used as an alternative method to develop *de novo* CGs, or as the first step of an implementation process of CGs, while preserving evidence-based principles by following a similar or systematic approach as the source CGs (86).

CG adaptation aims to improve the efficiency of the CG development process, saving time and resources. Based on existing CGs, the adaptation process may avoid duplicated efforts on evidence retrieving, synthesis, appraisal, etc. (66, 69, 86). In addition, CG adaptation facilitates the development of contextualised recommendations, as it allows the consideration of local contextual factors, including language, relevant stakeholders' cultural and ethical values, healthcare setting, accessibility, and availability of health services and resources (88-90).

1.2.2 Methodology for adapting clinical guidelines

CG adaptation frameworks have gradually evolved over the last three decades, along with the improvement of CG development methods, including initial adaptation frameworks and advanced adaptation frameworks that are based on the GRADE approach (Figure 04) (86, 88, 91, 92). CG adaptation methods include general steps for adapting CGs, while adaptation frameworks provide structured format for approaching CG adaptation (93).

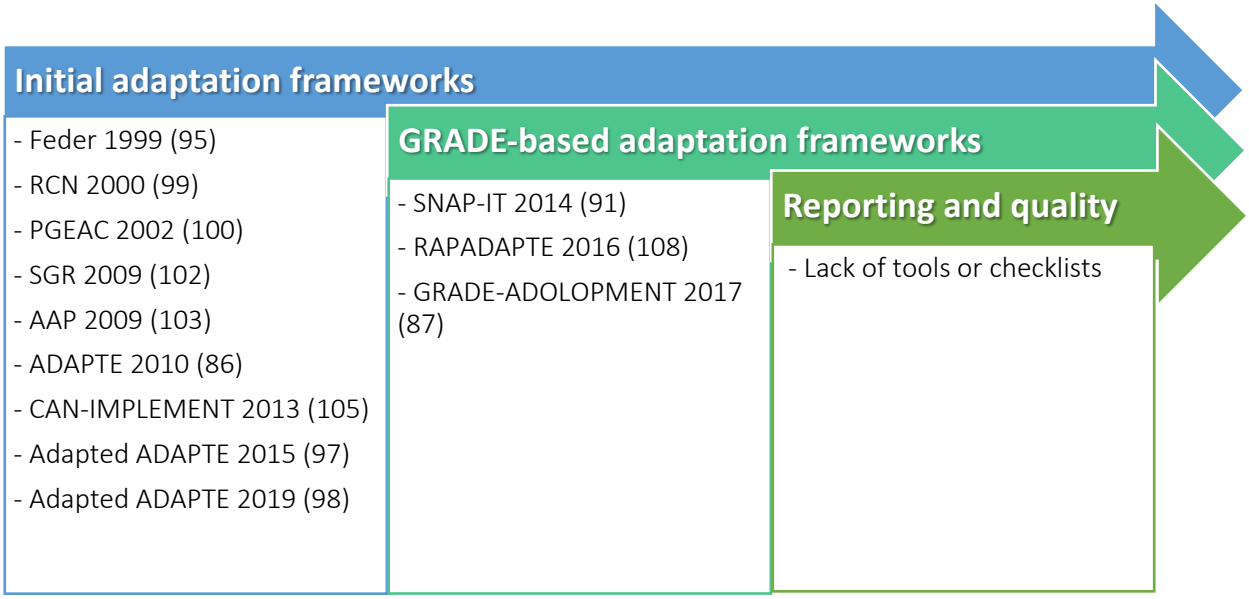


Figure 04. Clinical guideline adaptation methods

AAP: Alberta Ambassador program; ADAPTE: Resource Toolkit for Guideline Adaptation; CAN-IMPLEMENT: framework for guideline adaptation and implementation; GRADE-ADOLOPMENT: GRADE Evidence to Decision frameworks for adoption, adaptation, and de novo development of trustworthy recommendations; PGEAC: Practice Guideline Evaluation and Adaptation Cycle; RAPADAPTE: for rapid guidelines; RCN: Royal College of Nursing; SGR: Systematic Guideline Review.

1.2.2.1 History of adaptation frameworks

As shown in Figure 04, the concept of adaptation was brought into the CG concept in 1999 when CG were used to solve clinical questions, to save time and resources (94, 95). After a decade of exploration of the initial CG adaptation frameworks (e.g., PGEAC 2002 and AAP 2009), Fervers et al. developed and validated an adaptation framework in 2010, named ADAPTE, which has been widely implemented (86, 96). Since then, several modified versions of ADAPTE and other frameworks have been developed, based on real-life adaptation experiences from different countries or incorporating implementation considerations (92, 97, 98).

In 1999, Feder et al. discussed using CGs to improve clinical effectiveness within a series of publications (95). They stated that CG developers should identify existing rigorous developed CGs and adapt them for local use if CG organisations did not have the resources and skills to develop valid CGs. The proposed methods for adaptation include: 1) finding valid CGs to use, 2) appraising CGs, and 3) adapting valid CGs by reformatting the recommendations (95).

In 2000, Rycroft-Malone et al. described an alternative strategy for the local CG development process of the Royal College of Nursing (RCN), adapting existing CGs to local circumstances (99). This adaptation framework contains five key steps to identify source CGs and, based on them, to develop a national CG for local use. The steps included: 1) identifying a priority topic, 2) locating a guideline on the chosen topic, 3) appraising the quality of the CG, 4) appraising the applicability of the clinical guideline for local use, and 5) adapting it for local use (99).

In 2002, Graham et al. described a framework named Practice Guideline Evaluation and Adaptation Cycle (PGEAC) that healthcare organisations and groups could follow to evaluate and adapt existing CGs for local use (100). According to the authors, CG adaptation groups could conduct the CG adaptation process by: 1) adopting the entire CG with all recommendations, 2) adopting and endorsing some recommendations from specific CGs, for example, not endorsing recommendations that lack robust evidence or cannot be implemented or adapted for local use, or 3) developing new CGs by adopting or adapting the best-fit recommendations from different source CGs (100). The PGEAC framework includes ten comprehensive steps: 1) identify a clinical area in which to promote best practice, 2) establish a local interdisciplinary guideline evaluation group or task force, 3) establish a guideline appraisal process, 4) searching and retrieval of guidelines, 5) guideline appraisal, 6) adaptation of existing guidelines for local use, 7) external review of the proposed local guideline, 8) finalise the local guideline, 9) official endorsement and adoption of the guideline by the organisation, and 10) scheduled review and revision of guidelines (100, 101).

In 2009, Muth et al. proposed an adaptation framework named Systematic Guideline Review (SGR) as a new approach to developing CGs through retrieving, assessing, and summarising existing CGs (102). The SGR framework contains nine steps: 1) systematic search CGs, 2) selection of existing CGs according to predefined criteria, 3) assessment of the methodological quality of the included guidelines, 4) development of the question framework, 5) data extraction, 6) consistency analysis, 7) information synthesis, 8)

validation, and 9) formulation of the draft guideline and identification of evidence gaps for further research (102).

In the same year, Harstall et al. reported an adaptation framework derived from the Alberta Ambassador program (AAP) for low back pain CG (103). This framework provides an alternative way to develop a single overarching CG for a specific topic, including: 1) identifying and recruiting adaptation group participants, 2) formulating research questions according to local need, 3) identifying and screening source guidelines, 4) appraising source guidelines, 5) extracting data into evidence inventory tables, 6) drafting guideline document for general process, including dealing with inconsistencies through ad hoc subcommittees, rationale and process for developing and classifying recommendations, 7) reviewing and refining the draft guideline, 8) finalising and endorsing the guideline, 9) disseminating guideline, 10) planning update, and 11) next steps.

In 2010, Fervers et al. developed and validated an adaptation framework, and developed the Resource Toolkit for Guideline Adaptation – ADAPTE (86). ADAPTE is the first comprehensive adaptation framework, that provides a stepwise and systematic process for adapting source CGs to local use, aiming to improve the efficiency of CG development and utilisation (86). The ADAPTE framework for CG adaptation was developed based on a literature review and a validation process (86). ADAPTE contains 24 steps grouped into three stages, with nine modules, covering: the preparation, scope and purpose, search and screen of source CGs, assessment of recommendations, decision and selection of adapted recommendations, customisation, external review and acknowledgement, and follow-up activities (Table 03) (86). In 2014, the usability of ADAPTE was evaluated by an Australian research team, concluding that there are several challenges for using this tool, including the lack of clarity of the required expertise and resources and the efficiency of the CG adaptation process (104).

Table 03. ADAPTE framework outline*

Phases	Modules	Steps
Set-Up	Preparation module	Step 1. Establishing an organising committee
		Step 2. Selecting a guideline topic
		Step 3. Checking whether adaptation is feasible
		Step 4. Identifying necessary resources and skills
		Step 5. Completing tasks for the set-up phase
		Step 6. Writing adaptation plan
Adaptation	Scope and purpose module	Step 7. Determining the health (clinical/policy questions)

	Search and screen module	Step 8. Searching for guidelines and other relevant documents
		Step 9. Screening retrieved guideline
		Step 10. Reducing the number of retrieved guidelines
	Assessment module	Step 11. Assessing guideline quality
		Step 12. Assessing guideline currency
		Step 13. Assessing guideline content
		Step 14. Assessing guideline consistency
		Step 15. Assessing acceptability/applicability of the recommendations
	Decision and selection module	Step 16. Reviewing assessments
		Step 17. Selecting guidelines and recommendations to create an adapted guideline
	Customisation module	Step 18. Preparing draft adapted guideline
Finalization	External review and acknowledgement	Step 19. External review by target users
		Step 20. Consulting with relevant endorsement bodies
		Step 21. Consulting with developers of source guidelines
		Step 22. Acknowledging source documents
	Aftercare planning module	Step 23. Planning scheduled review and update of an adapted guideline
		Step 24. Final production including producing final guidance document

* Adapted from ADAPTE framework (67)

Five years later, Amer et al. adapted in 2015 the ADAPTE framework based on the real-life CG adaptation experience in Egypt, for the context of paediatrics and emergency medicine (97). The same authors validated this framework in Saudi Arabia in 2019 (98). The adapted ADAPTE framework follows the same steps as the ADAPTE, with additional updated tools for eligible criteria, a decision support table, and a postgraduate thesis support tool.

In 2013, Harrisons et al. proposed a framework for guideline adaptation and implementation named CAN-IMPLEMENT, based on the ADAPTE framework and the Knowledge-to-Action model (86) (105), to provide practical assistance, by augmenting the ADAPTE framework with experiences and needs of user groups and facilitation elements (106). CAN-IMPLEMENT framework focuses on the contextualisation process and implementation considerations, comprising three phases: 1) identification, appraisal, and adaptation of existing knowledge, and clarification of the practice issue, 2) solution building to align adapted knowledge with the local practice environment or context, and 3) solution implementation, evaluation and sustainability (106). In 2016, an online software named CAN-IMPLEMENT.pro was developed to operate the knowledge-to-action (KTA) model and to improve its dissemination and utilisation (107).

1.2.2.2 Advances of adaptation frameworks

As shown in Figure 04, CG adaptation frameworks have advanced notably by considering methods used in source CGs, including the GRADE approach, the GRADE EtD frameworks (87, 91, 108).

In 2014, the SNAP-IT project was launched to develop an adaptation framework, by combining the ADAPTE and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (91). It combines a five-step adaptation process into the Making GRADE the Irresistible Choice (MAGIC) app, improving the efficiency and transparency of the adaptation process. The steps are: 1) planning, including establishing an editorial committee, choosing topics to adapt, choosing chapter editors, convening start-up conference, and plan implementation strategies, 2) initial assessment of the recommendations, including COI of panellists, 3) modifications of recommendations, including the updated search for new documentation, submission of the final draft to the editorial committee, and peer review, 4) publication, and 5) evaluation and planning for the future, including evaluation of the adaptation process, and future updates (91).

In 2016, the RAPADAPTE framework was created based on the CG development and adaptation experience in the context of breast cancer in Costa Rica (108). This framework includes ten steps, and goes into detail about the supportive evidence for each recommendation and the assessment of the quality of the evidence, including: 1) identifying and selecting team and schedule resources, 2) training team members, 3) defining clinical questions, 4) identifying candidate guidelines for adaptation, 5) selecting most useful guidelines, 6) identifying existing summarised evidence for each clinical question, 7) searching for evidence for clinical questions for which existing summarised evidence is inconsistent or lacking, 8) grading the quality of the body of evidence for each question, 9) creating draft recommendations considering the body of evidence for benefits and harms, values, preferences and costs, 10) sharing draft recommendations and supporting evidence with expert review panels, 11) adjusting recommendations, and 12) external review process (108).

In 2017, the GRADE WG put forward the GRADE-ADOLOPMENT (GRADE Evidence to Decision frameworks for adoption, adaptation, and *de novo* development of trustworthy recommendations) approach, building on the advantages of source CGs developed with GRADE EtD frameworks, adapting, adopting, or developing additional *de novo* recommendations (87). These EtD frameworks enable adapting recommendations or healthcare decisions to specific context, and facilitate the consideration of priority problems, benefits and

harms, the certainty of the evidence, the importance of healthcare problems, patients' values and preferences, resource use, equity, acceptability, etc. (35, 87).

CG adaptation has also been included in organisational handbooks or CG development standards. In 2014, WHO updated their CG development standards, and indicated adapted CG as one type of WHO guidelines (3). WHO considers adapting CGs when appropriate, for example, in the case that a WHO guideline does not exist, an existing WHO CG is outdated, and the source CGs have met the minimum WHO standards (3).

In 2016, the Australian National Health and Medical Research Council (NHMRC) included CG adaptation into the NHMRC Standards for Guidelines development (109). The adaptable components for adopting or adapting are CG questions, evidence tables, a summary of findings table, GRADE EtD frameworks, evidence statements, recommendations, and supporting contents (109). The NHMRC adaptation method includes: 1) finding out what CG is available, 2) checking if a guideline is suitable to adopt or adapt regarding relevance, currency, trustworthiness, access to evidence, implementability, and applicability, 3) deciding which parts of the CG to adopt or adapt, and 4) adopting or adapting a CG or its recommendations.

1.2.2.3 Variability of adaptation frameworks

Two studies have recently systematically reviewed published adaptation frameworks and identified several similarities and differences between CG adaptation frameworks (89, 93). In 2017, Darzi et al. reviewed eight CG adaptation frameworks published from 2000 to 2017, and found a similarity in the initial and final phases, including: planning, the external review process, dissemination and updating strategy, and concluding notable differences in the adaptation phase (89). In 2018, Wang et al. analysed published adaptation frameworks from 2002 to 2017 (93), concluding that the limitations of adaptation frameworks need to be optimised to ensure the adapted recommendations remain evidence-based. However, the authors found differences between published adaptation processes regarding the committee structure, selection of adaptation panels, evaluation of source materials, and formulation of recommendations (93). As there are no adaptation standards that could ensure the minimal critical criteria for the adaptation process, it is unclear whether the variability in specific steps between the adaptation frameworks will affect the quality of adapted CGs (93). Furthermore, the development process of published CG adaptation frameworks is also different. Most of them were developed from real-life adaptation experience, without a formal validation process (93), for example, the AAP framework or the adapted ADAPTE framework (97, 103).

1.2.2.4 Main adaptation steps

Despite the variability across CG adaptation frameworks, there are common steps for adapting CGs, such as identifying and evaluating source CGs and recommendations (93). The comparison of main steps between adaptation frameworks is listed in Table 04. Adapted ADAPTE has not been included as it has similar main steps as ADAPTE. The main steps for adapting CGs are summarised in Figure 05, including: 1) planning, 2) defining the health questions, 3) searching and selecting source CGs, 3) source materials assessment, 4) formulation of recommendations, 5) external review process, and 6) follow-up activities (i.e., publication and dissemination, updating and future steps) (86, 93, 105).

Table 04. Main steps of adaptation frameworks (2010-2017)

Main steps		ADAPTE, 2010 (86)	CAN-IMPLEMENT, 2013 (106)	SNAP-IT, 2014 (91)	RAPADAPTE, 2016 (108)	GRADE-ADOLOPMENT, 2017 (87)
Planning	**Establish CG adaptation group**	Establish an organising committee	Call to action	Establish an editorial committee	Identify and select team and schedule resources	Establish groups and define roles, including COIs.
	Choose CG topic	Select a guideline topic	-	Choose topics to adapt	-	Select guideline topics and source CGs
	Planning	Check whether adaptation is feasible	Guideline development plan	Choose chapter editors	Train team members as needed in content domain and evidence-based methodology	General organisation and planning
		Identify necessary resources and skills	-	Convene start-up conference	-	-
		Complete tasks for the set-up phase, including COI	-	Plan implementation strategies	-	-
		Write adaptation plan	-	-	-	-
Defining questions	**Define health questions**	Determine the health (clinical/policy) questions and target settings	-	-	Define clinical questions	Prioritize questions from selected source CGs by the panel
Selection of source CGs	**Search and select source CGs**	Search for CGs and other relevant documents and Screen retrieved CGs	Search and screen	-	Identify candidate guidelines for adaptation	-
	Prioritize the source CGs	Reduce a large number of retrieved CGs	-	-	Select most useful guidelines for adaptation	-
	Assessment of source CG	Assess CG quality	Assess and select	-	-	-
Source materials assessment	**Assessment of source recommendation content**	Assess CG content	-	Initial assessment of the recommendation, including COI of panelists	-	-
		Assess acceptability/applica	-	-	-	-

		bility of the recommendations				
		Assess CG consistency	-	-	-	-
	Assessment and updating source evidence	Assess whether source evidence is up to date	-	-	Identify existing summarised evidence for each clinical question	-
		-	-	-	Search for evidence for clinical questions where existing summarised evidence is inconsistent or lacking	Update systematic reviews of health effects and identifying local data
		-	-	-	Grade the quality of the body of evidence for each question	Prepare GRADE evidence tables and being reviewed by expert panel
	Assessment of evidence to decision factors	-	-	-	-	Checking the EtD frameworks availability of source CGs
Formulation of recommendations	**Review assessment results**	Review assessments	-	-	-	-
	Adapt, adopt or develop de novo recommendations	Select among CGs and recommendations to create an adapted CG	-	Modifications, including updated search for new documentation	-	Completing the GRADE EtD frameworks
	Formulation of the adapted recommendations	Prepare draft adapted CG	Draft, revise, and endorse	Submission of final draft to the editorial committee	Share and adjust draft recommendations based on expert review panel	Formulating recommendations through consensus or voting
External review	**External review process**	External review by target users	-	Peer review	External review	-
		Consult with relevant endorsement bodies	-	-	-	-
		Consult with developers of source CGs	-	-	-	-
		Acknowledge source documents	-	-	-	-
Follow-up activities	**Dissemination**	-	-	Publication	-	-
	Implementation	-	Select and tailor implementation interventions Assess barriers and facilitators to knowledge use Align knowledge to local context practice and system	-	-	-
	Updating	Plan scheduled review and update of adapted CG	-	-	-	-
	Future step	Produce final guidance document	Evaluate outcomes and nature change, and sustain knowledge use	Evaluation and planning for the future	-	-

CG: Clinical guideline; COI: Conflict of Interests; EtD frameworks: Evidence to Decision frameworks; GRADE: Grading of Recommendations, Assessment, Development and Evaluations; WG: Working group.

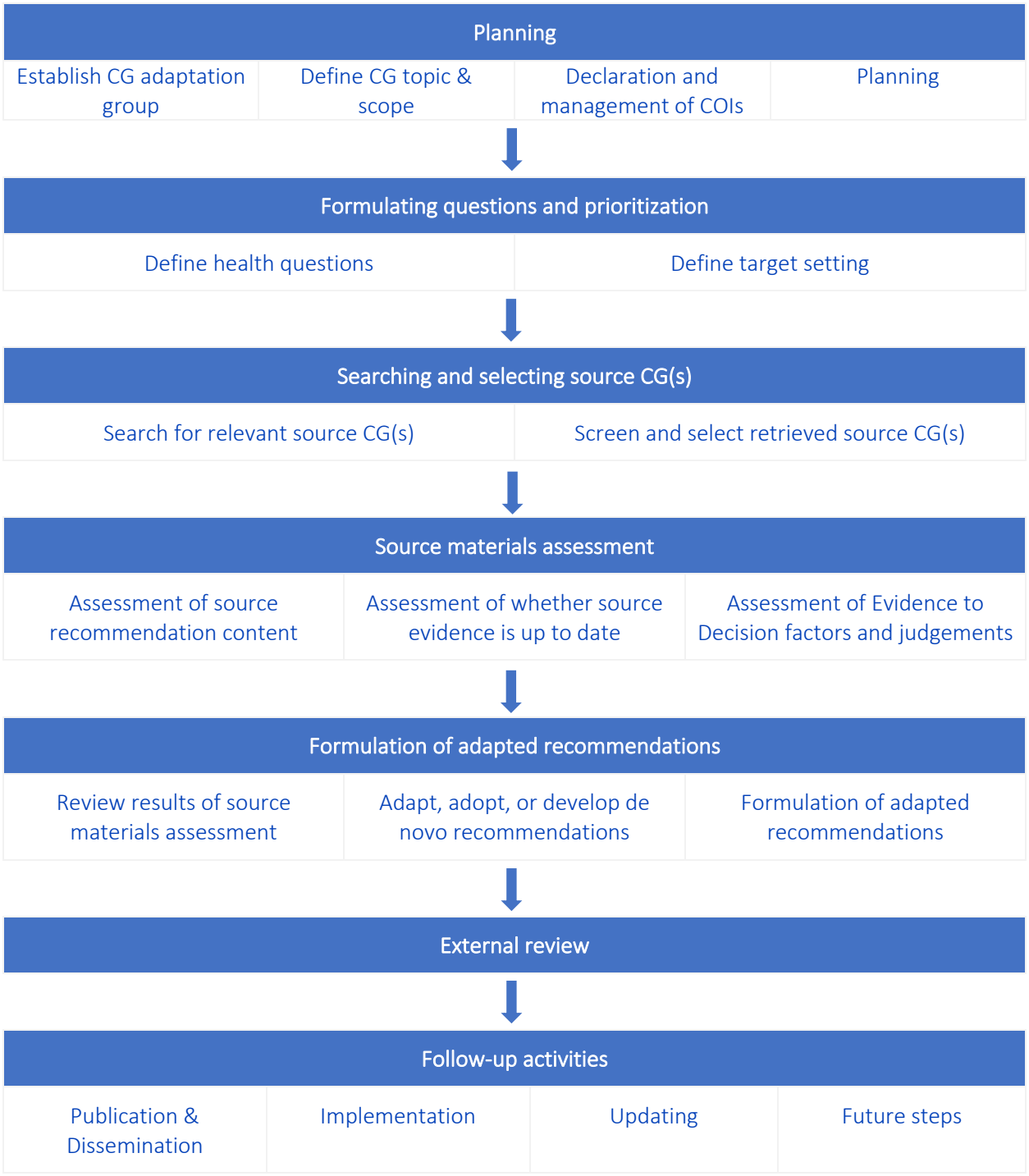


Figure 05. Main steps of adaptation frameworks

CG: Clinical guideline; COI: Conflict of Interests

1) Planning

Before the CG adaptation process starts, a multi-disciplinary adaptation group should be established, including the management of COI of all group members. In addition, a clinical area or health topic should be identified in the early stage of the CG adaptation process (5, 105). Several CG adaptation frameworks also involve a planning stage for the appraisal process of source CG(s), the feasibility assessment of the adaptation process, necessary resources and skills, start-up conference, or writing up adaptation or implementation strategies (86, 91).

2) Defining the health questions

CG adaptation group needs to specify the health questions for the adapted CG based on 1) the need of the target context (86, 100, 102), or 2) a high-quality CG with an aligned scope and health questions (87, 91). In addition, the ADAPTE framework also suggested specifying the target setting for the clinical questions defined (86).

3) Search and selection of source CGs

Given that the quality of adapted CGs relies on the source CGs, the selection of source CG(s) should follow a rigorous process. The selection process of source CGs mostly depends on the CG quality and other criteria, such as whether source CGs apply to the target setting. Different tools are helpful for assessing the quality of source CGs, for example, the AGREE II (37). Some CG adaptation groups also lean towards adapting CGs developed by well-known organisations or use rigorous methodology such as the GRADE approach, instead of searching and selecting source CGs through a comprehensive process (87, 91).

4) Source materials assessment

Once the source CGs are selected, an assessment process of source recommendations will take place. The crucial aspects are to assess recommendations' content, the linkage between evidence and recommendations, the interpretation of the evidence, the Evidence to Decision factors and judgements from source CGs, if available (86, 87, 103). If the evidence is outdated or did not sustain with the target context, updating or supplementing with new evidence would need to be considered.

5) Formulation of recommendations

According to the assessment results, the CG adaptation group discusses the assessment results, based on which to select the recommendations and decide whether to adapt, adopt or develop *de novo* recommendations for local use. The three recent CG adaptation frameworks formulate the recommendations by updating evidence, completing or refining the EtD frameworks, and reaching consensus with the CG panel (87, 91, 108).

6) External review

Considering the potential limitation of the representativeness of the included experts and perspectives in the guideline group, CG adaptation groups should conduct an external review or peer review process to ensure its comprehensiveness (1, 86, 91, 100). External reviewers may include different professionals or relevant stakeholders (e.g., CG users, clinical experts, allied organisations, etc.). Based on the feedback received from the external review, CG adaptation groups may improve and finalise the adapted CGs.

7) Follow-up activities

Follow-up activities include a dissemination strategy, updating plan, and future steps. The dissemination of adapted CGs could be an official endorsement of the adapted CG, by national or local organisations or a scientific publication. CG adaptation groups should also plan and report the future updating strategy, and further steps (86, 91, 100, 102, 103).

1.2.3 Quality of adapted clinical guidelines

Currently, there is no specific tool for assessing the quality of adapted CGs and the rigour of the CG adaptation process. As AGREE II exists for general appraisal of CG quality, some authors applied the AGREE II to assess the quality of adapted CGs (96). However, the AGREE II was not explicitly developed for adapted CGs, and it might not fully address all the aspects required for a rigorous adaptation process, for example, how the adapted recommendation was formulated.

A systematic survey evaluated the quality of published adapted CGs using the AGREE II and ADAPTE framework, and found that the quality of adapted CGs is suboptimal (96). The mean score assessed with the AGREE II was 57% for the "rigour of development" domain, and 50% for the "applicability" domain; meanwhile, the adaptation processes have poor adherence to the ADAPTE, especially to the step of source materials assessment. Less than 30% of adapted CGs assessed the quality of source CGs, and the coherence

between recommendations and supporting evidence, while less than 10% of adapted CGs assessed the consistency of recommendations content (96). Another assessment on the adaptation process of WHO CGs, found a similarly low adherence to the ADAPTE framework; out of 32 adapted CGs that reported their adaptation methodology used, around 50% followed the set-up steps in ADAPTE, but no CG followed all the steps in ADAPTE (96).

1.2.4 Reporting adapted clinical guidelines

Similarly to the lack of quality assessment tools for adapted CGs, the reporting of adapted CGs has not been standardised yet, despite the fact that previous CG adaptation frameworks have included some reporting components (86, 87). The ADAPTE framework included reporting components as a supplementary tool under the "ADAPTATION PHASE – Customization module", specifically for the general presentation format of adapted CGs (86). These reporting components cover the overview material, introduction and background, scope and purpose, target audience, health questions, recommendations, supporting evidence, external review, updating, summary, implementation, and editorial independence. As the reporting components are supplements of the ADAPTE resource toolkits, they have no specific guidance, and it is unclear how the supplementary tool is developed and implemented.

The GRADE-ADOLOPMENT framework provides a presentation format to record judgements on the factors of EtD frameworks during the assessment of source materials. However, as the GRADE-ADOLOPMENT relies on the EtD factors considered by source CGs, it may apply only to the adaptation of source CGs that have used the GRADE approach and provide details on the judgments made on the different EtD factors (35, 87).

The reporting of adapted CGs is considered suboptimal, assessed according to the adherence to published adaptation frameworks (96, 110). A systematic survey on the methods used for adapted CGs found that out of 72 adapted CGs included, 57 did not report any type of detail about the adaptation methods used, and only 23 reported using specific adaptation methods (23/57; 40%) (96). Another assessment on the national adaption of WHO CGs, similarly found poor reporting of adapted WHO CGs: out of 170 eligible adapted CGs, only 32 (19%) reported the methods used when adapting (110).

1.2.5 Adapting clinical guidelines in low- and middle-income countries

As adapting CG intends to save time and resources while retaining good quality, it is supposed to be an efficient and promising option to develop high-quality, evidence-informed CGs for LMICs to optimise healthcare (69, 86, 87). For example, in Tanzania, before the adaptation of international high-quality CGs for local use, the stillbirth rate during maternal and perinatal periods is relatively high in the low-resource tertiary hospital. However, after 12 months of implementation of locally adapted international CGs, the stillbirth rate decreased by 34%; meanwhile, the knowledge and skills of local healthcare practitioners significantly improved (111).

Unfortunately, only few CG adaptation frameworks have been applied in resource-constrained settings (93). A SR on the advantages and limitations of CG adaptation frameworks showed that most of the CG adaptation frameworks were developed and implemented by HICs. Meanwhile, only one CG adaptation framework (i.e., adapted ADAPTE) has been implemented in a LMIC – Egypt (93, 97). However, the local adaptation process might not be trustworthy if it does not follow any CG adaptation frameworks. In this case, local clinicians are unlikely to adhere to adapted CGs, consequently hindering its implementation (83). Take maternal health and COVID-19 as examples; there are international recommendations for healthcare interventions; however, in LMICs, the fundamental gaps between the clinical practice and the global recommendations still exist (112, 113). Therefore, the adaptation of high-quality and trustworthy CGs at national and regional level are urgently needed in resource-constrained settings, following a standardised and pragmatic adaptation methodology (112).

1.3 Justification

1.3.1 Justification of the research topic

Clinical guidelines (CGs) have been increasingly used to provide guidance for clinical practice and to minimise clinical practice variation (3, 5). Methodology of CG development has improved gradually over the years, and has become more systematic and rigorous in the last two decades (40). However, it has also become a very resource-intensive process, and organisations struggle to develop rigorous guidelines and keep their portfolios up to date, especially in resources-constrained settings. Therefore, CG adaptation has been proposed to be an efficient alternative to develop high-quality CGs with contextualised recommendations (66, 67, 86, 88).

CG adaptation methods are less well-developed compared to guideline development. Furthermore, the quality of adapted CGs is relatively low. Despite over eight published CG adaptation frameworks being available, most of the published adapted CGs do not follow a published adaptation framework (89, 93). Little is known about the reason for the low quality of adapted guidelines and the poor adherence to different adaptation frameworks. In addition, as opposed to guideline development, there is no reporting guidance to ensure transparency of the adaptation processes. More methodological research is warranted to improve and standardise the methodology of adapted guidelines, including the reporting.

1.3.2 Justification of the publications

Justification of study I

CGs in China have been consistently evaluated as low quality and poorly adhered by clinicians (74, 79, 81, 82). Although most Chinese CGs were developed based on existing CGs, the reporting of the CG development and adaptation process has been suboptimal, hindering the improvement of Chinese CG quality. Therefore, it is important to clarify the current methods Chinese CG development organisations have been using for CG development, adaptation and updating practices at the national level, identify the gaps, and suggest potential solutions.

Justification of study II

CG adaptation frameworks have noticeable variability among adaptation phases, and the practice for adaptation is unclear. Furthermore, although more than one adaptation framework has been implemented internationally, adapted CGs are generally of poor quality (89, 93). Consequently, fundamental gaps exist between international recommendations on healthcare interventions and realistic best practices, highlighting the need to better understand the global adaptation experience (97, 104). Therefore, a deep assessment of CG adaptation current practice and challenges is necessary.

Justification of study III

Transparent reporting in adapted guidelines could ensure the rigour, clarity, and reproducibility of the adaptation process, and improve the credibility and reliability of adapted CGs (114). However, the completeness of reporting for adapted CGs is suboptimal, and there is no existing reporting guidance to standardise and improve the reporting of adapted CGs. Although the Reporting Items for practice Guidelines in HealThcare (RIGHT) statement (51) can inform the reporting of CGs developed in general, it

fails to cover essential steps of the adaptation process. Therefore, there is a need for a well-developed reporting checklist to ensure rigour, transparency, clarity, and reproducibility of the adaptation process.

2. OBJECTIVES

2 Objectives

2.1 Main objective

This thesis aims to produce new knowledge on the methodology and reporting of CG adaptation, by investigating national CG development and adaptation methods, exploring the current practice and challenges of CG adaptation internationally, and developing a reporting checklist for adapted CGs.

In study I, we conducted a national survey in a middle-income country, China, to collect data on CG development methods, understand how CGs are developed, adapted, and updated. We aim to gain more insight into the methodology used by Chinese CG developers, and provide potential strategies to improve CG quality in China, and similar LIC settings.

In study II, we conducted a qualitative analysis based on semi-structured interviews, with international CG adaptation experts. On the one hand, to better understand the current practice of CG adaptation and identify main challenges, and on the other hand, to inform the development of the reporting checklist for adapted CGs.

In study III, we developed a reporting checklist based on the RIGHT statement to ensure rigour, transparency, clarity, and reproducibility of adapted guidelines.

2.2 Specific objectives

- To explore how CGs are developed, adapted, and updated in China.
- To explore the current practice of CG adaptation, and identify main challenges faced by organisations.
- To develop a reporting tool for adapted CGs in healthcare.

3. METHODS

3 Methods

3.1 Study I. "The development of clinical guidelines in China: insights from a national survey"

3.1.1 Design

Cross-sectional online national survey.

3.1.2 Participants

We conducted a survey with key informants and experts affiliated with CG development organisations, and expert committees that had developed Chinese CGs in the past three years. We adopted a purposive sampling method to recruit participants, identified as follows: 1) corresponding contacts of affiliated CG development organisations, 2) recommendations from Chinese CG developers, and 3) recommendations from Chinese clinical discipline experts.

3.1.3 Data collection

We developed a self-administered questionnaire based on several methodological and evaluation resources (11, 35, 37, 59, 86). The questionnaire consisted of 45 items in five sections: 1) characteristics of the organisation, 2) de novo CG development, 2) CG adaptation, 3) CG updating and monitoring, 4) conflict of interest (COI) management, and 5) funding. A free-text box in 33 items collected additional information and comments. We piloted and refined the questionnaire based on the feedback received. We used online software to design the questionnaire and collect responses. We invited participants through email or WeChat message. On receiving consent from the participants, we sent the survey link by email or WeChat.

3.1.4 Data analysis

We performed a descriptive analysis of quantitative data (absolute frequencies and proportions). We stratified CG development as de novo or adaptation. We hypothesized that using a CG development methodology handbook would be associated with a more rigorous development process (Pearson's chi-square test or Fisher's exact test, alpha was set at 0.05). For qualitative data, one author coded the data and extracted themes related to CG de novo development or adaptation, and another author double-

checked the codes and the corresponding quotations. The most relevant topics, raised by respondents in free-text areas of the questionnaire, were selected based on consensus among three authors.

3.2 Study II. "Current practices and challenges in adaptation of clinical guidelines: A qualitative study based on semi-structured interviews"

3.2.1 Design

Qualitative study based on semi-structured interviews.

3.2.2 Participants

We sampled a group of CG developers, who had been involved in CG adaptation over the past three years. We identified potential participants from: 1) attendees of the 2019 GIN conference, 2) authors of published adapted CGs, and 3) suggestions from the advisory group of the RIGHT-Ad@pt project. We continued recruitment and data collection until no new information emerged.

3.2.3 Data collection

We designed an interview guide that included four sections: 1) characteristics of participants, 2) characteristics of participants' CG developing organisations, 3) participants' experiences about current practice in the CG adaptation process, and 4) participants' views and experiences about challenges in the adaptation process. We audio-recorded each interview with the participant's permission and transcribed them verbatim.

3.2.4 Data analysis

For quantitative variables, we calculated absolute frequencies and proportions. For qualitative data, we conducted a framework deductive analysis, including the following steps: 1) generation of a priori thematic framework for the main steps of adaptation processes, 2) identification of additional concepts from the methodological evidence provided by participants, 3) codification of semi-structured interviews findings against the resulting thematic framework, revised and merged codes into themes as new aspects emerged, and 4) proposed subthemes under the drafted thematic framework. For participants' views and experiences about challenges, we applied an inductive thematic analysis, including: 1) codification of the interview transcripts 'line by line', 2) proposed descriptive themes following the coding process, and 3) generated analytical themes by analysing, organising, and creating descriptive subthemes. One author coded and extracted qualitative data, and two other authors double-checked selected codes and the

corresponding quotations. One author drafted the framework and proposed themes, and another author reviewed the framework and themes. We used Nvivo for the qualitative analysis.

3.3 Study III. "A reporting tool for adapted guidelines in health care: the RIGHT-Ad@pt checklist"

3.3.1 Design

We followed a multi-step process to develop the RIGHT-Ad@pt checklist, including establishing a Working Group (WG), generating an initial checklist, optimising the checklist (through an initial assessment of adapted CGs, semi-structured interviews, a Delphi consensus survey, an external review, and a final assessment of adapted CGs), and approval of the final checklist by the WG. A detailed description of methods is available in a previously published protocol (Appendix I) (115).

Establishment of the RIGHT-Ad@pt Working Group

The RIGHT-Ad@pt Working Group included the coordination team, advisory group, and Delphi panel. We collected the conflicts of interests of all members involved in the RIGHT-Ad@pt Working Group to manage the participation of members. After each step of the development process, the coordination team discussed the results, drafted a report, agreed on major or minor modifications, produced a new version of the checklist, and refined with the advisory group's feedback.

Generation of the initial checklist

The coordination team generated the initial version of the checklist through online discussions, based on the RIGHT statement (51), research evidence in the field (89, 93, 96, 110, 116), and advisory group's feedback.

Optimisation the checklist

- Initial assessment of adapted clinical guidelines

  We applied the initial checklist to a randomly selected convenience sample of published adapted CGs. We included adapted CGs that 1) were developed by a formal organisation, 2) included a description of the adaptation process, 3) reported at least one recommendation, 4) were available in English, and 5) were published in the last five years. We explored the adequacy of each item. Two reviewers from the coordination team independently applied the checklist and resolved disagreements by discussion and, if necessary, by consulting a third reviewer.

- Semi-structured interviews

We conducted semi-structured interviews with CGs developers who had experience with CG adaptation in the past three years. We identified potential participants from 1) attendees of the 2019 GIN conference, 2) authors of published adapted CGs, and 3) suggestions from the advisory group. We continued recruitment and data collection until no new information emerged (sampling saturation). We explored participants' views and experiences on CG adaptation and collected their feedback on each item, potentially missing items, and the overall usefulness of the checklist. Each interview was recorded and transcribed with participant's permission.

- Delphi Consensus Survey

  We conducted a Delphi consensus survey with CG methodological experts, CG developers, CG users, and journal editors of CG-related journals. We identified potential participants from: 1) GIN Adaptation WG, 2) WHO, 3) authors of published adapted CGs, and 4) suggestions from the advisory group. The Delphi panel assessed the inclusion of items in the checklist and reached a consensus on the inclusion. We conducted two Delphi rounds until consensus about each item's inclusion was reached (median score, 6 to 7), and no further substantial comments on the items were provided. We also recorded panel members' perceptions about understandability, usability, completeness of reporting, reporting quality of each item, and overall usefulness of the checklist.

- External review by clinical guideline developers and users

  - *External review with CG developers:* We conducted an online survey with CG developers who were involved in guideline adaptation in the past three years. We identified potential participants by contacting members of the GIN community through GIN connect. Participants ranked the usefulness of the items and the overall usefulness of the checklist using a 7-point scale.

  - *External review with CG users:* We conducted semi-structured interviews with CG users who have used CGs in the past three years. We identified the participants with the support of the advisory group. We continued recruitment and data collection until information became repetitive and no new information emerged. We collected participants' feedback on the understanding and usefulness of each item, and the overall checklist. We audio-recorded each interview with the participant's permission and transcribed them verbatim.

- Final assessment of adapted clinical guidelines

We used another randomly selected convenience sample of published adapted CGs to explore the adequacy of each item of the checklist and recorded the time to apply the checklist. We used the same eligibility criteria as in the initial assessment. Two reviewers from the coordination team independently applied the checklist and recorded the time to apply it. Disagreements were resolved by discussion and, if necessary, by consulting a third reviewer.

Approval of the final version of the checklist

The coordination team generated the final version of the checklist. All members of the RIGHT-Ad@pt WG reviewed and approved the final version.

3.3.2 Data analysis

We performed a descriptive analysis of the categorical variables (absolute and relative frequencies), and the continuous variables (median and range). We used content analysis to summarise and draw conclusions for qualitative variables.

4. RESULTS

4 Results

4.1 Study I. "The development of clinical guidelines in China: insights from a national survey"

4.1.1 Summary of the results

A total of 114 Chinese CG development organisations and expert committees were contacted, and 48 completed questionnaires were collected (42.1% response rate).

Participating organisations

Participating organisations represent six regional economic divisions, 13 provinces, 13 clinical disciplines, and were mostly professional/medical associations (45.8%) or CG expert committees (43.8%). More than a half of the organisations had more than five years of experience in CG development (60.6%), and obtained CG guidance from different sources (62.5%). Most organisations developed CGs based on scientific evidence (89.6%), the adaptation of source CGs (75%), or only expert experience and opinion (64.6%). Organisations that used a CG development methodology handbook were more likely to develop CGs based on scientific evidence (Fisher's exact test; p = 0.005). Only a few organisations had a specific CG development division (6.3%).

Developing de novo clinical guidelines

Most organisations reported developing de novo CGs (88.4%), reporting the inclusion of the following steps: forming/assembling a CG development group (55.3%); conducing a systematic search to retrieve evidence (92.1%); applying eligibility criteria to select evidence (97.4%); assessing the quality of evidence using specific tools (72.4%); rating the strength of recommendations (92.1%); formulating recommendations based on a formal decision-making process (76.3%); and conducting an external review (89.5%). The CG development group consisted of clinicans (95.2%), methodologists (85.7%), policy-makers (33.3%), and patients (42.9%).

Adapting clinical guidelines

Half of the organisations reported an adaptation process (52.8%), including the following steps: forming/assembling an adaptation group (31.6%); conducting a systematic search to retrieve source CGs (84.2%); appling eligibility criteria to select source CGs (68.4%); assessing the source CGs for quality using methodological tools (16.7%) and currency (100%); assessing the source recommendations (73.7%) and its inconsistency (63.2%); addressing population (84.2%), health system (73.7%) ,and clinical practice (63.2%) differences with source CGs; and conducting an external review (94.7%). Only one organisation reported using a published adaptation framework (5.3%). CG adaptation groups consisted of clinicans (83.3%), methodologists (83.3%), policy-makers (50.0%), and patients (16.7%).

Updating clinical guidelines and plans to investigate adherence

More than half of the organisations reported updating CGs (68.8%), and a few used a formal updating process (17.5%). A minority of organisations reported plans for investigating the adherence of clinicians (33.3%) and target users (18.8%) to CGs.

Conflict of interest management and funding

A few organisations reported receiving funding for CG development (33.3%), including non-profit associations, governments, industry, medical associations, and other sources. A few organisations reported having COI during CG development (31.2%), including professional or intellectual interests of CG development group members, and financial interests of organisations. However, only a minority of organisations reported a specific COI management policy (23.4%).

4.1.2 Publication of the study I

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Health Research Policy and Systems

RESEARCH Open Access

The development of clinical guidelines in China: insights from a national survey

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Abstract

Background: Previous research suggests that the quality of clinical guidelines (CGs) in China is suboptimal. However, little is known about the methodology that CGs follow. We conducted a national survey of methods used by Chinese CG developers for CG development, adaptation, and updating.

Methods: We used a previously piloted questionnaire based on methodologies of CG development, adaptation, and updating, which was distributed during September–November 2020 to 114 organizations identified from published Chinese CGs (searched 2017–2020), recommended by Chinese CG developers, and recommended by clinical discipline experts.

Results: We collected 48 completed questionnaires (42.1% response). Most organizations developed CGs based on scientific evidence (89.6%), existing CGs (75%), or expert experience and opinion (64.6%). Only a few organizations had a specific CG development division (6.3%), a CG monitoring plan (on clinicians 33.3%; on patients 18.8%), funding (33.3%), or a conflict-of-interest (COI) management policy (23.4%). Thirty (62.5%) organizations reported using a CG development methodology handbook, from international organizations (14/30, 46.7%), methodology or evaluation resources (3/30, 10.0%), expert experience and opinion (3/30, 10.0%), or in-house handbooks (3/30, 10.0%). One organization followed a published adaptation methodology. Thirty-eight organizations (88.4%) reported de novo CG development: 21 (55.3%) formed a CG working group, and 29 (76.3%) evaluated the quality of evidence (21 [72.4%] using a methodological tool). Nineteen organizations (52.8%) reported CG adaptation: three (31.6%) had an adaptation working group, and 12 (63.2%) evaluated the quality of source CGs (2 (16.7%) using the AGREE II instrument). Thirty-three organizations (68.8%) updated their CGs, seven (17.5%) using a formal updating process.

Conclusions: Our study describes how CGs are developed in a middle-income country like China. To ensure better healthcare, there is still an important need for improvement in the development, adaptation, and updating of CG in China.

Keywords: Practice guideline, Surveys and questionnaires, Evidence-based practice, China

Background

A clinical guideline (CG) is defined by the Institute of Medicine as "a statement that includes recommendations intended to optimize patient care that is informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options" [1]. CGs are increasingly used to provide guidance for clinical practice, public health, and policy recommendations [2]. The goal of CGs is to improve clinical practice, minimize unjustified variations in clinical practice, and ensure effective use of healthcare resources [3]. However, developing CGs is a complex and time-consuming process that requires material resources and expert personnel [2, 4]. If resources to develop a high-quality CG are unavailable, adaptation is an alternative [5, 6].

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In low- and middle-income countries, the lack of appropriately developed CGs to assist healthcare practice is resulting in suboptimal clinical practice [7, 8]. Although reviews of CGs show that their methodological quality has improved in the past decade [9, 10], in China the quality of CGs continues to be inferior [11–16]. The evidence shows that Chinese CG quality, as assessed by the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument [17], is scored at under 30% in most domains [16]. A 2015 study of 109 Chinese CGs reported that only a handful were developed based on research evidence (16; 14.7%), while even fewer critically assessed the certainty of evidence (14; 12.8%) or the strength of recommendations (13; 11.9%) [12].

Empirical evidence shows that China lacks high-quality clinical and epidemiological studies or other types of studies as evidence-based resources [18], which may hinder the adequate updating of Chinese CGs or adaptation for local use. Factors that could influence recommendations or informed decision-making, including resources, cost, feasibility, applicability, and equity, are seldom considered in Chinese CG development processes [11, 14, 15, 19]. Lack of proper incorporation of cost and other considerations potentially hinders adherence to Chinese CGs, but may also contribute to the documented tense relationship between doctors and patients [20]. Furthermore, the development process underlying some Chinese CGs based on existing CGs is also unclear. While previous evidence shows that many international CGs have been used to develop Chinese CGs [12]—for example, the National Comprehensive Cancer Network (NCCN) guidelines or National Institute for Health and Care Excellence (NICE) guidelines—how those source CGs were evaluated and adapted is poorly reported [21].

One important challenge, in terms of improving CG quality in China is the fact that little information is available on the methodology used by developers. To gain more knowledge on this, we conducted a national survey to collect data on Chinese CG development methods and to understand how CGs are developed, adapted, and updated, therefore providing the basis for future improvements in guideline quality in China.

Methods

Aim

This was a cross-sectional online national survey to better understand how CGs are developed, adapted, and updated in China.

Participants

Participants in our survey were key informants and experts affiliated with CG development organizations and expert committees that have developed Chinese CGs in the past 3 years. We adopted a purposive sampling method to recruit participants [22], identified as follows: (1) corresponding contacts of 74 affiliated CG development organizations extracted from 171 Chinese CGs published between January 2017 and February 2020, and retrieved from a literature search in the China National Knowledge Infrastructure database; (2) recommendations from Chinese CG developers; and (3) recommendations from Chinese clinical discipline experts. If initial contacts were not eligible for participation in the survey, they were asked to recommend an eligible person from their organization. The selection procedure is described in Additional file 1: Appendix 1.

Questionnaire

We developed a self-administered questionnaire based on several methodological and evaluation resources, including AGREE II [17], Grading of Recommendations Assessment, Development and Evaluation (GRADE) [23], GRADE Evidence to Decision (EtD) frameworks [24], Resource Toolkit for Guideline Adaptation (ADAPTE) [6], and the Checklist for the Reporting of Updated Guidelines (CheckUp) [25]. The questionnaire was drafted by one author (YS) and was subsequently reviewed and modified by two other authors (YZ, PAC). The Chinese version of the questionnaire, also available in English (Additional file 1: Appendix 2), was circulated to the contacts in the participating organizations.

The questionnaire consisted of 45 items in five sections: characteristics of the organization (10 questions), de novo CG development (13 questions), CG adaptation (16 questions), CG updating and monitoring (3 questions), and conflict-of-interest (COI) management and funding (3 questions). A free-text box in 33 items collected additional information and comments.

Survey

We used online software (http://www.wjx.cn) to design the questionnaire and collect responses. The questionnaire adopted a follow-up question format (only participants who answered "yes" needed to answer further questions) [26] and was piloted with four organizations (one national and three international). We refined the survey based on the feedback from pilot testing, which suggested creating follow-up questions and modifying response categories for optimal understanding and response efficiency. We invited participants through email or WeChat message and provided the following information: (1) a description of the study, (2) the purpose of the survey, (3) the main content of the questionnaire, and (4) instructions on completing the questionnaire. We sent two email reminders a month after delivering the invitation and, where possible, reminded potential

participants through a WeChat message. On receiving consent from the participants, we sent the survey link by email or WeChat between July and November 2020 and followed up with up to three email or WeChat reminders.

Analysis

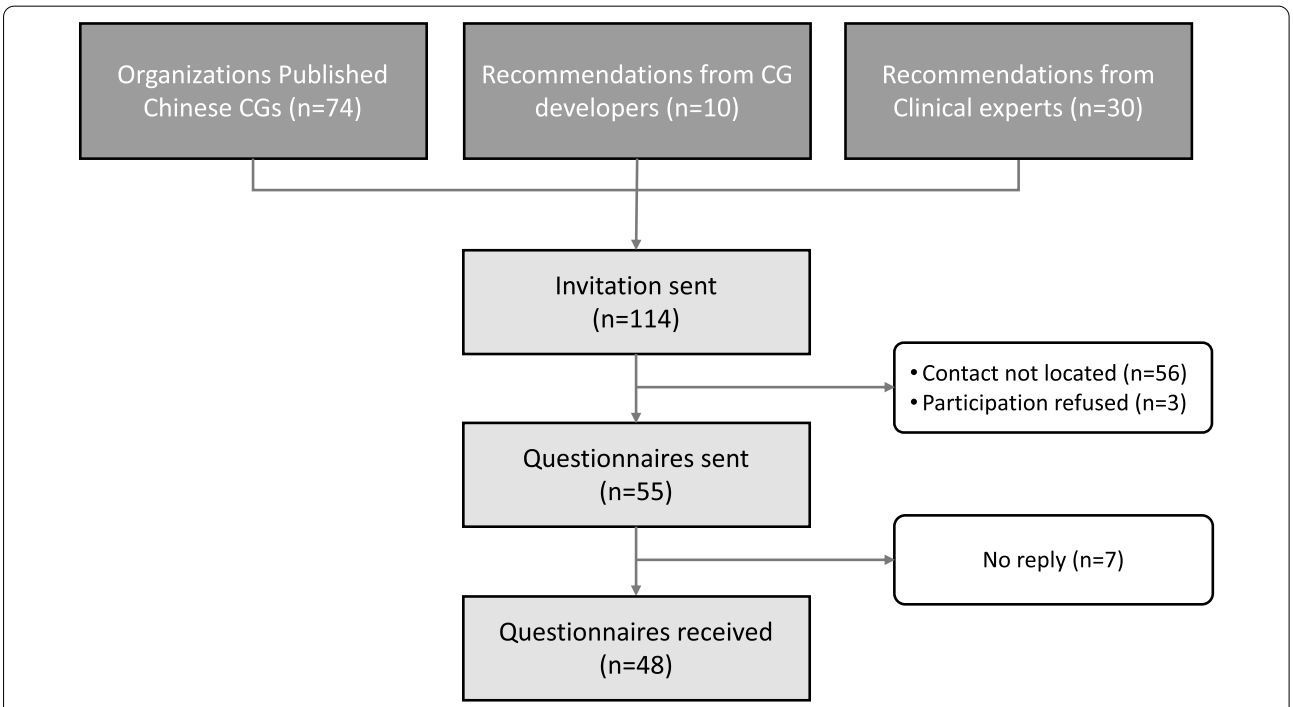
Descriptive statistics were used to analyse the study data. Absolute frequencies and proportions were calculated for all responses. Depending on the methodology used by organizations, we stratified CG development as de novo or adaptation. CGs used for adaptation purposes are referred to as "source CGs", and recommendations from source CGs are referred to as "source recommendations". We hypothesized that using a CG development methodology handbook would be associated with the rigour of the guideline development process. The association was determined by Pearson's chi-square test or Fisher's exact test (alpha was set at 0.05). Data were analysed using SPSS version 23.0 statistical software (IBM Corp., Armonk, NY, USA). For qualitative data, one author (YS) coded the data and extracted themes related to CG de novo development or adaptation [27], and another author (JL) double-checked the codes and the corresponding quotations. The most relevant topics raised by respondents in free-text areas of the questionnaire were selected on the basis of consensus among the three authors (YS, YZ, JL).

Results

A total of 114 Chinese CG development organizations and expert committees were contacted by email and WeChat. Responses were received from 55 CG development organizations. After three reminders, we obtained 48 complete responses (42.1% response rate) (Fig. 1) (Additional file 1: Appendix 3).

Organization characteristics

The organizations, profiled in Table 1, represent six regional economic divisions, 13 provinces, and 13 clinical disciplines as per the Subject Classification of the People's Republic of China [28]. Most respondents worked in hospitals (78.4%), mainly as divisional directors or vice-directors (81.3%). Participating organizations were mostly professional/medical associations (45.8%) or CG expert committees (43.8%). Over half of the organizations (28; 60.6%) had more than 5 years of experience in CG development, and a similar number (30; 62.5%) obtained CG guidance from different resources as their CG development methodology handbook, including international organization or national institute handbooks (46.7%); methodology or evaluation resources such as Guidelines



Abbreviations: CG: Clinical Guideline.

Fig. 1 Recruitment flowchart

Table 1 Clinical guideline (CG) development organizations and procedures (respondents $n=48$)

Characteristics	Category	No. (%)
Contact source ($n=114$)	Published Chinese CG	17/74 (23.0)
	CG developer recommendations	10/10 (100)
	Clinical expert recommendations	21/30 (70.0)
Responder employment[a] ($n=48$)	Hospital	40 (78.4)
	Research/knowledge production institution	9 (17.6)
	Government	2 (3.9)
Region[A] ($n=48$)	North China	16 (33.3)
	East China	13 (27.1)
	South Central China	12 (25.0)
	Northeast China	3 (6.3)
	Southwest China	2 (4.2)
	Northwest China	1 (2.1)
	Unclear	1 (2.1)
CG scope[B] ($n=48$)	Internal medicine	13 (27.1)
	Obstetrics and gynaecology	10 (20.8)
	Clinical epidemiology	5 (10.4)
	Paediatrics	4 (8.3)
	Surgery	4 (8.3)
	Oncology	3 (6.3)
	Acupuncture and tuina science	2 (4.2)
	Geriatrics	1 (2.1)
	Ophthalmology	1 (2.1)
	Nursing	1 (2.1)
	Dermatology and venereology	1 (2.1)
	Pharmaceutics	1 (2.1)
	Chinese medicine	1 (2.1)
	Unknown	1 (2.1)
Organizations	Category	n (%)
Type ($n=48$)	Professional/medical association	22 (45.8)
	CG expert committee	21 (43.8)
	Research institution	5 (10.4)
Development experience ($n=48$)	> 10 years	21 (43.8)
	3–5 years	14 (29.2)
	6–10 years	7 (14.6)
	< 3 years	5 (10.4)
	Do not know	1 (2.2)
Use of a handbook[b] ($n=48$)	Yes	30 (62.5)
	No	18 (37.5)
Handbook used ($n=30$)	International organization (e.g., WHO, NICE)	14(46.7)
	Not reported	6 (20.0)
	CG development tool/methodology (e.g., GRADE, AGREE II, or GRADE-ADOLOPMENT)	4 (13.3)
	In-house handbook	3 (10.0)
	Expert experience and opinion	3 (10.0)
Guideline development unit (n = 48)	No	45 (93.8)
	Yes	3 (6.3)

Table 1 (continued)

Characteristics	Category	No. (%)
Development process[a] ($n=48$)	De novo based on scientific evidence	43 (89.6)
	Adapted from other CGs	36 (75.0)
	De novo based on expert experience and opinion	31 (64.6)
	Adopted directly/translated from other CGs	13 (27.1)
	Updating of other CGs	13 (27.1)

GRADE Grading of Recommendations Assessment, Development and Evaluation; *AGREE II* Appraisal of Guidelines for Research and Evaluation II; *NICE* National Institute for Health and Care Excellence

[A] Based on China's regional economic divisions, one participant from abroad collaborates with Chinese CG development

[B] Scope classified according to clinical discipline

[a] More than one response possible

[b] Open-ended response

2.0 checklist, AGREE II, or GRADE (13.3%); in-house handbooks (10.0%); or expert experience and opinion (10.0%). One organization reported following a published adaptation framework—the GRADE EtD frameworks for adoption, adaptation, and de novo development of trustworthy recommendations (GRADE-ADOLOPMENT), specific for CG adaptation. The vast majority of organizations did not have a specific division in charge of CG development (93.8%). Most Chinese organizations developed CGs based on scientific evidence (89.6%), the adaptation of source CGs (75.0%), or expert experience and opinion (64.6%). Organizations that used a CG development methodology handbook were more likely to develop CGs based on scientific evidence (Fisher's exact test; $p=0.005$) (Additional file 1: Appendix 4).

CG de novo development

Thirty-eight of 43 organizations (88.4%) reported de novo CG development (Table 2). Only around half of organizations formed a CG working group (55.3%), mainly composed of clinicians (95.2%) and methodologists (85.7%). Most organizations reported conducting a systematic search to retrieve evidence (92.1%), applied eligibility criteria to select evidence (97.4%), assessed the certainty of evidence (94.7%), rated the strength of recommendations (92.1%), and conducted an external review (89.5%). Approximately one out of four organizations that reported having conducted a systematic search did not implement a rigorous search strategy or search in more than two databases, and although most organizations used the GRADE approach to rating the certainty of evidence (92.1%) and the strength of recommendations (89.5%), only around 70% assessed the risk of bias or methodological limitations (a key domain in the GRADE Confidence in the Evidence from Reviews of Qualitative Research (GRADE-CERQual) approach) [29], while 27.6% of organizations evaluated evidence limitations without using any methodological tool.

Twenty-nine (76.3%) organizations formulated recommendations based on a formal decision-making process, whether voting (55.2%), using Delphi consensus (51.7%), or based on expert opinion (27.6%) (Table 2). Organizations that reported using a CG development methodology handbook were more likely to use a formal decision-making process (Fisher's exact test; $p=0.009$) (Additional file 1: Appendix 4). When formulating recommendations, most organizations reported considering the balance between benefits and harms (81.6%), patient values and preferences (86.8%), cost and resources (86.8%), and other factors (81.6%) (e.g., equity, acceptability, and feasibility). The basis for formulating recommendations varied from expert opinion to the use of research evidence (Table 2, Fig. 2). The reasons for not considering specific aspects were lack of knowledge or expertise.

CG adaptation

Nineteen of 36 organizations developing CGs through guideline adaptation (52.8%) reported a CG adaptation process (Table 3). Six organizations (31.6%) had an adaptation working group, mainly composed of clinicians (83.3%) and methodologists (83.3%). Most organizations conducted a systematic search to retrieve source CGs (84.2%) and conducted an external review (94.7%). About one in five organizations that conducted a systematic search ultimately did not implement a rigorous search strategy. Eligibility criteria were applied to selecting source CGs by 13 organizations (68.4%), with those who used a CG development methodology handbook being more likely to use a formal eligibility procedure (Fisher's exact test; $p=0.007$) (Additional file 1: Appendix 4).

Over 60% of organizations assessed the source CGs for quality (63.2%), currency (100%), content (73.7%), and

Table 2 De novo clinical guideline (CG) development (n = 38)

Methods (yes responses)		**n (%)**
The institution has a formal CG working group		21 (55.3)
Evidence is retrieved using systematic searching		35 (92.1)
Eligibility criteria are used to select evidence		37 (97.4)
Evidence limitations are assessed		29 (76.3)
Evidence quality/certainty is rated		36 (94.7)
Strength of recommendations is rated		35 (92.1)
A formal decision-making process is followed		29 (76.3)
The balance between benefits and harms is considered		31 (81.6)
Patient values and preferences are considered		33 (86.8)
Cost and resources needed are considered		33 (86.8)
Other factors are considered		31 (81.6)
An external review is conducted		34 (89.5)
Specific methods (open-ended responses)		**n (%)**
Stakeholder involvement[a]		
Stakeholders	**Working group (*n* = 21)**	**External review (*n* = 34)**
Clinicians	20 (95.2)	34 (100.0)
Methodologists	18 (85.7)	30 (88.2)
Policy-makers	7 (33.3)	18 (52.9)
Patient representatives	9 (42.9)	9 (26.5)
Other	1 (4.8)	4 (11.8)
Systematic search[a] (*n* = 35)		
Search is conducted in at least two databases		27 (77.1)
Formal/rigorous search strategy is used		26 (74.3)
Other		1 (2.9)
Evidence limitations (*n* = 29)		
Methodological tools (e.g., Cochrane RoB, ROBINS I)		21 (72.4)
Expert opinion		8 (27.6)
Formal decision-making[a] (*n* = 29)		
Voting system		16 (55.2)
Delphi consensus		15 (51.7)
Informal consensus or expert opinion		8 (27.6)
Cost/resources[a] (*n* = 33)		
Based on expert opinion		26 (78.8)
Based on evidence synthesis		19 (57.6)
Based on studies (e.g., cost-effectiveness, cost–utility, budgetary impact)		14 (42.4)
Other factors[a] (*n* = 31)		
Based on expert opinion		26 (83.9)
Based on evidence synthesis (e.g., local data)		16 (51.6)
Based on studies (e.g., interviews)		9 (29.0)
Patient values/preferences[a] (*n* = 33)		
Based on expert opinion		21 (63.6)
Based on consultation with patient representatives		14 (42.4)
Based on evidence synthesis		12 (36.4)
Based on studies (e.g., reviews, surveys)		9 (27.3)

RoB risk of bias; *ROBINS I* Risk of Bias in Non-randomised Studies of Interventions

[a] More than one response possible

How does your organization consider health benefits, side effects, and risks when formulating recommendations?

Quotes:

- *"Through panel discussion, according to opinions of clinical experts and methodologists". (Expert opinion)*
- *"We did a Delphi consensus through a panel discussion with different disciplinary group members". (Formal consensus)*
- *"We followed the GRADE EtD framework". (GRADE EtD framework)*

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation; EtD, Evidence to Decision.

Fig. 2 Relevant quotes regarding de novo clinical guideline (CG) development

inconsistency in source recommendations (63.2%). However, only two organizations (16.7%) used AGREE II to assess the quality of source CGs (the other organizations relied on expert opinion). A summary table was used to assess recommendation content by 11 organizations (78.6%). The methods used to solve source recommendation inconsistency included (1) analysing the reason for an inconsistency, (2) selecting recommendations from prioritized source CG or based on the applicability of the recommendations to the target setting, and (3) discussion among experts (Fig. 3).

In relation to contextualization, most organizations took into consideration differences between the target setting and the source CG setting, including 16 (84.2%) population differences, 14 (73.7%) health system differences, and 12 (63.2%) clinical practice differences. Approaches to contextualizing source CG recommendations included (1) analysing the reason for differences, (2) supplementing with local evidence, (3) considering expert opinion, and (4) modifying recommendations according to the target context (Fig. 3). In the case that differences could not be solved, reporting differences was considered.

Most organizations reported considering patient values and preferences (94.7%), cost and resources (94.7%), constraints or barriers for implementation (84.2%), and other factors (89.5%). As with de novo CG development, the basis for formulating recommendations varied from expert opinion to considering research evidence (Table 3). The reasons for not considering specific aspects were lack of knowledge or expertise.

CG updating and plans to investigate adherence

Thirty-three of 48 (68.8%) organizations reported having an updating strategy for their CGs, with seven of them (17.5%) confirming a formal updating process (Table 4). Around 60% of the organizations reported an updating frequency of 3–5 years for their CGs. Plans for investigating clinician adherence and target user adherence to CGs were reported by 16 (33.3%) and nine (18.8%) of 48 organizations, respectively.

COI management and funding

Sixteen of 48 (33.3%) organizations reported having received funding for CG development (Table 5). Funding sources included nonprofit associations (50.0%), governments (37.5%), industry (31.3%), medical associations (12.5%), and other sources (18.8%). As for COI management, the type of COI reported included professional or intellectual interests of working group members (27.1%), and financial interests of organizations (6.3%) or of working group members (8.3%). A specific COI policy was reported by 11 (23.4%) organizations.

Discussion

Main findings

Our study describes the current CG development process in China, including de novo development, as well as adaptation and updating practices. While CG development in China is broadly in line with international standards, the methods used for specific steps tend to be both variable and informal. CG development is based on varied sources of CG development methodology handbooks and even expert experience and opinion; many developers perform only informal quality assessment of evidence or of source CGs; few organizations have specific CG development divisions, multiple stakeholder engagement, formal updating systems, a COI policy, or funding to support CG development. Similarly, standard methods are not used to adapt source CGs, even though CGs have been adapted for many years in China.

Table 3 Clinical guideline (CG) adaptation (n = 19)

Methods (yes responses)		**n (%)**
The institution has a formal CG adaptation working group		6 (31.6)
Evidence is retrieved using systematic searching		16 (84.2)
Eligibility criteria are used to select source CGs		13 (68.4)
Source CG quality is assessed		12 (63.2)
Source CG currency is assessed		19 (100.0)
Source CG recommendations are assessed		14 (73.7)
Source CG recommendation inconsistency is assessed		12 (63.2)
Population differences with source CGs are addressed		16 (84.2)
Health system differences with source CGs are addressed		14 (73.7)
Clinical practice differences with source CGs are addressed		12 (63.2)
Patient values and preferences are considered		18 (94.7)
Cost and resources needed are considered		18 (94.7)
Constraints/barriers are considered		16 (84.2)
Other factors are considered		17 (89.5)
An external review is conducted		18 (94.7)
Specific methods (open-ended responses)		**n (%)**
Stakeholder involvement[a]		
Stakeholder	**Working group (*n* = 6)**	**External review (*n* = 18)**
Clinicians	5 (83.3)	18 (100.0)
Methodologists	5 (83.3)	13 (72.2)
Policy-makers	3 (50.0)	10 (55.6)
Patient representatives	1 (16.7)	4 (22.2)
Other	0 (0.0)	3 (27.8)
Systematic search[a] (*n* = 16)		
Search is conducted in at least two databases		14 (87.5)
Formal/rigorous search strategy is used		12 (75.0)
Source CG quality[a] (*n* = 12)		
Expert opinion		8 (66.7)
Methodological tools (e.g., AGREE II)		2 (16.7)
Source CG content (*n* = 14)[a]		
Summary tables		11 (78.6)
Other		3 (21.4)
Recommendations matrix		0 (0.0)
Cost/resources[a] (*n* = 18)		
Based on studies (e.g., cost-effectiveness, cost–utility, budgetary impact)		14 (77.8)
Based on expert opinion		13 (72.2)
Based on evidence synthesis		10 (55.6)
Other factors[a] (*n* = 17)		
Based on expert opinion		13 (76.5)
Based on evidence synthesis (e.g., local data)		11 (64.7)
Based on studies (e.g., interviews)		7 (41.2)
Patient values/preferences[a] (*n* = 18)		
Based on expert opinion		15 (83.3)
Based on studies (e.g., reviews, surveys)		11 (61.1)
Based on evidence synthesis		10 (55.6)
Based on consultation with patient representatives		6 (33.3)

Table 3 (continued)

AGREE II Appraisal of Guidelines for Research and Evaluation II

[a] More than one response possible

How does your organization consider the inconsistency of recommendations for the same topic?

Relevant quotes:

- *"We will analysis the reason for inconsistency, discussed based on supportive evidence and the applicability for target settings" (Analyse the reason for inconsistency)*
- *"Prioritize according to the level of source guideline developers." (Select recommendations from prioritized source CGs)*
- *"Inconsistency is solved by considering recommendation applicability to Chinese setting" (Prioritize recommendations)*
- *"Expert discussion" (Expert opinion)*

How does your organizations consider population differences between source CG(s) and the target context?

Relevant quotes:

- *"We adopted clinical research from China to address differences". (Supplement with local evidence)*
- *"We analysed the difference in population from source CGs. If the recommendations apply to children, then we only adopt the section for children. We also make sure that there is no obvious difference between races". (Analyse the reason for difference)*
- *"We modified the recommendations according to the clinical practice of China. Panel experts discussed the difference and finally made a consensus". (Modify the recommendations according to target context)*
- *"We will report the difference separately". (Report the difference)*
- *"According to experts' opinion" (Expert opinion)*

How does your organization consider differences in settings/health systems between source CG(s) and the target context?

Relevant quotes:

- *"If a systematic review or other relevant evidence suggests a difference, we will consult the expert's opinion". (Supplement with local evidence, Expert opinion)*
- *"Suppose the recommended intervention from source CGs is not available from the target setting. In that case, we will consult evidence of other intervention/health management of the target setting and then develop a de novo recommendation" (Modify the recommendations according to target context).*
- *"We mainly based this on the experts' opinions". (Expert opinion)*
- *"We reported the difference separately". (Report the difference)*

How does your organization consider differences in practices and target users between source CG(s) and the target context?

Relevant quotes:

- *"We consulted the opinions of clinical experts and methodologies". (Expert opinion)*
- *"We modified the recommendations according to clinical practice and clinical research from China". (Modify the recommendations according to target context)*
- *"We reported the difference separately". (Report the difference)*

Fig. 3 Relevant quotes regarding clinical guideline (CG) adaptation

Table 4 Clinical guideline (CG) updating and monitoring ($n=48$)

Methods (yes responses)	No. (%)
Updating ($n=48$)	
The institution has a CG updating strategy	33 (68.8)
The institution has a formal CG updating procedure	7 (17.5)
Monitoring ($n=48$)	
The institution has a plan to check adherence by clinicians	16 (33.3)
The institution has a plan to check adherence by target users	9 (18.8)
Specific methods (open-ended responses)	**No. (%)**
Updating frequency ($n=33$)	
3–5 years	22 (66.7)
< 3 years	5 (15.2)
> 5 years	3 (9.1)
Unknown	3 (9.1)

Our study in the context of previous research

Our findings, compared to those of previous quality assessment studies, show that the rigour of CG development in China is gradually improving. Zhou et al. (2020), for instance, found that CGs published after 2014 were of significantly higher quality than older CGs [30]. Similarly, a quality assessment of Chinese CGs by Wang et al. [31], published in 2020, reported "rigour of development" scores for CGs published specifically in 2018–2019 that were higher (65.1%) than the overall average median score of below 50%. A new series regarding the development process of evidence-based medicine and clinical guidelines in China published in the *Journal of Clinical Epidemiology* is also in line with our study findings [32].

Table 5 Clinical guideline (CG) conflict-of-interest (COI) management and funding ($n=48$)

Methods (yes responses)	No. (%)
COI management and funding ($n=48$)	
The institution has funding for CG development	16 (33.3)
The institution has a COI management policy	11 (23.4)
Specific methods (open-ended responses)	n (%)
Funding source ($n=16$)	
Nonprofit association	8 (50.0)
Government	6 (37.5)
Industry	5 (31.3)
Medical association	2 (12.5)
Other	3 (18.8)
COI types ($n=48$)	
No COI	33 (68.8)
Professional and intellectual interests of working group members	12 (27.1)
Financial interests of working group members	4 (8.3)
Financial interests of institution	3 (6.3)

Unlike quality assessment studies, our survey identified the methodologies that Chinese CG developers follow, which is not limited to what is reported. The reporting of Chinese CGs is very suboptimal as assessed by the Reporting Items of Practice Guidelines in Healthcare (RIGHT) statement [33–35]. Considering that the completeness of reporting impacts quality assessment results for CGs, the assessment scores based on AGREE II are likely to be lower, thereby underestimating the methodological quality of Chinese CGs. Moreover, around 2 years is needed to develop a CG; hence, previous assessment studies reporting poor quality in the AGREE II "rigour of development" domain with the last search date around 2019 or earlier may reflect CG development in or before 2017 [30, 31].

Although the rigour of CG development in China is improving, the methods used vary widely. More than 30% of Chinese CG development organizations in our study did not follow any handbooks or guidance on developing CGs, and the handbooks they used were not only standards from different international organizations, but also methodological tools or expert experience and opinion. Given that evidence rating systems and decision-making procedures vary across international organizations, such discrepancies introduce variability in the Chinese CG development process. NCCN, for instance, uses a different evidence rating system from that used by WHO [36], while NICE also has its own decision-making procedure [37]. In addition, the methods used for specific steps, such as assessing the limitations of evidence or the quality of source CGs, tend to be informal.

However, as was reported by a previous study [11], most Chinese CG development organizations do not have a specific division or group for CG development; this makes our findings regarding inconsistent CG development methodology handbook use and lack of quality assurance monitoring less surprising. The funding sources for CG development point to the involvement of industry funding and, therefore, of COIs. Without proper COI management policies, the evidence-based framework and credibility of CGs is inevitably hampered [38, 39]. Furthermore, few CG organizations have formal updating or adherence monitoring procedures in place. Although around 20% of recommendations become outdated within 3 years, only 15.2% of organizations update their CGs within this period of time [40]. Another area of concern is that most organizations mainly rely on clinicians and so lack participation by other stakeholders, such as patient representatives and policy-makers.

Stakeholder engagement is essential for improving CG recommendation uptake and implementation, which should be considered during the CG development process [4, 41]. A lack of stakeholder engagement may lead to controversy and uncertainty, thereby hindering CG implementation [42].

We found that 75% of Chinese CG organizations developed CGs by adapting source CGs, which highlights the widespread use of CG adaptation in China. However, precisely how CG adaptation methods are used is unclear. Of the CG organizations in our study that adapted source CGs, only half reported their adaptation process, and hardly any mentioned following a published adaptation methodology. In addition, as happens with de novo CG development, CG adaptation is informal and lacks monitoring. Only six CG organizations in our study had created an adaptation working group, and only two mentioned having used a validated tool to evaluate the quality of source CGs. Since the quality of adapted CG relies mainly on the source CG, this informality undoubtedly contributes to the low quality of Chinese CGs.

Limitations and strengths

Our study has some limitations. First, the response rate was relatively low, despite sending two reminders and contacting potential participants using different approaches. However, our sample included 48 Chinese CG development representatives of 13 clinical disciplines and 13 provinces. We did not explore CG development on the basis of consensus, which is yet to be studied and understood.

There are several strengths of our study. First, the survey format with follow-up questions allows us to describe in depth the specific methods used in China and to explore the underlying reasons for the low-level quality of Chinese CGs. Additionally, our study comprehensively describes the CG development process in one middle-income country, including CG de novo development, adaptation, and updating process, which contributes to the improvement of the CG development process as a whole in China. Furthermore, we designed the study questionnaire following international standards and piloted it with both national and international organizations. This allows our methods to provide more reference value to other countries with similar issues.

Implications for practice and research

CG development in China needs to be standardized. A good CG development process requires a multidisciplinary working group, a rigorous methodology, sufficient and independent funding, sound COI management, and a monitoring and updating system [1]. Stakeholder engagement should be emphasized in the development process of Chinese CGs to ensure that guideline topics are relevant and prioritized and that other factors like acceptability and feasibility are adequately considered, thus facilitating policy-maker adoption of recommendations into policy and practice [43–45]. In addition, sufficient nonprofit public funding and strict COI management strategies should be ensured for CG development, to reduce the potential COI impact on health-related decision-making and clinical practice. Medical associations and government institutions need to assume responsibility for CG monitoring and quality assurance, thereby ensuring the proper implementation of formal development and adaptation methodologies for CGs. CG developers in China need to collaborate closely in standardizing and improving the rigour of CG development, for example, by implementing a standard CG development methodology/handbook and following published reporting guidance such as the RIGHT statement for de novo CGs or CheckUp for updated CGs [25, 46]. Future practices need to build on those aspects so as to improve the quality and reliability of Chinese CGs, and therefore improve healthcare nationwide.

While CG adaptation is an efficient way to develop contextualized recommendations, adapted CGs will only benefit from the quality of source CGs by implementing a rigorous adaptation process [6, 47, 48]. Of the quality published adaptation methodologies available [49], Chinese CG developers could adopt and validate an optimal methodology applicable to the national context. Future research could therefore focus on exploring efficient and rigorous adaptation methods that ensure CG quality and also improve CG implementation.

Conclusions

CG development and adaptation methodologies, including for updating, as used in China tend to be variable and informal, and so need to be standardized. CG development in general is poorly managed and monitored. Greater effort and more funds need to be invested in improving the quality of Chinese CGs so as to ensure better healthcare.

Abbreviations

ADAPTE: Resource Toolkit for Guideline Adaptation; AGREE II: Appraisal of Guidelines for Research and Evaluation II; CheckUp: Checklist for the Reporting of Updated Guidelines; CG(s): Clinical guideline(s); COI: Conflict of interest; EtD: Evidence to Decision; GRADE: Grading of Recommendations Assessment, Development and Evaluation; GRADE-ADOLOPMENT: GRADE EtD frameworks for adoption, adaptation, and de novo development of trustworthy recommendations; NCCN: National Comprehensive Cancer Network; NICE: National Institute for Health and Care Excellence; RIGHT: Reporting Items of Practice Guidelines in Healthcare.

Supplementary Information

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Additional file 1. Appendices.

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Authors' contributions
YS and PAC participated in study conception and design. YS, PAC, YZ, YLC, and RXG drafted the protocol. YS, YZ, JL, YLC, and RXG collected the data. YS, YZ, and JL analysed the data. YS drafted the first version. All authors critically reviewed the draft and have approved the final version to be published.

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Availability of data and materials
All data generated or analysed during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate
As our study did not involve patients, biological samples, or clinical data, we obtained a waiver of approval from the Clinical Research Ethics Committee of the Hospital de la Santa Creu i Sant Pau (Barcelona). In addition, we received participants' consent and guaranteed the confidentiality of their data. Participants could withdraw their consent at any stage of the survey.

Consent for publication
Not applicable.

Competing interests
Dr. Yaolong Chen reports that he is Co-Director of the WHO Collaborating Centre for Guideline Implementation and Knowledge Translation, Chair of Guidelines International Network—Asia, and Director of the Chinese GRADE Centre. No other author has anything to declare.

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References

1. Institute of Medicine. Clinical practice guidelines we can trust. Washington: The National Academies Press; 2011.
2. World Health Organization. WHO handbook for guideline development. WHO handbook for guideline development. 2014.
3. Woolf SH. Practice guidelines, a new reality in medicine. II. Methods of developing guidelines. Arch Intern Med. 1992;152(5):946–52.
4. Schünemann HJ, Wiercioch W, Etxeandia I, Falavigna M, Santesso N, Mustafa R, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. CMAJ. 2014;186(3):E123–42.
5. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 1. Guidelines for guidelines. Health Res Policy Syst. 2006;4:13.
6. Fervers B, Burgers JS, Voellinger R, Brouwers M, Browman GP, Graham ID, et al. Guideline adaptation: an approach to enhance efficiency in guideline development and improve utilisation. BMJ Qual Saf. 2011;20(3):228–36.
7. Olayemi E, Asare EV, Benneh-Akwasi Kuma AA. Guidelines in lower-middle income countries. Br J Haematol. 2017;177(6):846–54.
8. Maaløe N, Ørtved AMR, Sørensen JB, Sequeira Dmello B, van den Akker T, Kujabi ML, et al. The injustice of unfit clinical practice guidelines in low-resource realities. Lancet Glob Health. 2021;9(6):e875–9.
9. Alonso-Coello P, Irfan A, Solà I, Gich I, Delgado-Noguera M, Rigau D, et al. The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. Qual Saf Health Care. 2010;19(6):e58.
10. Armstrong JJ, Goldfarb AM, Instrum RS, MacDermid JC. Improvement evident but still necessary in clinical practice guideline quality: a systematic review. J Clin Epidemiol. 2017;81:13–21.
11. Chen YL, Yao L, Xiao XJ, Wang Q, Wang ZH, Liang FX, et al. Quality assessment of clinical guidelines in China: 1993–2010. Chin Med J (Engl). 2012;125(20):3660–4.
12. Jiang M, Liao LY, Liu XQ, He WQ, Guan WJ, Chen H, et al. Quality assessment of clinical practice guidelines for respiratory diseases in China: a systematic appraisal. Chest. 2015;148(3):759–66.
13. Deng W, Li L, Wang Z, Chang X, Li R, Fang Z, et al. Using AGREE II to evaluate the quality of traditional medicine clinical practice guidelines in China. J Evid Based Med. 2016;9(3):152–62.
14. Yao S, Wei D, Chen YL, Wang Q, Wang XQ, Zeng Z, et al. Quality assessment of clinical practice guidelines for integrative medicine in China: a systematic review. Chin J Integr Med. 2017;23(5):381–5.
15. Wu D, Jiang W, Yu L, Wang Y, Tao Y, Tang H, et al. Quality assessment of clinical practice guidelines for infectious diseases in China. J Evid Based Med. 2018;11(2):95–100.
16. Chen Y, Wang C, Shang H, Yang K, Norris SL. Clinical practice guidelines in China. BMJ. 2018;360:j5158.
17. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ. 2010;182(18):E839–42.
18. Li B, Yan Y, Lv M, Zhao G, Li Z, Feng S, et al. Clinical Epidemiology in China series. Paper 1: Evidence-based medicine in China: an oral history study. J Clin Epidemiol. 2021. https://doi.org/10.1016/j.jclinepi.2021.08.012.
19. Jiang L, Krumholz HM, Li X, Li J, Hu S. Achieving best outcomes for patients with cardiovascular disease in China by enhancing the quality of medical care and establishing a learning health-care system. Lancet. 2015;386(10002):1493–505.
20. Ending violence against doctors in China. Lancet. 2012;379(9828):1764
21. [Chinese guideline on menopause management and menopause hormone therapy (2018)]. Zhonghua Fu Chan Ke Za Zhi. 2018;53(11):729–39.
22. Taherdoost H. Sampling methods in research methodology; how to choose a sampling technique for research. Int J Acad Res Manag (IJARM). 2016;5:hal-02546796.
23. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924–6.
24. 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.
25. Vernooij RW, Alonso-Coello P, Brouwers M, Martínez GL. Reporting items for updated clinical guidelines: checklist for the reporting of updated guidelines (checkup). PLoS Med. 2017;14(1):e1002207.
26. Allen M. The SAGE encyclopedia of communication research methods. 2017; survey:follow-up questions:1708–10.
27. Bengtsson M. How to plan and perform a qualitative study using content analysis. NursingPlus Open. 2016;2:8–14.
28. Subject Classification of the People's Republic of China. https://zh.wikipedia.org/wiki. Accessed 20 May 2021
29. Lewin S, Booth A, Glenton C, Munthe-Kaas H, Rashidian A, Wainwright M, et al. Applying GRADE-CERQual to qualitative evidence synthesis findings: introduction to the series. Implement Sci. 2018;13(1):2.
30. Zhou X, Xu S, Ren Q, Chen J. Quality and specific concerns of clinical guidelines for integrated chinese and western medicine: a critical appraisal. Evid Based Complement Alternat Med. 2020;2020:9254503.
31. Wang Y, Yu S, Wang L, Liang D, Shen Q, Xue H, et al. The methodology for developing nursing clinical practice guidelines over recent decades in China: a critical appraisal using AGREE II. J Nurs Manag. 2020;28(4):976–97.
32. Zhou Q, Wang Z, Shi Q, Zhao S, Xun Y, Liu H, et al. Clinical Epidemiology in China series. Paper 4: The reporting and methodological quality of Chinese clinical practice guidelines published between 2014 and 2018: A Systematic Review. J Clin Epidemiol. 2021;S0895–4356(21):00256.
33. Yun X, Yaolong C, Zhao Z, Qi Z, Yangyang W, Runshen X, et al. Using the RIGHT statement to evaluate the reporting quality of clinical practice guidelines in traditional Chinese medicine. PLoS ONE. 2018;13(11):e0207580.
34. Wang Q, Duan Y, Liang J, Chen Z, Chen J, Zheng Y, et al. Reporting quality of 2014–2018 clinical practice guidelines on diabetes according to the RIGHT checklist. Endocrine. 2019;65(3):531–41.
35. Xiao Y, Jiang L, Tong Y, Luo X, He J, Liu L, et al. Evaluation of the quality of guidelines for assisted reproductive technology using the RIGHT checklist: a cross-sectional study. Eur J Obstet Gynecol Reprod Biol. 2019;241:42–8.
36. NCCN. Development and Update of Guidelines. https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines. Accessed 20 May 2021.
37. NICE. Developing NICE guidelines: the manual. https://www.nice.org.uk/process/pmg20/chapter/decision-making-committees. Accessed 1 December 2020.
38. Thompson DF. Understanding financial conflicts of interest. N Engl J Med. 1993;329(8):573–6.
39. Schünemann HJ, Al-Ansary LA, Forland F, Kersten S, Komulainen J, Kopp IB, et al. Guidelines international network: principles for disclosure of interests and management of conflicts in guidelines. Ann Intern Med. 2015;163(7):548–53.
40. Martínez García L, Sanabria AJ, García Alvarez E, Trujillo-Martín MM, Etxeandia-Ikobaltzeta I, Kotzeva A, et al. The validity of recommendations from clinical guidelines: a survival analysis. CMAJ. 2014;186(16):1211–9.
41. Gagliardi AR, Brouwers MC. Integrating guideline development and implementation: analysis of guideline development manual instructions for generating implementation advice. Implement Sci. 2012;7:67.
42. Sonnad SS. Organizational tactics for the successful assimilation of medical practice guidelines. Health Care Manage Rev. 1998;23(3):30–7.
43. Armstrong MJ, Rueda JD, Gronseth GS, Mullins CD. Framework for enhancing clinical practice guidelines through continuous patient engagement. Health Expect. 2017;20(1):3–10.
44. Oliver K, Lorenc T, Innvær S. New directions in evidence-based policy research: a critical analysis of the literature. Health Res Policy Syst. 2014;12:34.
45. Gillard S, Simons L, Turner K, Lucock M, Edwards C. Patient and public involvement in the coproduction of knowledge: reflection on the analysis of qualitative data in a mental health study. Qual Health Res. 2012;22(8):1126–37.
46. Chen Y, Yang K, Marušic A, Qaseem A, Meerpohl JJ, Flottorp S, et al. A reporting tool for practice guidelines in health care: the RIGHT statement. Ann Intern Med. 2017;166(2):128–32.
47. Burgers JS, Anzueto A, Black PN, Cruz AA, Fervers B, Graham ID, et al. Adaptation, evaluation, and updating of guidelines: article 14 in Integrating and coordinating efforts in COPD guideline development. An official ATS/ERS workshop report. Proc Am Thorac Soc. 2012;9(5):304–10.
48. Kristiansen A, Brandt L, Agoritsas T, Akl EA, Berge E, Flem Jacobsen A, et al. Applying new strategies for the national adaptation, updating, and dissemination of trustworthy guidelines: results from the Norwegian adaptation of the Antithrombotic Therapy and the Prevention of Thrombosis, 9th Ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2014;146(3):735–61.
49. Darzi A, Abou-Jaoude EA, Agarwal A, Lakis C, Wiercioch W, Santesso N, et al. A methodological survey identified eight proposed frameworks for the adaptation of health related guidelines. J Clin Epidemiol. 2017;86:3–10.

Publisher's Note

4.2 Study II. "Current practices and challenges in adaptation of clinical guidelines: a qualitative study based on semi-structured interviews"

4.2.1 Summary of the results

We conducted ten semi-structured interviews between November 2019 and January 2020 until data saturation on the reason for CG adaptation and methodology was reached.

Participants

Participants worked in nine different organisations from seven countries. Most of the included organisations were from high-income countries (60%), were research centres (67%), had over five years of experience in CG adaptation (78%), had a CG development or adaptation group size that ranged from 6 to 20 members (78%), spent less than 2 years to complete their adaptation process (78%), and had funding sources (78%).

Reasons for adapting clinical guidelines

We identified four main reasons for CG adaptation: 1) to develop their own CGs; 2) to implement or endorse source CGs; 3) to update an existing CGs; and 4) to analyse conflicting recommendations from different source CGs.

Current practice

We identified nine CG adaptation methodologies: 1) ADAPTE framework (86), 2) Adopt–Contextualise–Adapt (ACA) framework (117), 3) American College of Physicians (ACP) guidance statement (18), 4) American Society of Clinical Oncology (ASCO) CG endorsement/adaptation methodology (118), 5) Cancer Care Ontario's (CCO) endorsement protocol (119), 6) DynaMed editorial methodology (120), 7) German Instrument for Methodological Guideline Appraisal (DELBI) (121), 8) GRADE-ADOLOPMENT framework (87), 9) Piloted adaptation framework (122).

Based on the framework analysis, we identified four main steps in the process of adapting CGs: 1) selection of scope and source CGs, 2) assessment of source materials, 3) formulation of adapted recommendations, and 4) external review and follow-up process.

Challenges for adapting clinical guidelines

Challenges of the CG adaptation include 1) limitations from source clinical guidelines (poor quality or reporting); 2) limitations from adaptation settings (lacking resources or skills); 3) adaptation process intensity and complexity; 4) challenges arising from specific adaptation process (context differences between source CGs and adapted CG, inconsistencies between recommendations from different source CGs, updating source evidence), and 5) implementation barriers.

4.2.2 Publication of the study II

BMJ Open

Current practices and challenges in adaptation of clinical guidelines: a qualitative study based on semistructured interviews

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ABSTRACT

Objective This study aims to better understand the current practice of clinical guideline adaptation and identify challenges raised in this process, given that published adapted clinical guidelines are generally of low quality, poorly reported and not based on published frameworks.

Design A qualitative study based on semistructured interviews. We conducted a framework analysis for the adaptation process, and thematic analysis for participants' views and experiences about adaptation process.

Setting Nine guideline development organisations from seven countries.

Participants Guideline developers who have adapted clinical guidelines within the last 3 years. We identified potential participants through published adapted clinical guidelines, recommendations from experts, and a review of the Guideline International Network Conference attendees' list.

Results We conducted ten interviews and identified nine adaptation methodologies. The reasons for adapting clinical guidelines include developing *de novo* clinical guidelines, implementing source clinical guidelines, and harmonising and updating existing clinical guidelines. We identified the following core steps of the adaptation process (1) selection of scope and source guideline(s), (2) assessment of source materials (guidelines, recommendations and evidence level), (3) decision-making process and (4) external review and follow-up process. Challenges on the adaptation of clinical guidelines include limitations from source clinical guidelines (poor quality or reporting), limitations from adaptation settings (lacking resources or skills), adaptation process intensity and complexity, and implementation barriers. We also described how participants address the complexities and implementation issues of the adaptation process.

Conclusions Adaptation processes have been increasingly used to develop clinical guidelines, with the emergence of different purposes. The identification of core steps and assessment levels could help guideline adaptation developers streamline their processes. More methodological research is needed to develop rigorous international standards for adapting clinical guidelines.

Strengths and limitations of this study

- ► To ensure participants' representativeness, we invited clinical guideline (CG) adaptation experts through different ways, including adapted CGs, attendees from the Guideline International Network conference and additional strategies or sources.
- ► To reduce participant's bias, we complemented participants' views and experiences with their adaptation methodology publications.
- ► The interview format allowed us to explore the challenges of CG adaptation in depth and how the participants address specific issues.
- ► The challenges highlighted by our study are likely to be universal to experienced CG adaptation developers, since our participants' selection process limits the study samples to experts with sufficiently large experience in the CG adaptation or development field.
- ► Some specific challenges, such as particular contextualisation issues, might be under-reported in our study due to the small sample size and fewer participants from low-income/middle-income countries.

INTRODUCTION

Clinical guidelines (CGs) adaptation is an efficient methodology to develop contextualised recommendations.[1 2] CG adaptation tailors existing trustworthy CGs for local, regional or national guidance, by considering local contextual factors, such as language, availability and accessibility of services and resources, the healthcare setting and the relevant stakeholders' cultural and ethical values.[3] CG adaptation may lead to changes compared with the original recommendations in (1) the specific population, intervention or comparator, (2) the certainty of the evidence or (3) the strength of recommendations by including additional information regarding the health conditions,

monitoring, implementation and implications for research.[4] Besides, CG adaptation could also be used as an alternative method to develop *de novo* CGs, with the expectation of reducing waste of resources and avoiding duplication of efforts. However, this process should follow a similar and systematic approach as that of the source CGs to benefit from their quality.[3 5 6]

Currently, there is no single standard adaptation methodology.[7 8] One systematic review identified eight frameworks for CG adaptation[1]: Resource Toolkit for Guideline Adaptation—ADAPTE instrument,[9] Adapted ADAPTE,[10] Alberta Ambassador programme adaptation phase,[11] Grades of Recommendations, Assessment, Development and Evaluation (GRADE) Evidence to Decision frameworks for adoption, adaptation and de novo development of trustworthy recommendations (GRADE-ADOLOPMENT),[4] Making GRADE the irresistible choice,[12] RAPADAPTE for rapid guideline development,[13] Royal College of Nursing (RCN)[14] and Systematic Guideline Review.[15] Most of these frameworks are based on the ADAPTE instrument,[9] while some use the GRADE Evidence to Decision frameworks.[1 4] The comparison between frameworks showed similarities in the initial and final phases of the process, and notable differences in the 'adaptation' phase of the process.[1] Another recent review categorised the frameworks into formal and informal.[7] However, new methods and experiences of CG adaptation periodically emerge.[16–18]

Despite this, published adapted CGs seldom used a published adaptation methodology and their quality is still suboptimal.[19] A systematic survey that assessed 72 published adapted CGs found that only 57 reported any details on adaptation methods, and only 23 used a published adaptation methodology. The proportion of published adapted CGs satisfying the steps of ADAPTE ranges from 4% to 100%. In addition, the mean score of adapted CGs assessed using Appraisal of Guidelines for Research & Evaluation II (AGREE II) was 57% for the 'rigour of development' domain, and 50% for the 'applicability' domain. Similarly, another systematic assessment found that only 30% of adapted WHO CGs reported adaptation process methods.[20]

Challenges faced by adaptation groups are not well known and are likely to vary across CG organisations. A recent review described several limitations of published adaptation frameworks and showed that the time to adapt CGs using the same framework varies between 18 months and 3 years.[7] Besides, most adaptation frameworks require methodology expertise; this might be a barrier for many CG adaptation groups, especially those from low-income/middle-income countries (LMICs). Although international collaboration and providing staff training could help, this should be based on a standardised adaptation process. Furthermore, most published adaptation frameworks were developed from adaptation experiences and lacked validation.[7] No formal evaluation instrument or guidance could help expertise methodologists improve adaptation frameworks.[7]

In addition, fundamental gaps between international recommendations and realistic best practice are being reported due to poorly CG adaptation, which leaves health providers with non-useful guidance.[21] There is an urgent need to explore the proper adaptation process and share the global adaptation experience. This study aims to better understand the current practice of CG adaptation and identify the challenges raised in this process, thus providing accordance for the improvement of the adaptation process.

METHODS

We applied a qualitative design using semi-structured interviews. This study is part of the RIGHT-Ad@pt project, which aims to develop a reporting checklist for CG adaptation.[22] We reported findings using the Consolidated criteria for Reporting Qualitative research checklist.[23]

From now on, we will refer to the CGs selected for adaptation as 'source CGs', and to the evidence from the source CGs as 'source evidence'.

Participants

We sampled a group of CG developers, who had been involved in CG adaptation over the past 3 years using a snowball sampling method.[24] We identified potential participants from (1) authors lists of 16 published adapted CGs retrieved from a search for adapted CGs via PubMed (from 1992 to December 2019) (online supplemental appendix 01);[25] (2) suggestions from the advisory group of the RIGHT-Ad@pt project and (3) attendees of the 2019 Guideline International Network (G-I-N) conference.

We contacted potential participants by email with an invitation letter including (1) an introduction to the RIGHT-Ad@pt project, (2) the eligibility criteria, (3) the purpose of the semistructured interview, (4) the topics to be discussed and (5) the expected contribution from participants. We sent two email reminders within 1 month. After receiving consent for participation and before starting the semi-structured interviews, we circulated a more detailed description of the RIGHT-Ad@pt project, the interview guide, and collected the Conflicts of interest (CoI) form from each participant. We continued to recruit participants and collect data until we reached saturation.

Data collection

We designed an interview guide based on checklists previously developed by our group, and the experience obtained from the development of the RIGHT-Ad@pt checklist.[22 26 27] The interview guide included four sections (online supplemental appendix 02): (1) characteristics of participants (country, experience in the field of health-related CGs and CG adaptation), (2) characteristics of participants' CGs developing organisation, (3) participants' experiences about current practice in the adaptation process and (4) participants' views and

experiences about challenges in the adaptation process. Participants completed the first two sections before the interview. We also asked participants to provide the published methodology that supported their adaptation processes if applicable. Interviews were conducted face to face or via teleconference and lasted approximately 40 min. We audiorecorded each interview with the participant's permission. One researcher (YS, PhD(c), female, with guideline development and adaptation experience) conducted the semistructured interviews and transcribed them verbatim.

Data analysis

For quantitative variables (characteristics of participants and organisations), we calculated absolute frequencies and proportions.

For qualitative data regarding adaptation processes, we followed a framework deductive analysis.[28] First, we generated a priori thematic framework for the main steps of adaptation processes, based on relevant systematic reviews.[1 7] Second, we sought additional concepts from the methodological evidence provided by participants. Third, we coded semistructured interviews findings against the resulting thematic framework, revised and merged codes into themes as new aspects emerged. Finally, we proposed subthemes under the drafted thematic framework. For participants' views and experiences about challenges, we applied an inductive thematic analysis; we coded the interview transcripts 'line by line', proposed descriptive themes following the coding process; and generated analytical themes by analysing, organising and creating descriptive subthemes.[29 30] One author (YS) coded and extracted qualitative data, drafted the framework and proposed themes independently. Two authors (MB and JL) double-checked selected codes and the corresponding quotations. A second senior author (PA-C) reviewed the framework and themes. A final structure was confirmed by discussion and approved by consensus. We used NVivo (V.12 for Mac, QSR International) for qualitative analysis.[31]

Patient and public involvement

The patient and public were not involved in the study.

RESULTS

We invited 39 CG adaptation developers to participate. Participants were identified from published adapted CGs (49%; 19/39), suggestions from the Advisory Group of the RIGHT-Ad@pt project (28%; 11/39), attendees of G-I-N conference (2019) (15%; 6/39) and eligible participants' recommendations (7%; 3/39) (See figure 1). Finally, we conducted ten semistructured interviews between November 2019 and January 2020 until data saturation on the reason for CG adaptation and methodology was reached. Data from published methodologies of different participating organisations were included in framework analysis to avoid individual bias. In addition, data from individuals were included in the thematic analysis to reflect participants' views and experiences.

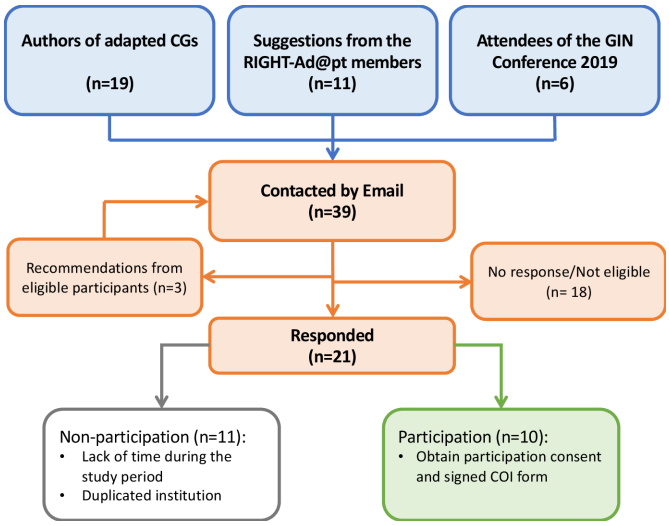

Figure 1 Participant recruitment flow diagram. Relevant conference attendees were identified by screening the list of conference attendees and oral presentation regarding CG adaptation. CGs, clinical guidelines; CoI, conflict of interest; GIN, Guideline International Network.

Participants

The main characteristics of participants, as well as their organisations, are summarised in table 1. Participants worked in nine different organisations from seven countries, the majority being from high-income countries (60%; 6/10). Most participants had over 5 years of experience in CG adaptation (70%; 7/10). Most of the included organisations were research/knowledge-producing centres (67%; 6/9), had over 5 years of experience in CG adaptation (78%; 7/9), had a working group size that ranged from 6 to 20 members (78%; 7/9) and spent less than 2 years to complete their adaptation process (78%; 7/9). Most of these organisations had funding sources from government, medical association operation fees, national/international foundations, or the combination of those above (78%; 7/9). Three participants declared a CoI as a coauthor of published adaptation methodology. Other participants have nothing to declare.

Reasons for adapting CGs

We identified four main reasons for CG adaptation (table 2, online supplemental appendix 03): (1) to develop their own CGs; (2) to implement or endorse source CGs; (3) to update an existing CG and (4) to analyse conflicting recommendations from different source CGs. The most common reason to adapt was to develop CGs for their intended setting based on other existing CGs, by first retrieving and adapting existing CGs that could potentially answer their questions, saving resources and time and avoiding duplication of efforts.

Table 1 Characteristics of study sample

Characteristics of interviewees (n=10)	n (%)
Continents (n=10)	
Africa	1 (10)
Asia‡	3 (30)
Europe	2 (20)
North America	4 (40)
Experience in the CG field (n=10)	
Experience in developing CGs*	8 (80)
Experience in adapting CGs*	8 (80)
Methodological experience in developing CGs†	7 (70)
Methodological experience in adapting CGs†	9 (90)
CG user	4 (40)
Years of CG adaptation experience (n=10)	
0–5 years	3 (30)
6–10 years	3 (30)
11–20 years	4 (40)
Characteristics of organisations (n=9)	**n (%)**
Type of organisations (n=9)	
Hospital	1 (11)
Research/knowledge producing organisation	6 (67)
Service provider organisation (community)	1 (11)
University	2 (22)
Professional medical association	2 (22)
Years of CG adaptation practice (n=9)	
0–5 years	2 (22)
6–10 years	3 (33)
11–20 years	3 (33)
>20 years	1 (11)
The average size of CG adaptation working group (n=9)	
0–5	1 (11)
6–10	2 (22)
11–20	5 (56)
>20	1 (11)
Average time for CG adaptation (n=9)	
0–1 year	3 (33)
1–2 years	4 (44)
2–3 years	1 (11)
NR	1 (11)
Funding source (n=9)	
Government funding	2 (22)
Medical association operational fee	2 (22)
National/international foundations	4 (44)
Self-service fee	1 (11)
Pharmacy company	1 (11)
Multiple funding without industry	3 (33)
Multiple funding including industry	1 (11)

*Participation in a CG development/adaptation group at least once in the past year.
†Participation in a CG technical team at least once in the past year or participation in methodological research.
‡One expert is from Australia but develops CG adaptation in Philippines, we classified the country as Philippines.
CG, clinical guideline; NR, not reported.

Some organisations focused on implementing source CGs in the target setting through CG adaptation. Three organisations also updated their own CGs by adapting newly published CGs, while another conducted adaptation processes only when there were discrepancies among different recommendations for the same topic.

Current practice

Six participants reported using their own adaptation methodology.[8 32–36] Three of them were based on the ADAPTE instrument and/or the GRADE-ADOLOPMENT framework.[4 9] One participant used a published adaptation framework[9] and supplemented it with GRADE to rate the certainty of the evidence.[37] Two used a guideline quality assessment tool named German Instrument for Methodological Guideline Appraisal (DELBI) to inform the CG adaptation process in their setting.[38] Lastly, one participant reported not using a formal methodology. See online supplemental appendix 04 for detailed new methodologies.

Participants reported using the following nine CG adaptation methodologies (table 3):

1. ADAPTE instrument.[9]
2. Adopt–Contextualise–Adapt framework.[36]
3. American College of Physicians guidance statement.[34]
4. American Society of Clinical Oncology CG endorsement/adaptation methodology.[32]
5. Cancer Care Ontario's endorsement protocol.[35]
6. DynaMed editorial methodology.[33]
7. DELBI[38]
8. GRADE-ADOLOPMENT framework.[4]
9. Piloted adaptation Framework.[8]

Seven of the nine methodologies were not identified in previous publications. Based on the framework analysis, we identified four main steps in the process of adapting CGs (figure 2 and table 3).

Selection of the scope and source CG(s)

CG adaptation groups defined or identified CG topic, scope and key questions before or after the selection of source CGs. Most organisations reported first predefining the topic, scope and key questions, then searching for existing relevant or implementable CGs.[9 32 33 35] Some also identified key questions from newly released, well-known

Table 2 Views and experiences of CG adaptation

Themes	No of participants
Reasons for adapting CGs	
Develop their CGs	
As part of de novo CG development process	3
To avoid duplicates and save efforts	1
To save resources and time	3
Implementing/endorsing for target settings	5
Updating existing CGs	3
Solving recommendations' controversy	1
Challenges for adapting CGs	
Poor reporting or the limitations of source CG(s)	2
Limited skills in advanced CG development and adaptation	3
The intensity in terms of resources and time for adaptation	2
Specific steps of adaptation process:	
Addressing context differences between source CG(s) and adapted CG	4
Addressing inconsistency and integrate recommendations from different source CG(s)	3
Updating or supplementing with research evidence	1
Implementation barriers	5
Addressing context differences between source CG(s) and the adapted CG	
Through panel discussion	7
Adapting to the target context (at CG level)	
Prioritising the source CG(s) according to different factors	2
Discarding the source CG(s)	1
Adapting to the target context (at recommendation level)	
Evaluating the reason behind and reconsidering the strength of the recommendations	1
Contextualising by considering different factors	3
Formulating new recommendations for a specific population (eg, subgroups)	1
Adapting to the target context (at evidence level)	
Supplementing new evidence/other considerations	2
Reporting the differences when drafting the recommendation	3
Addressing inconsistencies between recommendations from different source CG(s)	
Through panel discussion	2
Selecting source CG(s) with different criteria (at CG level)	
Good quality/rigorous development of source CG(s)	5
Content relevance/suitability to the target context	2
Most up to date	2
Trustworthy source CG(s)	1
Assessing the reason for inconsistency	
At recommendation level	4
At evidence level	3
Not applicable when single CG was included	4
Updating source evidence	
Trigger for supplement/update search of source CG(s)	
Source CG(s) do not answer all the questions of interest	3
Source CG(s) are outdated	1
Source CG(s) are consensus-based	2
Experts' suggestions	2
Way of including new evidence	
Literature search (eg, pragmatic search or a full de novo search)	6
Update the search from source CG(s)	3
Experts' suggestions	3
If the source CG(s) are not evidence-based or do not answer the questions	
Start CG de novo development process	3
Discard the recommendation	1
Conduct the consensus process	1
Considering implementation barriers	
Way of obtaining information	
Experts' opinion	4
Literature search	5
Group discussion	5
Decision making after consideration of implementation barriers	
Modifying the practice instead of change recommendations	1
Modifying the recommendations	1
Reporting the differences if needed	4

CGs, clinical guidelines.

and trustworthy CGs.[4 35] The screening criteria of source CGs for a further appraisal at this preliminary stage were: (1) stakeholders' preferences of CG topic;[4 32 35] (2) a good reputation of the CGs developers;[32 34 35] (3) methodological quality of the source CGs;[8 9] (4) clinical relevance to the target context[33] and (5) CoIs management and funding independence of the source CGs.[32]

Assessment of source materials

CG adaptation groups reviewed and assessed source CGs. We stratified this step into three levels based on participants' reported practice:

- Guideline level: The guideline quality, trustworthiness, transparency of the process, value and relevance to clinical practice, resource availability and inclusion of latest evidence (up to date) were assessed.[9 32–36] To rate the CG quality, most participants applied the AGREE II instrument. To ensure source CGs were up

Table 3 Main steps of the adaptation process

Adaptation methodology/year	Selection of the scope and source CG(s)	Assessment of source materials	Decision-making process	External review and follow-up
ADAPTE 2010[9]	▶ Determining the health question ▶ Search for existing CGs/other relevant documents ▶ Source CG(s) screening and selection	▶ Source CG quality assessment ▶ Source CG currency assessment ▶ Source CG content assessment ▶ Source CG consistency assessment ▶ Acceptability and applicability of recommendations assessment	▶ Review assessment ▶ Choosing between source CGs and recommendations	▶ External review and acknowledgement of source CG(s) ▶ Consulting source CG(s)
Adopt–Contextualise–Adapt Framework 2016[36]	▶ Predefining CG topics [1] ▶ Search for international existing CGs ▶ Source CG(s) selection by evaluating the implementability of the question to the target setting	▶ Evaluation of methodological quality of the source CG(s) [a] ▶ Content review and recommendations and evidence summary ▶ Identifying recommendations relevant to steps along the patient journey ▶ Dealing with two or more relevant recommendations ▶ Supplementing with local evidence [a]	▶ Developing composite recommendations [α] ▶ Decision making as adoption, contextualisation/adaptation according to the local context	▶ Plan Implementation ▶ Focused public consultation ▶ Planning and evaluation of the CG adaptation roll out ▶ Establishing partnerships
ACP guidance statement 2019[34]	▶ Choosing topics with recommendation conflictions ▶ Search and selection of national-level source CG(s) within 5 years [2]	▶ Assessing quality and process transparency of source CG(s) ▶ Assessing the interpretation of the evidence (benefits, harms, costs, and patient values and preferences) ▶ Source evidence review [b]	▶ Presenting evidence summary and proposing recommendations ▶ Reaching consensus by discussion or voting	▶ Public panel review ▶ Peer review process ▶ Publication ▶ Financial support ▶ Reporting ▶ Updating
ASCO CG endorsement/ adaptation methodology 2019[32]	▶ Based on the ASCO's priority topics ▶ Selection of source CGs matched by criteria [3]	▶ Quality of source CGs appraisal using AGREE II [c] ▶ Content review with expert's agreement on recommendations ▶ SRs appraisal using AMSTAR and search for new evidence (eg, when the evidence base is outdated.)	▶ Evidence synthesis with a matrix containing recommendations and supporting evidence ▶ Independent evidence review by the expert panel ▶ Modification decision (eg, contextualisation, clarification, or new evidence addressing) made by the expert panel ▶ Full committee approval or voting for consensus	▶ Review by applicant organisations of source CG(s) ▶ Peer review by journal ▶ Publication ▶ Derivative clinical tools/ resources ▶ Updating

Continued

Table 3 Continued

Adaptation methodology/year	Selection of the scope and source CG(s)	Assessment of source materials	Decision-making process	External review and follow-up
CCO endorsement protocol 2019[35]	► Defining key topics based on the release of well-known CGs that meet the interest of CCO or ► Defining key topics based on CG-related project and identify existing CG addressing CCO's topic	► Initial assessment and selection of source CG(s) [d] ► Source recommendations assessment [e] ► Likelihood of new evidence assessment (if so, a de novo development will start)	► Review of the draft endorsement document by an expert panel ► Consensus and approval	► Professional Consultation ► Final Publication ► Maintenance/Updating
DynaMed editorial methodology 2019[33]	► Based on the current existing topics of Dynamed ► Screening and selection of the best available evidence based on relevance and potential impact on clinical decision-making and patient care	► Critically appraisal of source CGs regarding trustworthiness, relevance, and clinical value ► Rating of the strength of the recommendations (eg, net benefit, cost and burdens, and patients' value) [f] ► Rating of potential source of bias and certainty of the evidence	► Evidence reporting and review by clinicians ► Synthesis of multiple evidence reports [β] ► Based on conclusions of the overviewed evidence with direct links provided	► Review by the editorial team, topic/section editors, and EBM experts ► Updating daily
DELBI 2019[38]	► Defining key questions before source CG selection [4] ► Systematic search for existing CGs ► Criteria description for source CG selection	► Quality review of source CG(s) [g] ► Source recommendation review [g] ► Systematic update of searches for primary evidence	► Describing the modifications of recommendations	► External review CG adaptation process*
GRADE-ADOLOPMENT 2017[4]	► CG topic and source CG selection[5] ► Questions prioritisation by the panel from selected source CGs	► Checking Evidence to Decision frameworks availability of source CGs ► Completing the GRADE Evidence to Decision frameworks ► Updating systematic reviews of health effects and identifying local data [h]	► Preparing GRADE Evidence to Decisions frameworks and review by an expert panel ► Formulating recommendations through consensus or voting	► NA
Piloted adaptation framework 2017[8]	► CG topic prioritisation and Ministry of Health approval ► CG search from National guideline Clearinghouse	► Source CG quality assessment [i] ► Identifying relevant recommendations from source CG(s) based on panel expertise and clinical practice settings	► Adopted/adapted/ new recommendations compilation ► Expert review	► External review ► Online access for public consultation ► Updating
Adaptation experience 2019	► Predefining health questions [6] ► Searching for existing CG [6]	► Source CG quality assessment using AGREE II [j] ► Identifying evidence from the most up-to-date CGs [j] ► Underlying evidence review [j]	► Evidence review from source CG(s) ► Decision-making by national-level experts with no further details provided [μ]	► National external review [ł]

Continued

Table 3 Continued

Adaptation methodology/year	Selection of the scope and source CG(s)	Assessment of source materials	Decision-making process	External review and follow-up
The criteria or clarification for topic/scope/questions selection and source CG screening: **1:** Quote: '*At that time we have identified the top of the conditions for stroke and low back pain. We look at the literature, even at that time, there were so many CGs published already for those two topics.*' (Participant 10) **2:** Sources were from PubMed and GIN library in the last five years or current practice, and Web of science. **3:** Criteria are: high-quality CG developers, detailed CoI management, and financially independence; or applicant organisations' preferable. **4:** Quote: '*If the CG adaptation groups plan to develop a new CG, they will search for the existing evidence from published CGs first.*' (Participant 06) **5:** Assessed the relevance to stakeholders, proposed by a professional group or prioritised by stakeholders; In addition, GRADE approach and Evidence to Decision frameworks availability are required. **6:** Quote: '*A lot of kind of process will be in a national process, and there will be specific health questions and PICOs. Then we will be asked to conduct SRs. We do have in that particular process is that the SR would include first to look at what CGs are out there, and then we will look at what SRs are out there before we conduct our systematic review.*' (Participant 09)				
The considerations or clarifications for the assessment of source materials: **a:** Quote: '*We quickly appraise source CGs using AGREE II to ensure the source CG you are basing on are good quality; … To adapt, we update the search and include new evidence. …It means you take evidence surrounded for instance in the local context settings, there might be a new paper has been published locally, not internationally, but it answers the questions the local context actually asked. Then the recommendation could change.*' (Participant 10) **b:** Quote: '*We will look at the evidence and do the assessment ourselves. If we do the quality assessment, we look at the systematic review, and if the systematic review doesn't make sense, we will look at the primary studies.*' (Participant 07) **c:** Quote: '*We do not have a numeric cut-off for AGREE II.*' (Participant 02) **d:** Criteria: Scope, relevance, and timing, quality and methods, resource availability; acceptability; **e:** Interpretation and justification, applicability/relevance, qualifications & clarifications. **f:** Quote: '*If we see many CGs agree, and we know the evidence is high quality, we don't need to go into a lot of greater depth because everything is pointing into the right direction. If we see the CGs are disagreeing, then we may have to evaluate and see why they are disagreeing and that where we checked the currency of the content to help us to understand the disagreement.*' (Participant 01) **g:** Quote: '*We don't have a critical cut off to choose which CG to use, we do prioritise by the quality of the CG. The CG adaptation group will create CG synopses, prefer methodologically sound recommendations. …The adaptation group should be transparent if they have appropriate changes in the recommendations when the adaptation process and provide the scientific rationale behind the change.*' (Participant 03) **h:** We conducted rapid SRs of patient's value, cost-effectiveness; We considered local data suggested by panel members (patients' value and preference, cost, resource use, population prevalence and incidence). **i:** Quote: '*We request the adaptation group to assess the quality of the CGs using the AGREE II instrument. We do not have a cut-off of the AGREE score, because sometimes there are few source CGs for the consideration of adaptation. … If there are no clear answers for several questions in the source CG(s), they looked at existing Cochrane SRs but do not conduct a new one. No cost-effectiveness evidence was searched, but patients' values and preferences, yes.*' (Participant 08) **j:** Quote: '*If there is a CG of good quality, those are the recommendations. So, if I see a CG from NICE, or from European, our society will have both or do an AGREE appraisal. If there are good quality, I transparently put in my review about what the quality it was, and I pooled out the recommendations that could be relevant for that health question. And then I also look at the underlying evidence from those CGs, also the SRs, that independent of pooling out the if possible, a GRADE evidence table, or something that explains the magnitude of the effect and the certainty of evidence.*' (Participant 09)				
The considerations or clarifications for the decision-making process: **α**: Quote: '*In the most recent CG we published, we extracted the source recommendations from the source CGs, we have developed composite recommendations, which is the new recommendation based on the other CG have said…*' (Participant 10) ***β***: 'Current evidence, current CGs, and clinical expertise's recommendations to support clinical decision making'. **μ**: Quote: '*For people who work in the CG adaptation group they have any Evidence to Decision framework, so they will look at the quality of evidence from source CGs or other SRs.*' (Participant 09)				

Continued

Table 3 Continued

Adaptation methodology/year	Selection of the scope and source CG(s)	Assessment of source materials	Decision-making process	External review and follow-up
The considerations or clarifications for the external review process: * Quote: *'Our organisation doesn't do for the CG adaptation group, but they do the external review process by themselves'*. (Participant 03) ‖ Quote: *'The national group I am referring to send the adapted CG out for comment, feedback, and input as external review. We don't have a specific small external review team broadly.'* (Participant 10)				

DELBI is a CG assessment tool used by adaptation group to inform CG adaptation.
ACP, American College of Physicians; ADAPTE, Resource Toolkit for Guideline Adaptation; AGREE II, Appraisal of Guidelines for Research & Evaluation II; ASCO, American Society of Clinical Oncology; CCO, Cancer Care Ontario; CGs, clinical guidelines; CoI, conflict of interest; DELBI, German Instrument for Methodological Guideline Appraisal; GRADE, Grading of Recommendations, Assessment, Development and Evaluations; NA, not applicable; NICE, National Institute for Health and Care Excellence; SR, systematic review.

to date, some participants conducted a comprehensive search and chose the most recent CG among those with similar quality.

- Recommendation level: The recommendation content, the formulation process of source recommendations (eg, how the net benefit, resources, patients' values and other criteria were considered), as well as the strength of recommendation were reviewed.[8 9 32–35] Some participants used a CG summary format to display recommendations and facilitate panel discussion.[8 32 38] Recommendations were modified as needed based on the discussion of the evidence.[4 33 34]
- Evidence level: The certainty of the evidence of the source recommendations was reviewed.[4 6 9 33–35] Some participants assessed the risk of bias of included primary studies and systematic reviews, and the certainty of the source evidence.[32 33] Besides, updating the original search or supplementing with new evidence was also conducted at this level, if necessary.[4 6 8 32 33 38] The reasons to update source evidence were: (1) it did not clearly answer all the key questions; (2) it was not adequately searched or appraised; (3) it was considered outdated (eg, more than 3 years since the last search) or (4) when panel experts recommended it (table 2, online supplemental appendix 03).

Decision-making process

CG adaptation groups review the summarised evidence and decide whether to adapt (with modifications) or adopt (without modifications) the source recommendations. To support the decision, some participants presented the summarised evidence using a matrix or direct links containing both recommendations and evidence. Where CG developers of source CGs used GRADE-ADOLOPMENT, the GRADE Evidence to Decision frameworks of source CGs were reviewed or completed by the CG adaptation groups.[4] Decisions were made mostly through panel discussion or voting.

External review and follow-up

Following the decision-making process, an external review or a peer review process was conducted. Moreover, a follow-up process was scheduled, including the plan for dissemination, monitoring and updating. Those processes were similar to *de novo* CG development processes. However, some organisations also consulted source CG developers on the changes made to source recommendations.[9 32]

Challenges for adapting CGS

Most participants reported challenges to the adaptation and development of CGs in general (table 2, online supplemental appendix 03). Challenges of the adaptation process were: (1) limitations from source CGs, including poor reporting and quality; (2) limited advanced CG development and adaptation skills of the CG adaptation group; (3) resource and time intensity required for

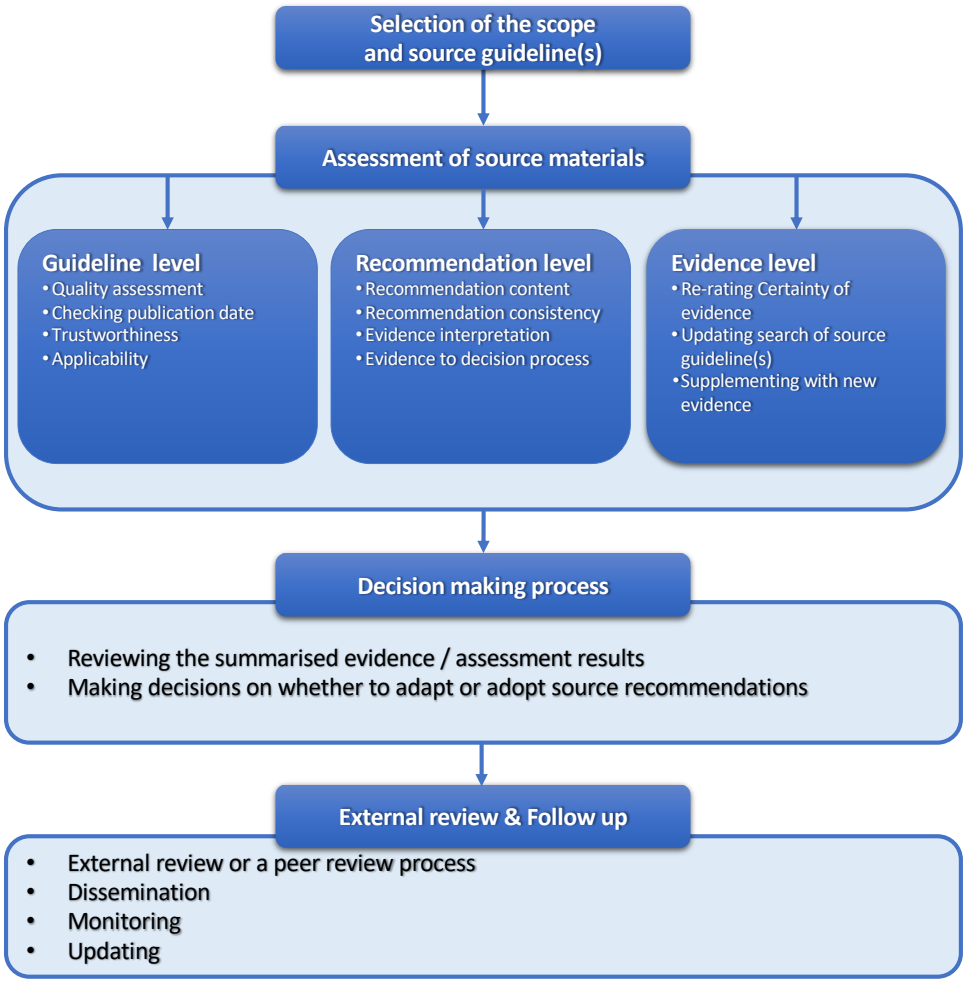

Figure 2 Main steps of the adaptation process. CGs, clinical guidelines.

adaptation; (4) challenges arising from specific adaptation process, including how to address and report context differences between source CGs and adapted CGs; how to address inconsistency and integrate recommendations from different source CGs, and how to update source evidence, including update search and supplement with additional evidence and (5) implementation barriers of CG adaptation.

We identified participants' strategies for dealing with the specific challenges within the adaptation process and implementation issues (table 2, online supplemental appendix 03).

Addressing context differences between source CG(s) and adapted CG

According to participants' views and experiences, the differences in setting or population between source CGs and target context were addressed mainly through panel discussion and experts' opinions. CG adaptation groups could address these differences at multiple levels: (1) at CG level, by prioritising source CGs according to different criteria or discarding the entire source CGs if the difference was large enough; (2) at recommendation level, by modifying the strength of recommendations due to differences after considering the balance of the benefits and harms, other factors (eg, acceptability or feasibility) or formulating new recommendations (eg, new recommendations for subgroup population) and (3) at evidence level, by supplementing with new evidence (eg, local data). Finally, participants stated that differences and modifications were reported or documented along with the adapted CG.

Addressing inconsistencies between recommendations from different source CG(s)

The inconsistency between recommendations was addressed by prioritising those source CGs that (1) had good quality or rigorous development process, (2) were relevant to the target context, (3) were most up to date and (4) were considered trustworthy. The reasons behind the inconsistency were also assessed on the recommendation and evidence level. At the recommendation level, whether (1) the inconsistency was due to a different target population, (2) the evidence was sufficient or up to date and (3) the evidence was appropriately interpreted. At the evidence level, whether the source evidence was appropriately assessed.

Updating source evidence

CG adaptation groups sometimes used evidence that is more recent or relevant in addition to the source evidence. To identify new evidence, participants relied on literature searches, including full *de novo* search or pragmatic search (eg, PubMed, local databases or Cochrane database), updating the source search or experts' suggestions. However, half of the participants expressed their unwillingness to supplement with new evidence since they generally based on the source CGs, maintaining the merits of adaptation to save resources and time. If the evidence base of the source CGs was unclear or did not answer their questions, participants conducted a *de novo* CG development process, discarded the recommendation or formulated recommendations based on the discussion.

Considering implementation barriers

CG adaptation groups considered different implementation barriers, including medical policy, cost of the intervention or management, equity, applicability or feasibility. The implementation barriers were identified through experts' opinions (eg, policymakers, primary carers or CG adaptation panel) or literature search (eg, local data). Most of the CG adaptation groups held a discussion to address implementation barriers by considering the applicability of their settings. As a result, either the recommendations or the implementation plan were modified to facilitate the CG adaptation. Finally, the differences in implementation considerations with the source CGs and the modifications were reported in the adapted CGs.

DISCUSSION

Our study summarises the current practice of CG adaptation derived from different methodologies used by nine organisations worldwide. We structured adaptation processes into four steps, including three-level source materials assessment (guideline, recommendation and evidence level). We identified the reasons of CG adaptation groups for adaptation, the challenges faced during the process, and their strategies to overcome these. Most of the identified methodologies were not discussed in previous systematic reviews.

Our findings in the context of previous research

We described reasons for conducting adaptation processes, which has not been previously highlighted in the literature.[1 7] Fervers *et al* defined CG adaptation as an alternative methodology to developing *de novo* CGs or as a systematic method to improve implementation.[39] Our findings reflect this definition and suggest that most adaptation groups are conducting adaptation processes as part of their CG *de novo* development. Besides, we identified that adaptation processes could also play a role in updating and harmonising source recommendations.

We identified nine adaptation methodologies that CG adaptation groups have been using, two of which had been described by previous reviews, while seven had not.[1 7] Unlike previous reviews, our study—in addition to summarising and comparing published frameworks—describes the used adaptation processes in a novel structured way, including the stratified assessment of source materials. This stratification fits the conceptual progression of CG adaptation; Fervers *et al* considered two levels in this process, the guideline level (quality of source CGs) and recommendation level (coherence between evidence and recommendations, and the applicability of specific recommendations).[39] More recently, Wang *et al* described a shift towards an evidence level (evidence of recommendations).[7]

To this day, very few studies have explored the challenges arising from the adaptation process. Only one review has described the limitations of using adaptation frameworks and gaps for adaptation knowledge.[7] Our study identified that adaptation challenges arise from limitations of source CGs (poor quality or reporting), limitations of adaptation settings (lacking resources or skills), and the complexity of the adaptation process. In addition, we described the strategies used by the participants to address specific steps of the adaptation process, thereby providing new knowledge to inform more streamlined adaptation processes: for contextualisation and reconciliation, adaptation groups could address different issues at three levels of source materials assessment; for updating source evidence, they could add new evidence through a literature search or experts' suggestions; for implementation, adaptation groups could hold a panel discussion, and consider modifying recommendations or the implementation plan if necessary.

Limitations and strengths

Our study has some limitations. We only conducted ten interviews and hence could have missed additional adaptation methods from other countries. In addition, we recruited participants from published adapted guidelines and G-I-N attendees, limiting the study samples to experts with sufficiently large experience in CG adaptation or development field. Besides, we did not interview non-English-speakers, which may bias the study results. Finally, we did not conduct data analysis based on country income due to the small sample size and fewer participants from LMICs that lack resources and technical/methodological experts.[21] The challenges highlighted by our study are likely to be universal within experienced guideline adaptation developers (eg, intensity and complexity of adaptation process, limitations of source CGs, and implementation barriers). However, some specific challenges, such as specific contextualisation issues, would be underreported in our study.

Our study also has some strengths. We invited CG adaptation experts from identified adapted CGs, attendees from the G-I-N conference, and other additional strategies or sources to ensure representativeness. To reduce participant's bias, we complemented participants' views and experiences with their adaptation methodology

publications. The interview format allowed us to explore the challenges of CG adaptation in depth and how the participants address specific issues. Moreover, we conducted a framework analysis based on published adaptation frameworks, ensuring our findings' comprehensiveness. Finally, we presented the results in a user-friendly format, including tables and figures.

Implication for practice

CG adaptation has been increasingly used in the guideline arena with diverse initiatives emerging and can be used as a pragmatic methodology to develop recommendations. In 2020, an international WHO collaboration project developed a living map of the latest evidence-based recommendations for the prevention and treatment of COVID-19.[40] This project makes the source materials available online and allows CG developers to adopt or adapt relevant recommendations for their questions of interest. CG developers could therefore avoid duplication of efforts and focus on how to implement scientific guidance to tackle this public health crisis.

Adaptation processes should be conducted rigorously. The identified core steps of the adaptation process and assessment levels could help CG adaptation groups streamline their future initiatives. CG adaptation groups could predefine the level of source materials to evaluate, simplifying the adaptation process while remaining rigorous. The adaptation process overlaps with the CG *de novo* process when assessing source materials at the recommendation level and the evidence level. At the recommendation level, CG adaptation groups need to review the factors considered to formulate source recommendations. This process uses an approach similar to that applied by the source panels and requires explicit and transparent reporting on the formulation of source recommendations to achieve feasibility. For example, if source CGs followed the GRADE Evidence to Decision frameworks, the adaptation groups need to review the interpretation of evidence regarding each factor considered under the Evidence to Decision frameworks. Not all robust source CGs use the GRADE Evidence to Decision frameworks, but yet, describe in detail how they make recommendations. Similarly, at the evidence level, the boundary between the CG adaptation process and the *de novo* process blurs. The notable difference could be that a *de novo* process conducts a full *de novo* search while the adaptation process updates the source search or supplements it with local evidence. Although the structured adaptation process could be used as a framework, its usability should be further formally assessed and validated.

Implication for future research

There is still room for improving adaptation methodology, especially the efficiency of adaptation processes and the quality as well as credibility of CG adaptation. Besides, there is no framework to guide CG adaptation groups to make judgements on whether to adapt, adopt or develop de novo recommendations based on the assessment of source materials. Although the GRADE-ADOLOPMENT is available, it requires the Evidence to Decisions frameworks from source CGs. A standardised and pragmatic adaptation methodology, including guidance on how to make judgements, should be developed. Furthermore, there is still a need of a validated quality assessment tool and comprehensive reporting guidance to improve the rigorous CG adaptation. The structured adaptation process could be considered as a critical aspect of the quality assessment.

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REFERENCES

1 Darzi A, Abou-Jaoude EA, Agarwal A, *et al*. A methodological survey identified eight proposed frameworks for the adaptation of health related guidelines. *J Clin Epidemiol* 2017;86:3–10.
2 Okely AD, Ghersi D, Hesketh KD, *et al*. A collaborative approach to adopting/adapting guidelines - The Australian 24-Hour Movement Guidelines for the early years (Birth to 5 years): an integration of physical activity, sedentary behavior, and sleep. *BMC Public Health* 2017;17:869.
3 Burgers JS, Anzueto A, Black PN, *et al*. Adaptation, evaluation, and updating of guidelines: article 14 in integrating and coordinating efforts in COPD Guideline development. An official ATS/ERS workshop report. *Proc Am Thorac Soc* 2012;9:304–10.
4 Schünemann HJ, Wiercioch W, Brozek J, *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.
5 Fervers B, Burgers JS, Voellinger R, *et al*. Guideline adaptation: an approach to enhance efficiency in Guideline development and improve utilisation. *BMJ Qual Saf* 2011;20:228–36.
6 Kristiansen A, Brandt L, Agoritsas T, *et al*. Adaptation of trustworthy guidelines developed using the grade methodology: a novel five-step process. *Chest* 2014;146:727–34.
7 Wang Z, Norris SL, Bero L. The advantages and limitations of guideline adaptation frameworks. *Implement Sci* 2018;13:72.
8 Mehndiratta A, Sharma S, Gupta NP, *et al*. Adapting clinical guidelines in India-a pragmatic approach. *BMJ* 2017;359:j5147.
9 The ADAPTE Collaboration. The ADAPTE process: resource toolkit for guideline adaptation. version 2.0, 2009. Available: http://www.g-i-n.net
10 Amer YS, Elzalabany MM, Omar TI, *et al*. The 'Adapted ADAPTE': an approach to improve utilization of the ADAPTE guideline adaptation resource toolkit in the Alexandria Center for Evidence-Based Clinical Practice Guidelines. *J Eval Clin Pract* 2015;21:1095–106.
11 Harstall C, Taenzer P, Zuck N, *et al*. Adapting low back pain guidelines within a multidisciplinary context: a process evaluation. *J Eval Clin Pract* 2013;19:773–81.
12 Kristiansen A, Brandt L, Agoritsas T, *et al*. Applying new strategies for the National adaptation, updating, and dissemination of trustworthy guidelines: results from the Norwegian adaptation of the antithrombotic therapy and the prevention of thrombosis, 9th ED: American College of chest physicians evidence-based clinical practice guidelines. *Chest* 2014;146:735–61.
13 Alper BS, Tristan M, Ramirez-Morera A, *et al*. RAPADAPTE for rapid Guideline development: high-quality clinical guidelines can be rapidly developed with limited resources. *Int J Qual Health Care* 2016;28:268–74.
14 Rycroft-Malone J, Duff L. Developing clinical guidelines: issues and challenges. *J Tissue Viability* 2000;10:144–53.
15 Muth C, Gensichen J, Beyer M, *et al*. The systematic guideline review: method, rationale, and test on chronic heart failure. *BMC Health Serv Res* 2009;9:74.
16 Amer YS, Wahabi HA, Abou Elkheir MM, *et al*. Adapting evidence-based clinical practice guidelines at university teaching hospitals: a model for the eastern Mediterranean region. *J Eval Clin Pract* 2019;25:550–60.
17 McCaul M, Ernstzen D, Temmingh H, *et al*. Clinical practice guideline adaptation methods in resource-constrained settings: four case studies from South Africa. *BMJ Evid Based Med* 2020;25:193–8.
18 Darzi A, Harfouche M, Arayssi T, *et al*. Adaptation of the 2015 American College of rheumatology treatment guideline for rheumatoid arthritis for the eastern Mediterranean region: an exemplar of the grade Adolopment. *Health Qual Life Outcomes* 2017;15:183.
19 Abdul-Khalek RA, Darzi AJ, Godah MW, *et al*. Methods used in adaptation of health-related guidelines: a systematic survey. *J Glob Health* 2017;7:020412.
20 Godah MW, Abdul Khalek RA, Kilzar L, *et al*. A very low number of national adaptations of the world Health organization guidelines for HIV and tuberculosis reported their processes. *J Clin Epidemiol* 2016;80:50–6.
21 Maaløe N, Ørtved AMR, Sørensen JB, *et al*. The injustice of unfit clinical practice guidelines in low-resource realities. *Lancet Glob Health* 2021;9:e875–9.
22 Song Y, Darzi A, Ballesteros M, *et al*. Extending the RIGHT statement for reporting adapted practice guidelines in healthcare: the RIGHT-Ad@pt Checklist protocol. *BMJ Open* 2019;9:e031767.
23 Tong ASP, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups 2007;19:349–57.
24 Palinkas LA, Horwitz SM, Green CA, *et al*. Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. *Adm Policy Ment Health* 2015;42:533–44.
25 Martínez García L, Sanabria AJ, Araya I, *et al*. Efficiency of pragmatic search strategies to update clinical guidelines recommendations. *BMC Med Res Methodol* 2015;15:57.
26 Vernooij RWM, Alonso-Coello P, Brouwers M, *et al*. Reporting items for updated clinical guidelines: checklist for the reporting of updated guidelines (checkup). *PLoS Med* 2017;14:e1002207.
27 Sanabria AJ, Pardo-Hernandez H, Ballesteros M, *et al*. The UpPriority tool was developed to guide the prioritization of clinical guideline questions for updating. *J Clin Epidemiol* 2020;126:80–92.
28 Gale NK, Heath G, Cameron E, *et al*. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Med Res Methodol* 2013;13:117.
29 Ritchie J, Lewis J, Nicholls CM, *et al*. *Qualitative research practice: a guide for social science students and researchers*. sage, 2013.
30 Braun V, Clarke V, Hayfield N, *et al*. Thematic Analysis. In: Liamputtong P, ed. *Handbook of research methods in health social sciences*. Singapore: Springer, 2019.
31 QSR International. NVivo Qualitative Data Analysis Software [Software], 1999. Available: https://qsrinternational.com/nvivo/nvivo-products/
32 Shah MA, Oliver TK, Peterson DE, *et al*. ASCO clinical practice guideline Endorsements and adaptations. *J Clin Oncol* 2020;38:834–40.
33 Dynamed evidence-based methodology, 2019. Available: https://www.dynamed.com/home/editorial/evidence-based-methodology
34 Qaseem A, Kansagara D, Lin JS, *et al*. The development of clinical guidelines and guidance statements by the clinical guidelines Committee of the American College of physicians: update of methods. *Ann Intern Med* 2019;170:863–70.
35 CCO guideline endorsement protocol 2019.
36 Dizon JM, Machingaidze S, Grimmer K. To adopt, to adapt, or to contextualise? the big question in clinical practice Guideline development. *BMC Res Notes* 2016;9:442.
37 Schünemann HBJ, Guyatt G, Oxman A, eds. *GRADE handbook for grading quality of evidence and strength of recommendations*. The GRADE Working Group, 2013. www.guidelinedevelopment.org/handbook
38 DELBI. German instrument for methodological guideline, 2019. Available: https://www.leitlinien.de/mdb/edocs/pdf/literatur/german-guideline-appraisal-instrument-delbi.pdf
39 Fervers B, Burgers JS, Haugh MC, *et al*. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. *Int J Qual Health Care* 2006;18:167–76.
40 COVID19 recommendations and gateway to Contextualization. Available: https://covid19.recmap.org/

4.3 Study III. "A reporting tool for adapted guidelines in health care: the RIGHT-Ad@pt checklist"

4.3.1 Summary of the results

We developed a reporting checklist for adapted CGs in health care, which started in May 2019 and was completed in October 2021.

Participants

A total of 119 professionals participated in a multi-step development process, including 38 members of the Working Group, 10 participants in the semi-structured interviews, and 71 participants in external review (61 guideline developers, and 10 guideline users). The development process of the RIGHT-Ad@pt checklist started in May 2019 and was completed in October 2021, with a total of seven iterations, culminating in the final version (the RIGHT-Ad@pt version 7) (Appendix II).

Generation of the initial checklist

The initial checklist retained all sections from the original RIGHT statement (51), although almost all items and topics were tailored for the adaptation process. The initial checklist comprised seven sections, 26 topics, and 40 items (RIGHT-Ad@pt checklist, version 1).

Optimisation of the Checklist

- Initial assessment of adapted clinical guidelines

  We assessed 10 adapted guidelines using version 1 of the checklist. Twenty-five items were deemed adequate for guideline reporting, whereas 15 required further review. We made 21 major and eight minor modifications to create version 2 of the RIGHT-Ad@pt checklist. We also developed a user guide that included explanations and examples for each item.

- Semi-structured interviews

  We conducted a total of 10 semi-structured interviews. The participants described four main steps of the adaptation process, including: selection of scope, assessment of source materials, formulation of adapted recommendations, and external review and follow-up process. We made 14 major and three minor modifications, improved the user guide, and created version 3 of the checklist.

- Delphi Consensus Survey

  Twenty-seven professionals agreed to participate in the Delphi consensus survey. Of these, 23 completed the first round of the survey (85.2% response rate). All items were rated as essential to be included and understandable. We received substantial feedback on both the checklist and user guide. We made 10 major and 13 minor modifications, and improved the user guide, to create version 4.1 of the checklist.

  A total of 23 professionals agreed to participate in the second round of the Delphi survey. Of these, 22 completed the second round of the survey (95.7% response rate). All items were understandable (except for 1 item) and maintained to be included. We received substantial feedback about three items. We made three major and 11 minor modifications, improved the user guide, and created version 4.2 of the checklist. We shared this version with the Delphi panel, and we did not receive further comments. Therefore, we did not conduct a third round of the Delphi survey.

- External review by clinical guideline developers and users
  - *External review with CG developers:* A total of 61 participants completed the survey (66.3% response rate). All items were rated as useful.
  - *External review with CG users:* We conducted a total of 10 semi-structured interviews. All participants judged the checklist as understandable and useful for reporting the adapted CGs.

  Based on external reviewers' feedback, we made four major and 11 minor modifications, improved the user guide, and created version 5 of the checklist.

- Final assessment of adapted clinical guidelines

  We assessed 10 adapted guidelines using version 5 of the checklist. Thirty-one items were considered adequate for the reporting, whereas three presented discrepancies in reporting. We made two major and 11 minor modifications, improved the user guide, and created version 6 of the checklist.

Approval of the final version of the checklist

We circulated version 6 of the checklist within the coordination team and advisory group for final feedback. We made one major modification on the basis of a substantial comment. The final version of the checklist (RIGHT-Ad@pt Checklist, version 7) was approved by the WG.

The final RIGHT-Ad@pt checklist contains 7 sections, 27 topics, 34 items, and the user guide (Appendix III). The sections comprise basic information (7 items); scope (6 items); rigour of development (10 items); recommendations (4 items); external review and quality assurance (2 items); funding, declaration, and management of interest (2 items); and other information (3 items). In addition, a user guide was developed to support the use of the checklist.

4.3.2 Publication of the study III

Annals of Internal Medicine RESEARCH AND REPORTING METHODS

A Reporting Tool for Adapted Guidelines in Health Care: The RIGHT-Ad@pt Checklist

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Background: Adaptation of existing guidelines can be an efficient way to develop contextualized recommendations. Transparent reporting of the adaptation approach can support the transparency and usability of the adapted guidelines.

Objective: To develop an extension of the RIGHT (Reporting Items for practice Guidelines in HealThcare) statement for the reporting of adapted guidelines (including recommendations that have been adopted, adapted, or developed de novo), the RIGHT-Ad@pt checklist.

Design: A multistep process was followed to develop the checklist: establishing a working group, generating an initial checklist, optimizing the checklist (through an initial assessment of adapted guidelines, semistructured interviews, a Delphi consensus survey, an external review, and a final assessment of adapted guidelines), and approval of the final checklist by the working group.

Setting: International collaboration.

Participants: A total of 119 professionals participated in the development process.

Measurements: Participants' consensus on items in the checklist.

Results: The RIGHT-Ad@pt checklist contains 34 items grouped in 7 sections: basic information (7 items); scope (6 items); rigor of development (10 items); recommendations (4 items); external review and quality assurance (2 items); funding, declaration, and management of interest (2 items); and other information (3 items). A user guide with explanations and real-world examples for each item was developed to provide a better user experience.

Limitation: The RIGHT-Ad@pt checklist requires further validation in real-life use.

Conclusion: The RIGHT-Ad@pt checklist has been developed to improve the reporting of adapted guidelines, focusing on the standardization, rigor, and transparency of the process and the clarity and explicitness of adapted recommendations.

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* For members of the RIGHT-Ad@pt Working Group, see the **Appendix** (available at Annals.org).

The World Health Organization defines guidelines as "systematically developed evidence-based statements which assist providers, recipients, and other stakeholders to make informed decisions about appropriate health interventions" (1). The development of high-quality de novo guidelines requires considerable resources, both financial and human (2). However, these resources are limited for almost all guideline development settings (3), especially those not able to develop their own guidelines (4–6). One option to address these barriers is the adaptation of published, high-quality guidelines (7–9).

We define guideline adaptation as adapting, adopting, or developing de novo recommendations from an existing, trustworthy guideline to create contextualized recommendations for a different health system (8–10). The adaptation of guidelines could save time and resources, avoid duplication of effort, and provide rapid and contextualized recommendations. This process has been especially important during the COVID-19 pandemic (7–9, 11).

Eight formal methodological frameworks for the guideline adaptation process have been identified (10, 12), and new methods and experiences are continuously emerging (13, 14). The ADAPTE framework was one of the earliest systematic approaches to adapt guidelines to local context (15). More recently, the GRADE-ADOLOPMENT (Grading of Recommendations Assessment, Development and Evaluation Evidence to Decision frameworks for adoption, adaptation, and de novo development of trustworthy recommendations) approach has been developed (9). However, the quality of adapted guidelines and their reporting still needs to be improved (16, 17).

Reporting guidelines enhance the accurate, complete, and transparent reporting of health research and evidence-based guidelines (www.equator-network.org). The RIGHT (Reporting Items for practice Guidelines in HealThcare) statement informs the reporting of the guideline development (18); however, it does not cover reporting of steps that are specific to guideline adaptation. Therefore, to ensure rigor, transparency, clarity, and reproducibility of reporting the adaptation process, we developed an extension of the RIGHT statement, the RIGHT-Ad@pt checklist. In this article, we report on the process for developing and refining the checklist.

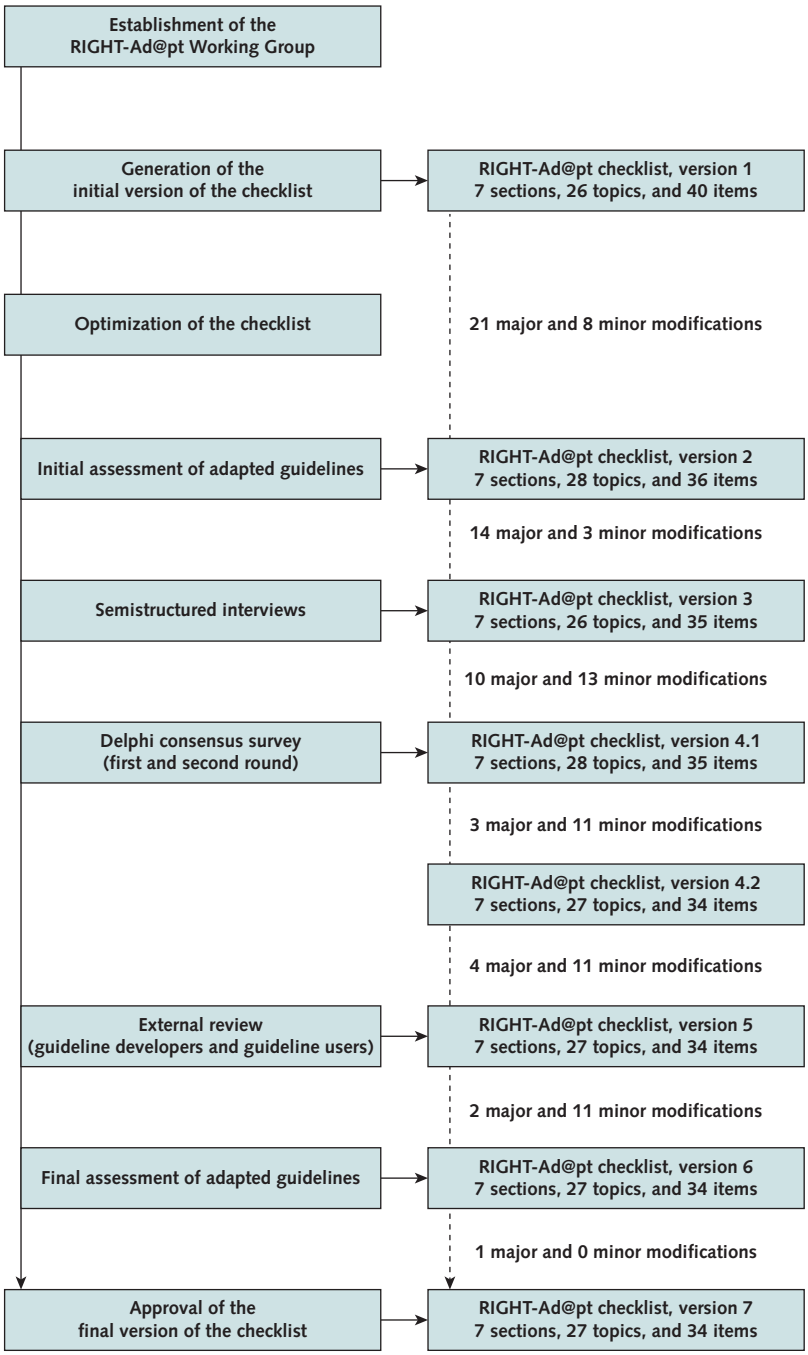
METHODS

A detailed description of methods is available in a previously published protocol (19). There was no deviation from

See also:

Web-Only
Supplement

Figure 1. Multistep development process of the RIGHT-Ad@pt checklist.



RIGHT = Reporting Items for practice Guidelines in HealThcare.

the protocol other than a timeline delay. Figure 1 shows the multistep development process of the RIGHT-Ad@pt checklist, which started in May 2019 and was completed in October 2021.

Establishment of the RIGHT-Ad@pt Working Group

The RIGHT-Ad@pt Working Group included the coordination team, advisory group, and Delphi panel. We collected the conflicts of interests of all members involved in the RIGHT-Ad@pt Working Group to manage the participation of members.

After each step of the development process, the coordination team discussed the results, drafted a report, agreed on major modifications (significant content changes) or minor modifications (writing style improvement), produced a new version of the checklist, and refined with the advisory group's feedback.

Generation of the Initial Checklist

The coordination team generated the initial checklist through online discussions, based on the RIGHT statement (18), research evidence in the field (10, 12, 16, 17, 20), and the advisory group's feedback.

Optimization of the Checklist

Initial Assessment of Adapted Guidelines

We applied the initial checklist to a randomly selected convenience sample of published adapted guidelines to explore the adequacy of each item (Table 1 of Supplement 1, available at Annals.org) (21).

Semistructured Interviews

We conducted semistructured interviews with guideline developers who had experience with guideline adaptation in the past 3 years. We explored participants' views and experiences on guideline adaptation and collected their feedback on each item, potentially missing items, and the overall usefulness of the checklist (Table 1 of Supplement 1).

Delphi Consensus Survey

We conducted a Delphi consensus survey with the Delphi panel to reach a consensus on the inclusion of items in the checklist (Table 1 of Supplement 1). For each Delphi round, we asked participants to rate whether each item should be included in the checklist using a 7-point scale (1 = strongly disagree and 7 = strongly agree) (22–25) (Table 1 of Supplement 1). We conducted 2 Delphi rounds until consensus about each item's inclusion was reached (median score, 6 to 7), and no further substantial comments on the items were provided. We also recorded panel members' perceptions about understandability, usability, completeness of reporting, reporting quality of each item, and overall usefulness of the checklist (Table 1 of Supplement 1).

External Review by Guideline Developers and Users

External Review With Guideline Developers. We conducted an online survey of persons who were involved in guideline adaptation in the past 3 years. Participants ranked the usefulness of the items and the overall usefulness of the checklist (Table 1 of Supplement 1).

External Review With Guideline Users. We conducted semistructured interviews with guideline users who have used practice guidelines in the past 3 years. We collected participants' feedback on the understanding and usefulness of each item and the overall checklist (Table 1 of Supplement 1).

Final Assessment of Adapted Guidelines

We used another randomly selected convenience sample of published adapted guidelines to explore the adequacy of each item of the checklist and recorded the time to apply the checklist (Table 1 of Supplement 1).

Approval of the Final Version of the Checklist

The coordination team generated the final version of the checklist. All members of the RIGHT-Ad@pt Working Group reviewed and approved the final version.

Institutional Review Board Approval

This project received a waiver of approval from the Clinical Research Ethics Committee at the Hospital de la Santa Creu i Sant Pau (Barcelona, Spain).

Role of the Funding Source

This work did not receive any funding support.

RESULTS

Figure 1 shows the multistep development process of the RIGHT-Ad@pt checklist and the results for each step. A total of 119 professionals participated in the development process (Table). The final version of the RIGHT-Ad@pt checklist is presented in Figure 2. In addition, in the supplements we included relevant intermediate results (Tables 4 through 8 of Supplement 1, available at Annals.org), the user guide (Supplement 2, available at Annals.org), and the comparison with the RIGHT statement (Table 9 of Supplement 1, available at Annals.org) (18).

Generation of the Initial Checklist

The initial checklist (RIGHT-Ad@pt checklist, version 1) retained all sections from the original RIGHT statement (18), although almost all items and topics were tailored for the adaptation process (10, 12). The initial checklist comprised 7 sections, 26 topics, and 40 items (Figure 1).

Optimization of the Checklist

Initial Assessment of Adapted Guidelines

We assessed 10 adapted guidelines using the RIGHT-Ad@pt checklist, version 1 (Table 2 of Supplement 1, available at Annals.org). Twenty-five items were deemed adequate for guideline reporting (25 of 40 [62.5%]), whereas 15 (15 of 40 [37.5%]) required further review (Table 3 of Supplement 1, available at Annals.org). We made 21 major and 8 minor modifications to create version 2 of the RIGHT-Ad@pt checklist (Table 4 of Supplement 1, available at Annals.org). We also developed a user guide that included explanations and examples for each item.

Semistructured Interviews

We conducted a total of 10 semistructured interviews. The participants described 4 main steps of the adaptation process, including selection of scope, assessment of source materials (which comprised 3 stepwise assessments: guideline, recommendations, and evidence levels), decision-making process, and external review and follow-up process (26). We made 14 major and 3 minor modifications and improved the user guide (Table 4 of Supplement 1).

Delphi Consensus Survey

Twenty-seven professionals agreed to participate in the Delphi consensus survey. Of these, 23 completed the first round of the survey (23 of 27; 85.2% response rate). All items were rated as essential to be included and understandable (Table 5 of Supplement 1, available at Annals.org). A few items (9 of 35 [25.7%]) raised concerns about their usability, completeness, and quality for

Table. Characteristics of Participants in the Multistep Development Process

Characteristic	RIGHT-Ad@pt Working Group			Semistructured Interviews	External Review		Total
	Coordination Team	Advisory Group*	Delphi Panel, First Round		Guideline Developers	Guideline Users	
Participants, *n*	7	8	23	10	61	10	119
Continents, *n* (%)							
Africa	–	–	1 (4.3)	1 (10.0)	3 (4.9)	1 (10.0)	6 (5.0)
Asia	1 (14.3)	3 (37.5)	4 (17.4)	3 (30.0)	8 (13.1)	3 (30.0)	22 (18.5)
Australia	–	1 (12.5)	3 (13.0)	–	2 (3.3)	–	6 (5.0)
Europe	6 (85.7)	2 (25.0)	7 (30.4)	2 (20.0)	28 (45.9)	3 (30.0)	48 (40.3)
North America	–	1 (12.5)	2 (8.7)	4 (40.0)	16 (26.2)	2 (20.0)	25 (21.0)
South America	–	1 (12.5)	6 (26.1)	–	4 (6.6)	1 (10.0)	12 (10.1)
Country income, *n* (%)†							
High income	6 (85.7)	6 (75.0)	12 (52.2)	6 (60.0)	47 (77.0)	5 (50.0)	82 (68.9)
Low to middle income	1 (14.3)	2 (25.0)	11 (47.8)	4 (40.0)	14 (23.0)	5 (50.0)	37 (31.1)
Organization, *n* (%)‡							
Hospital	2 (28.6)	1 (12.5)	5 (21.7)	1 (10.0)	10 (16.4)	8 (80.0)	27 (22.7)
Primary care/general practice	–	–	1 (4.3)	–	4 (6.6)	1 (10.0)	6 (5.0)
Research/knowledge production organization	6 (85.7)	4 (50.0)	10 (43.5)	5 (50.0)	26 (42.6)	–	51 (42.9)
Service provider organization (community)	–	–	–	–	3 (4.9)	–	3 (2.5)
University	1 (14.3)	3 (37.5)	9 (39.1)	1 (10.0)	17 (27.9)	2 (20.0)	33 (27.7)
Other	1 (14.3)	1 (12.5)	1 (4.3)	4 (40.0)	17 (27.9)	–	24 (20.2)
Current position, *n* (%)‡							
Clinician	1 (14.3)	4 (50.0)	6 (26.1)	3 (30.0)	22 (36.1)	10 (100.0)	46 (38.7)
Community member	–	–	–	–	3 (4.9)	–	3 (2.5)
Educator	–	2 (25.0)	6 (26.1)	–	11 (18.0)	1 (10.0)	20 (16.8)
Policymaker	–	2 (25.0)	4 (17.4)	1 (10.0)	9 (14.8)	–	16 (13.4)
Researcher/methodologist	7 (100.0)	4 (50.0)	17 (73.9)	7 (70.0)	34 (55.7)	3 (30.0)	72 (60.5)
Service provider	–	–	3 (13.0)	1 (10.0)	1 (1.6)	–	5 (4.2)
Student	–	–	–	–	1 (1.6)	–	1 (0.8)
Other	–	2 (25.0)	1 (4.3)	1 (10.0)	1 (1.6)	–	5 (4.2)
Experience in the guidelines field, *n* (%)‡							
Experience in developing guidelines	7 (100.0)	6 (75.0)	17 (73.9)	9 (90.0)	42 (68.9)	6 (60.0)	87 (73.1)
Experience in adapting guidelines	6 (85.7)	5 (62.5)	14 (60.9)	9 (90.0)	30 (49.2)	6 (60.0)	70 (58.8)
Methodological experience in developing guidelines	7 (100.0)	5 (62.5)	16 (69.6)	8 (80.0)	40 (65.6)	5 (50.0)	81 (68.1)
Methodological experience in adapting guidelines	7 (100.0)	4 (50.0)	13 (56.5)	9 (90.0)	26 (42.6)	5 (50.0)	64 (53.8)
Guidelines user	–	3 (37.5)	9 (39.1)	4 (40.0)	22 (36.1)	9 (90.0)	47 (39.5)
Other	–	–	5 (21.7)	–	6 (9.8)	1 (10.0)	12 (10.1)

RIGHT = Reporting Items for practice Guidelines in HealThcare.
* One member withdrew in 2020.
† Country income was classified according to The World Bank data (https://data.worldbank.org/country), accessed in May 2021.
‡ More than 1 response possible.

reporting adapted guidelines (items related to identification as an adapted guideline, year of publication, developer and country, abbreviations and acronyms, contact information, basic epidemiologic information of the problem, access, implementation, and update). We received substantial feedback on both the checklist and user guide. The panel members rated the checklist as useful for reporting and for assessing the reporting completeness of the adapted guidelines (Table 6 of Supplement 1, available at Annals.org). We made 10 major and 13 minor modifications, improved the user guide, and subsequently improved the checklist into version 4.1 (Table 4 of Supplement 1).

A total of 23 professionals agreed to participate in the second round of the Delphi survey. Of these, 22 completed the second round of the survey (22 of 23; 95.7% response rate). All items were maintained to be included and understandable (except for 1 item) (Table 5 of Supplement 1). The score improved for almost all 9 items that had some concerns for usability, completeness, and quality in the first round (Table 5 of Supplement 1). We received substantial feedback about 3 items. The rating of the checklist as useful for reporting and for assessing the reporting of the adapted guidelines was maintained (Table 6 of Supplement 1).

We made 3 major and 11 minor modifications, improved the user guide, and created the RIGHT-Ad@pt checklist, version 4.2 (Table 4 of Supplement 1). We shared this version and a modifications report with the Delphi panel, and we did not receive further comments. Therefore, we did not conduct a third round of the Delphi survey.

Figure 2. The RIGHT-Ad@pt checklist. RIGHT = Reporting Items for practice Guidelines in HealThcare.

7 sections, 27 topics, and 34 items		Assessment	Page(s)	Note(s)
Basic information				
Title/subtitle				
1	Identify the report as an adaptation of practice guideline(s), that is include "guideline adaptation", "adapting", "adapted guideline/recommendation(s)", or similar terminology in the title/subtitle.	☐ Yes ☐ No ☐ Unclear		
2	Describe the topic/focus/scope of the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
Cover/first page				
3	Report the respective dates of publication and the literature search of the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
4	Describe the developer and country/region of the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
Executive summary/abstract				
5	Provide a summary of the recommendations contained in the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
Abbreviations and acronyms				
6	Define key terms and provide a list of abbreviations and acronyms (if applicable).	☐ Yes ☐ No ☐ Unclear		
Contact information of the guideline adaptation group				
7	Report the contact information of the developer of the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
Scope				
Source guideline(s)				
8	Report the name and year of publication of the source guideline(s), provide the citation(s), and whether source authors were contacted.	☐ Yes ☐ No ☐ Unclear		
Brief description of the health problem(s)				
9	Provide the basic epidemiological information about the problem (including the associated burden), health systems relevant issues, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
Aim(s) and specific objectives				
10	Describe the aim(s) of the adapted guideline and specific objectives, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
Target population(s)				
11	Describe the target population(s) and subgroup(s) (if applicable) to which the recommendation(s) is addressed in the adapted guideline, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
End-users and settings				
12	Describe the intended target users of the adapted guideline, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
13	Describe the setting(s) for which the adapted guideline is intended, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		

Figure 2–Continued.

Rigor of development		
Guideline adaptation group		
14	List all contributors to the guideline adaptation process and describe their selection process and responsibilities.	☐ Yes ☐ No ☐ Unclear
Adaptation framework/methodology		
15	Report which framework or methodology was used in the guideline adaptation process.	☐ Yes ☐ No ☐ Unclear
Source guideline(s)		
16	Describe how the specific source guideline(s) was(were) selected.	☐ Yes ☐ No ☐ Unclear
Key questions		
17	State the key questions of the adapted guideline using a structured format, such as PICO (population, intervention, comparator, and outcome), or another format as appropriate.	☐ Yes ☐ No ☐ Unclear
18	Describe how the key questions were developed/modified, and/or prioritized.	☐ Yes ☐ No ☐ Unclear
Source recommendation(s)		
19	Describe how the recommendation(s) from the source guideline(s) was(were) assessed with respect to the evidence considered for the different criteria, the judgements and considerations made by the original panel.	☐ Yes ☐ No ☐ Unclear
Evidence synthesis		
20	Indicate whether the adapted recommendation(s) is/are based on existing evidence from the source guideline(s), and/or additional evidence.	☐ Yes ☐ No ☐ Unclear
21	If new research evidence was used, describe how it was identified and assessed.	☐ Yes ☐ No ☐ Unclear
Assessment of the certainty of the body of evidence and strength of recommendation		
22	Describe the approach used to assess the certainty/quality of the body/ies of evidence and the strength of recommendations in the adapted guideline and note any differences (if applicable) compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear
Decision-making processes		
23	Describe the processes used by the guideline adaptation group to make decisions, particularly the formulation of recommendations.	☐ Yes ☐ No ☐ Unclear
Recommendations		
Recommendations		
24	Report recommendations and indicate whether they were adapted, adopted, or *de novo*.	☐ Yes ☐ No ☐ Unclear
25	Indicate the direction and strength of the recommendations and the certainty/quality of the supporting evidence and note any differences compared to the source recommendations(s) (if applicable).	☐ Yes ☐ No ☐ Unclear
26	Present separate recommendations for important subgroups if the evidence suggests important differences in factors influencing recommendations and note any differences compared to the source recommendations(s) (if applicable).	☐ Yes ☐ No ☐ Unclear

Figure 2–Continued.

Rationale/explanation for recommendations		
27	Describe the criteria/factors that were considered to formulate the recommendations or note any relevant differences compared to the source guideline(s) (if applicable).	☐ Yes ☐ No ☐ Unclear
External review and quality assurance		
External review		
28	Indicate whether the adapted guideline underwent an independent external review. If yes, describe the process.	☐ Yes ☐ No ☐ Unclear
Organizational approval		
29	Indicate whether the adapted guideline obtained organizational approval. If yes, describe the process.	☐ Yes ☐ No ☐ Unclear
Funding, declaration, and management of interest		
Funding source(s) and funder role(s)		
30	Report all sources of funding for the adapted guideline and source guideline(s), and the role of the funders.	☐ Yes ☐ No ☐ Unclear
Declaration and management of interests		
31	Report all conflicts of interest of the adapted and the source guideline(s) panels, and how they were evaluated and managed.	☐ Yes ☐ No ☐ Unclear
Other information		
Implementation		
32	Describe the potential barriers and strategies for implementing the recommendations (if applicable).	☐ Yes ☐ No ☐ Unclear
Update		
33	Briefly describe the strategy for updating the adapted guideline (if applicable).	☐ Yes ☐ No ☐ Unclear
Limitations and suggestions for further research		
34	Describe the challenges of the adaptation process, the limitations of the evidence, and provide suggestions for future research.	☐ Yes ☐ No ☐ Unclear

RIGHT = Reporting Items for practice Guidelines in HealThcare.

External Review With Guideline Developers and Users

External Review With Guideline Developers. A total of 61 participants completed the survey (61 of 92; 66.3% response rate). All items were rated as useful (Table 5 of Supplement 1). The participants rated the checklist as useful for reporting, for assessing the reporting of the adapted guidelines, and for informing guideline adaptation process (Table 6 of Supplement 1).

External Review With Guideline Users. We conducted a total of 10 semistructured interviews. All participants judged the checklist as understandable and useful for reporting the guideline adaptation process.

On the basis of external reviewers' feedback, we made 4 major and 11 minor modifications, improved the user guide, and created the RIGHT-Ad@pt checklist, version 5 (Table 4 of Supplement 1).

Final Assessment of Adapted Guidelines

We assessed 10 adapted guidelines using version 5 of the RIGHT-Ad@pt checklist (Table 7 of Supplement 1, available at Annals.org). Thirty-one items were considered adequate for the reporting (31 of 34 [91.2%]), whereas 3 (3 of 34 [8.8%]) presented discrepancies about reporting (Table 8 of Supplement 1, available at Annals.org). The reviewers spent an average of 45 minutes (range, 40 to 54 minutes) assessing adapted guidelines using the checklist. We made 2 major and 11 minor modifications and improved the user guide (Table 4 of Supplement 1).

Approval of the Final Version of the Checklist

We circulated version 6 of the RIGHT-Ad@pt checklist within the coordination team and advisory group for

final feedback. We made 1 major modification on the basis of a substantial comment (**Table 4** of **Supplement 1**). The final version of the checklist (RIGHT-Ad@pt Checklist, version 7) was approved by the RIGHT-Ad@pt Working Group.

The final RIGHT-Ad@pt checklist, version 7, contains 7 sections, 27 topics, 34 items, and the user guide (**Figure 2** and **Supplement 2**). The sections comprise basic information (7 items); scope (6 items); rigor of development (10 items); recommendations (4 items); external review and quality assurance (2 items); funding, declaration, and management of interest (2 items); and other information (3 items) (**Figure 2**). In addition, a user guide was developed to support the use of the checklist (**Supplement 2**).

Discussion

We developed an extension of the RIGHT statement for the reporting of adapted guidelines–the RIGHT-Ad@pt checklist–through an exhaustive process that included a literature review as well as input and consensus from a full range of relevant stakeholders, including guideline adaptation experts. We also evaluated the applicability and usability of the checklist and did validity testing.

The RIGHT-Ad@pt checklist can be used to guide the reporting of adapted guidelines, including adaptation process ("rigor of development" section) and the adapted recommendations ("recommendations" section). The checklist can also be applied to assess the completeness of reporting and, in combination with available adaptation frameworks, to inform adaptation processes. Users should apply the checklist along with the user guide to report adapted guidelines. Response options ("yes," "no," and "unclear") can be used to provide judgments on the reporting content. We suggest at least 2 reviewers apply the RIGHT-Ad@pt checklist independently when assessing the completeness of reporting of an adapted guideline. Discrepancies should be solved by discussion or involve a third reviewer if there is a need to reach a consensus. It is recommended that users of the RIGHT-Ad@pt checklist do not score each item or create an overall score because that assumes equal weight across items, which may not be the case. Instead, we encourage users to interpret the reporting according to the responses and make an overall judgment.

Currently, there is no published guidance or checklist for reporting adapted guidelines. Similar to the RIGHT statement that focuses on reporting guideline recommendations, the RIGHT-Ad@pt checklist emphasizes the importance of methodological rigor in the adaptation process. The checklist includes 7 new items and improved 13 items by tailoring adaptation practice (**Table 9** of **Supplement 1**, available at Annals.org). Besides, we renamed the "evidence" section in the RIGHT statement to "rigor of development" to better highlight the adaptation process. We also combined 19 RIGHT items into 6 RIGHT-Ad@pt items to shorten the checklist and increase usability. Furthermore, we deleted 1 item because of duplication and modified the wording for all items.

Unlike previous frameworks that focus on the practical adaptation process (9, 10, 15), the RIGHT-Ad@pt checklist focuses on reporting aspects for recommendations and critical methodological processes. The RIGHT-Ad@pt checklist suggests stratifying the reporting of the evidence review process into guideline level (item 16), recommendation level (item 19), and evidence level (items 20 and 21). The stratification fits the guideline adaptation conceptual progression, which shifts from adapting guidelines to adapting recommendations, as a review of available frameworks suggests (12). The RIGHT-Ad@pt checklist also required explicitly reporting the decision-making process (item 23) and the rationale of the recommendations' modifications (item 27), which adaptation experts highlighted as an essential aspect to explore further (26). Besides, the RIGHT-Ad@pt checklist promotes transparency in the adaptation process by reporting differences about the guideline scope, recommendations, and the decision-making process compared with the source guidelines.

The RIGHT-Ad@pt checklist retains the strengths of the RIGHT statement while adequately contextualizing the guideline adaptation process. In addition, the checklist reflects a relatively strong overall consensus among a wide range of stakeholders, including guideline developers, users, journal editors, and policymakers, through a formal Delphi consensus survey. Finally, we also conducted usability testing with external reviewers and 2 assessments with published adapted guidelines, enhancing the validity of the RIGHT-Ad@pt checklist for reporting of and assessing the reporting of adapted guidelines. The RIGHT-Ad@pt checklist, despite having showed face and content validity, requires further validation in real-life use.

Different audiences may use the RIGHT-Ad@pt checklist for different purposes. First, guideline developers can use the checklist to report their adapted guidelines. Second, journal editors and reviewers could use the checklist to ensure the completeness and transparency of the reporting in the publication of adapted guidelines. Third, detailed and clear reporting would help clinicians accurately identify the adapted recommendations, whether they are different from the source recommendations, and the justifications for any differences. These details can assist clinicians applying adapted recommendations to their clinical practice. Finally, policymakers could evaluate the feasibility of adapted recommendations for local implementation on the basis of the reporting contents suggested by the checklist, therefore enhancing the applicability and potential effect of guidelines and supporting health decision making.

Future research should address the completeness of adapted guidelines and whether the publication of RIGHT-Ad@pt will have an influence on reporting. This research could also explore the potential effect of RIGHT-Ad@pt on the quality of adapted guidelines and efficiency of the adaptation process. Another aspect worth exploring is the development of an abridged version of the RIGHT-Ad@pt checklist that facilitates its application.

The RIGHT-Ad@pt checklist will be published on the EQUATOR Network's website (www.equator-network.org), the RIGHT website (www.right-statement.org), and the Guidelines International Network website (https://g-i-n.net/get-involved/resources/). We will also encourage its translation into other languages and engage the journal

editors to use the checklist to standardize the reporting of adapted guidelines to be published. We are preparing an online version of the RIGHT-Ad@pt checklist to facilitate its application, in which we will include a comment box to gather further feedback and update the checklist in the future.

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References

1. **World Health Organization.** WHO handbook for guideline development. 2nd ed. World Health Organization; 2014.
2. **Graham R, Mancher M, Miller Wolman D, et al, eds; Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines.** Clinical Practice Guidelines We Can Trust. National Academies Pr; 2011.
3. **Schünemann HJ, Fretheim A, Oxman AD; WHO Advisory Committee on Health Research.** Improving the use of research evidence in guideline development: 1. Guidelines for guidelines. Health Res Policy Syst. 2006;4:13. [PMID: 17118181]
4. **Bhaumik S.** Use of evidence for clinical practice guideline development. Trop Parasitol. 2017;7:65-71. [PMID: 29114482] doi:10.4103/tp.TP_6_17
5. **Kahale LA, Ouertatani H, Brahem AB, et al.** Contextual differences considered in the Tunisian ADOLOPMENT of the European guidelines on breast cancer screening. Health Res Policy Syst. 2021;19:80. [PMID: 33985535] doi:10.1186/s12961-021-00731-z
6. **Arayssi T, Harfouche M, Darzi A, et al.** Recommendations for the management of rheumatoid arthritis in the eastern Mediterranean region: an ADOLOPMENT of the 2015 American College of Rheumatology guidelines. Clin Rheumatol. 2018;37:2947-2959. [PMID: 30097896] doi:10.1007/s10067-018-4245-5
7. **Fervers B, Burgers JS, Haugh MC, et al.** Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. Int J Qual Health Care. 2006;18:167-76. [PMID: 16766601]
8. **Fervers B, Burgers JS, Voellinger R, et al; ADAPTE Collaboration.** Guideline adaptation: an approach to enhance efficiency in guideline development and improve utilisation. BMJ Qual Saf. 2011;20:228-36. [PMID: 21209134] doi:10.1136/bmjqs.2010.043257
9. **Schünemann HJ, Wiercioch W, Brozek J, et al.** GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. J Clin Epidemiol. 2017;81:101-110. [PMID: 27713072] doi:10.1016/j.jclinepi.2016.09.009
10. **Darzi A, Abou-Jaoude EA, Agarwal A, et al.** A methodological survey identified eight proposed frameworks for the adaptation of health related guidelines. J Clin Epidemiol. 2017;86:3-10. [PMID: 28412463] doi:10.1016/j.jclinepi.2017.01.016
11. **Maaløe N, Ørtved AMR, Sørensen JB, et al.** The injustice of unfit clinical practice guidelines in low-resource realities. Lancet Glob Health. 2021;9:e875-e879. [PMID: 33765437] doi:10.1016/S2214-109X(21)00059-0

12. **Wang Z, Norris SL, Bero L.** The advantages and limitations of guideline adaptation frameworks. Implement Sci. 2018;13:72. [PMID: 29843737] doi:10.1186/s13012-018-0763-4
13. **Amer YS, Wahabi HA, Abou Elkheir MM, et al.** Adapting evidence-based clinical practice guidelines at university teaching hospitals: a model for the eastern Mediterranean region. J Eval Clin Pract. 2019;25:550-560. [PMID: 29691950] doi:10.1111/jep.12927
14. **McCaul M, Ernstzen D, Temmingh H, et al.** Clinical practice guideline adaptation methods in resource-constrained settings: four case studies from South Africa. BMJ Evid Based Med. 2020;25:193-198. [PMID: 31292208] doi:10.1136/bmjebm-2019-111192
15. **ADAPTE.** The ADAPTE process: resource toolkit for guideline adaptation. Version 2.0 Accessed at https://g-i-n.net/wp-content/uploads/2021/03/ADAPTE-Resource-toolkit-March-2010.pdf on 1 August 2021.
16. **Godah MW, Abdul Khalek RA, Kilzar L, et al.** A very low number of national adaptations of the World Health Organization guidelines for HIV and tuberculosis reported their processes. J Clin Epidemiol. 2016;80:50-56. [PMID: 27565977] doi:10.1016/j.jclinepi.2016.07.017
17. **Abdul-Khalek RA, Darzi AJ, Godah MW, et al.** Methods used in adaptation of health-related guidelines: a systematic survey. J Glob Health. 2017;7:020412. [PMID: 29302318] doi:10.7189/jogh.07.020412
18. **Chen Y, Yang K, Marušic A, et al; RIGHT (Reporting Items for Practice Guidelines in Healthcare) Working Group.** A reporting tool for practice guidelines in health care: the RIGHT statement. Ann Intern Med. 2017;166:128-132. [PMID: 27893062] doi:10.7326/M16-1565
19. **Song Y, Darzi A, Ballesteros M, et al.** Extending the RIGHT statement for reporting adapted practice guidelines in healthcare: the RIGHT-Ad@pt Checklist protocol. BMJ Open. 2019;9:e031767. [PMID: 31551391] doi:10.1136/bmjopen-2019-031767
20. **Darzi A, Harfouche M, Arayssi T, et al.** Adaptation of the 2015 American College of Rheumatology treatment guideline for rheumatoid arthritis for the eastern Mediterranean region: an exemplar of the GRADE ADOLOPMENT. Health Qual Life Outcomes. 2017;15:183. [PMID: 28934978] doi:10.1186/s12955-017-0754-1
21. **Glenton C, Carlsen B, Lewin S, et al.** Applying GRADE-CERQual to qualitative evidence synthesis findings-paper 5: how to assess adequacy of data. Implement Sci. 2018;13:14. [PMID: 29384077] doi:10.1186/s13012-017-0692-7
22. **Likert R.** A technique for the measurement of attitudes. Archives of Psychology. 1932;22:140-155.
23. **Akins RB, Tolson H, Cole BR.** Stability of response characteristics of a Delphi panel: application of bootstrap data expansion. BMC Med Res Methodol. 2005;5:37. [PMID: 16321161]
24. **Sinha IP, Smyth RL, Williamson PR.** Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. PLoS Med. 2011;8:e1000393. [PMID: 21283604] doi:10.1371/journal.pmed.1000393
25. **Finstad K.** Response interpolation and scale sensitivity: evidence against 5-point scales. J Usability Stud. 2010;5:104-110.
26. **Song Y, Ballesteros M, Li J, et al.** Current practices and challenges in adaptation of clinical guidelines: a qualitative study based on semistructured interviews. BMJ Open. 2021;11:e053587. [PMID: 34857574] doi:10.1136/bmjopen-2021-053587

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5. DISCUSSION

5 Discussion

5.1 Main findings

This thesis explored current practice and main challenges of CG adaptation globally and has developed a reporting checklist through a multi-stage development process, providing guidance on the methodology for CG adaptation, and the reporting of adapted CGs. The thesis includes three studies: a national survey to explore how CGs are developed, adapted, and updated in China (Study I) (123), a qualitative study to explore current practice of CG adaptation and identify challenges presented along this process (Study II) (115), and the development of a tool for the reporting of adapted CGs in healthcare (Study III) (124).

In Study I, we described the current methods used for CG development, adaptation and updating practices in China. We found that CG development process in China was aligned with international standards, but methods used for specific steps tended to be both variable and informal. CG organisations based their practices on varied sources, like methodological handbooks or expert experience and opinion. However, only a few CG organisations had a specific CG development division, multiple stakeholder engagement, a formal process to assess the quality of evidence, a CG updating strategy, a COI management policy, or funding support. Similarly, we found that practices for adapting CGs were not supported by standard methods.

In Study II, we explored the current CG adaptation practice from nine organisations worldwide. We identified the current methods used for the CG adaptation and summarised the findings in a structured CG adaptation process, including four core steps (selection of scope and source CGs, assessment of source materials, formulation of recommendations, and external review and follow-up process). We stratified the level of assessment of source materials into three levels (guideline, recommendation, and evidence level). We also identified four reasons for adapting CGs (to develop own CGs, to implement or endorse source CGs, to update an existing CG, and to analyse conflicting recommendations from different source CGs), challenges for adapting CGs (limitations from source CGs, limitations from adaptation settings, adaptation process intensity and complexity, and implementation barriers), and described organisations' strategies for dealing with these challenges.

In Study III, we developed the RIGHT-Ad@pt checklist for the reporting of adapted CGs. The RIGHT-Ad@pt checklist includes 34 items grouped in seven sections: 1) basic information; 2) scope; 3) rigour of development; 4) recommendations; 5) external review and quality assurance; 6) funding, declaration, and management of interest; and 7) other information. We also developed a user guide that included explanations and real-world examples for each item.

5.2 Our results in the context of previous research

This thesis work extends the knowledge of the CG adaptation practice and methodology, and provides organisations with detailed reporting guidance. Previous reviews have described more than eight CG adaptation frameworks and summarised the existing adaptation methodology, mainly focusing on the general process of CG adaptation, highlighting the similarity and variability of the CG adaptation process (89, 93). The three studies included in this thesis illustrate the variability and informality of CG development and adaptation practice, propose core steps of the CG adaptation process to streamline future initiatives, and develop a reporting checklist to provide standardised guidance for reporting adapted CGs (124, 125). The discussion below compares the main findings of each study with the previously available research.

5.2.1 Developing and adapting clinical guidelines in China

Previous quality assessment studies on Chinese CGs found that the quality of Chinese CGs is gradually improving (126, 127). Zhou Q et al. in 2021, systematically reviewed the methodological and reporting quality of Chinese CGs published between 2014 and 2018, using AGREE II tool and the RIGHT checklist (126). They found that the quality of CGs published before 2014 was lower than those published during 2014-2018 (126). Specifically, the mean score for the domain of "rigour of development" was 7.0% versus 11.7%, respectively. Similarly, Zhou X et al. in 2020 conducted a critical analysis of the quality of Chinese CGs and described how the quality seemed to improve over time (127). These authors found that CG quality was significantly higher for CGs published after 2014, with the mean score for the domain of "rigour of development" increasing from 9.7% to 21.1% (127).

As shown in Study I, despite the improvement of Chinese CG methods and quality, specific steps tended to be both variable and informal. Some CG organisations (37.5%) did not follow any methodological guidance or handbook (123). Others based their practice on various organisational handbooks (e.g., WHO, NICE),

methodological resources (e.g., Guidelines 2.0 checklist, AGREE II, or GRADE), in-house handbooks, or solely on expert opinion. In addition, the specific steps from methodological resources that Chinese CG organisations have followed varied to some extent. In addition, some organisations (27.6%) reported having used GRADE methodology for CG development; however, the methods used to assess the quality of evidence and source CGs relied on expert consensus or other assessment processes rather than methodological assessment tools (27.6%) (123).

Similarly, a recent systematic review assessed the CG development process of Chinese CGs published between 2010 to 2020, and found that the process for formulation of recommendations and rating the strength of recommendations varied (128). Out of 2,654 included Chinese CGs, only 62 (2.34%) considered important factors, such as values and preferences of patients, resources use, equity, acceptability, and feasibility when formulating recommendations. None of the CG followed a standardised evidence to decision process for decision-making (128). Nevertheless, the inconsistent application of CG development methods, including the GRADE approach, also happens in high-income countries (HICs). For instance, a methodological study of Australian CGs found that the application of the GRADE approach varied between guidelines, with some CGs misreporting the CG methods or altered aspects of the GRADE approach without justification (129). Specifically, among 15 retrievable Australian CGs, published between 2011 to 2018, that followed the GRADE approach, only four (27%) considered all GRADE criteria (e.g., balance of desirable and undesirable effects; the certainty of the evidence; values and preferences, and resource use) when determining the strength of a recommendation (129).

Previous empirical evidence on the quality of Chinese CGs argued the necessity to establish a national CG system to improve the quality of Chinese CGs (73). However, to date, most Chinese CG development organisations still do not have a specific division to oversee the quality of the CG development process. This may cause problems, such as lacking stakeholder engagement or COI management, and funding support, poor updating strategies, and insufficient implementation and adherence monitoring (123). A similar situation happens in other low- and middle-income countries (LMICs), like in India (70). One quality appraisal study on Indian CGs showed that CG development was usually unplanned and ad hoc, without sufficient government structure and funding support (70).

A multiple stakeholder engagement could improve the adoption of recommendations and facilitate the implementation of CGs (20, 130). However, most Chinese CG organisations in Study I report including only

clinical experts and methodologists during CG development process, and lacked the participation of other stakeholders (e.g., patient representativeness, or policymakers) (123). Likewise, in India most CGs were developed by institutions with only elitism, lacking other stakeholder engagement, and affecting the implementation of guidelines (70). The quality appraisal study on Indian CGs showed that only one of the 11 CGs included was rated as "recommended". The authors also interviewed CG developers of included CGs; one of the ten interviewees reported they had involved patients in CG development (70).

As defined by Thompson in 1993, *"Conflict of interest is a set of conditions in which professional judgement concerning a primary interest (such as patients' welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)"* (24). Few Chinese CG organisations in Study I reported that they had a policy to manage COI. Potential COI can introduce bias in the decision-making process and impact the formulation of recommendations, and without proper management of COI the trustworthiness of Chinese CGs is likely to remain limited. Similarly, In India COI management faces important challenges, as CG developers are sometimes reluctant to report them or have a poor understanding of the impact of COI on health-related decisions (70).

Previous research shows that recommendations become outdated fairly quickly (20% of the recommendations probably need to be reviewed prior to three years) (131). It is, therefore, likely that a large number of Chinese CG and recommendations are out of date, as many CG organisations (82.5%) did not report having a formal updating strategy. Therefore, Chinese CG organisations should develop and implement updating strategies to ensure an updated catalogue of CGs.

Without monitoring adherence, CG organisations are not able to address potential barriers influencing the adoption of recommendations, and the implementation of CGs during the CG development process, hindering the uptake of health-related recommendations. The adherence to CGs and recommendations varies across different settings and is sometimes suboptimal (132, 133). For example, the CG adherence of endocrine therapy prescription for breast cancer patients was 90% in European countries (132) and 67% in Mexico (133); and the CG adherence for the overall breast cancer care process in Europe ranged from 54% to 69% (132). The internal barriers for CG adherence include clinician's perceptions, preferences, lack of knowledge, or intentional decisions (132). Similarly, CG adherence in China is also suboptimal and varies widely, ranging from 0% to 72.87% (134, 135). Study I shows that CG adherence monitoring was not performed sufficiently by CG developers in China (33.3%) (123). Two survey studies on the barriers and

enablers of the implementation of Chinese CGs, showed that clinicians did not consider recommendations appropriate or applicable because few or no Chinese patients had been considered during the CG development (82, 83).

CG adaptation has been widely used in different countries; however, the methods and processes used are varied and often informal, especially in LMICs (70, 123). In a previous review, Wang et al. summarised and analysed the implementation of the CG adaptation frameworks and found that only one framework, the adapted ADAPTE (97), was applied in a low-middle income country – Egypt (93). In China, the majority of Chinese organisations reported having adapted existing CGs; however, they rarely reported the use of an adaptation framework (123). Similarly, CG developers in India have gradually considered CG adaptation as an efficient way for CG development, and highlighted the need to improve the CG adaptation methods (67, 70). A quality appraisal study on CG development and the use of evidence in India found a transition towards the adoption of systematic, transparent and evidence-based guidelines (70). However, several barriers hinder the CG adaptation process in India, including the increasing preference for integrating local data and lack of methodological capacity (70).

5.2.2 Adapting Clinical Guidelines

5.2.2.1 Initiatives for adapting clinical guidelines

As shown in study II, CG adaptation processes are being increasingly used over the last years (125). An early review listed the initiatives for CG adaptation, including adapting CGs as an alternative methodology for the *de novo* CG development process, saving time and resources, or using CG adaptation as a systematic method to enhance CG implementation, and developing contextualised recommendations (69). More recently, CG adaptation also plays a role in CG updating, by adapting existing published CGs, and as a strategy to harmonise source recommendations when there are discrepancies among recommendations for the same topic (125).

5.2.2.2 Methods for adapting clinical guidelines

CG adaptation methods have also been gradually improving over the last two decades. Previous systematic reviews identified a total of nine CG adaptation frameworks (89, 93), including several based on the ADAPTE framework (e.g., adapted ADAPTE (97, 108)), on the GRADE approach (e.g., SNAP-IT (91)), or on the GRADE EtD framework (e.g., GRADE-ADOLOPMENT (87)). In Study II, only three to four years after these reviews,

we managed to identify seven additional adaptation methodologies, which speaks of the important activity around CG adaptation methods by organisations widely (125).

CG adaptation methods that CG organisations currently use, identified in study II, are diverse (125). Four of the identified methods are organisational standards from HICs, developed by organisational expert committees, including the American College of Physicians (ACP) guidance statement (18), the American Society of Clinical Oncology (ASCO) CG endorsement/adaptation methodology (118), the Cancer Care Ontario's (CCO) endorsement protocol (119), and the DynaMed editorial methodology (120). The other two derived from CG adaptation experiences in the Philippines and India (the Piloted adaptation framework and the Adopt–Contextualise–Adapt (ACA) framework) (117, 122): the Piloted adaptation framework was proposed by the UK National Institute for Health and Care Excellence (NICE), and was piloted in the Indian national CG development programme (122); the ACA framework has also been used in another LMIC – South Africa (136). Another adaptation method, used by the Association of the Scientific Medical Societies in Germany, was an appraisal tool named DELBI (121). Similarly, El-Khoury et al. have recently reviewed CG development guidance documents and identified 48 documents describing CG adaptation methods. Among the 48 documents, 19% were dedicated entirely to CG adaptation, and 50% referred to the ADAPTE-toolkit (137).

A recent SR summarised methodological tools for CG development, reporting, and quality assessment, published between 2010 and 2020 (138). The authors identified 17 publications that reported CG adaptation frameworks, validity testing results of CG adaptation frameworks or methods (138). Apart from CG adaptation frameworks identified by previous SRs (89, 93), there are seven additional CG adaptation frameworks or methods (138). Five of them were CG adaptation methods, developed based on national CG development processes, including adaptation methods in Korea (139), Turkey (140), and Iran (141-143). The other two are newly emerged CG adaptation frameworks. One adaptation framework, named the European Federation of Internal Medicine (EFIM) methodology, was developed based on the AGREE II and ADAPTE frameworks (144). The EFIM methodology aims to facilitate the adaptation of valid CGs within the context of elderly patients with comorbidities (144). Another adaptation framework, named Principles for Adapting Guidelines in Emergencies (PAGE), was developed specifically for the emergency healthcare context in the United States (144).

5.2.2.3 Variability of the clinical guideline adaptation processes

Previous SRs have emphasised notable differences in CG adaptation (86, 93), mainly in the steps of selection of the scope and source CGs, assessment of source materials, and formulation of recommendations. This variability is also present in the methodologies, identified in study II (125).

1) Selection of scope and source CGs

The differences among different adaptation frameworks in the selection of CG scope and source CGs, depend on the objectives of the CG adaptation, whether to develop CGs, through the CG adaptation of source CGs or to implement a source CG in the target setting (69, 93, 125). Sometimes CG adaptation groups intend to adapt existing CGs as part of or as an alternative way of developing *de novo* CGs; the CG adaptation process should include a similarly rigorous process as the *de novo* CG development process, plus the additional assessment on the source materials. The CG adaptation process consists of a systematic search to retrieve and select source CGs, assessing the source CGs, recommendations and evidence, to rate certainty of the body of evidence, and going through the process of decision-making on whether to adapt or adopt recommendations (86, 91). On some occasions, adaptation groups have the intention to use adaptation to implement a specific source CG. In such scenarios, the CG adaptation process will focus on the evidence to decision process, including implementation and monitoring/evaluation considerations. GRADE-ADOLOPMENT and CAN-IMPLEMENT are two examples of this approach (87, 92), in which the source CGs that are being adapted usually are chosen before the adaptation process starts.

From the perspective of organisations that provide methodological support for CG adaptation, the variability of the CG adaptation processes could also be differentiated into two (145). A qualitative study of WHO staff experiences, described two approaches (145), the "Copy or Customize Model" and the "Capacity Building Model". The "Copy or Customize Model" adopts source recommendations and focuses on the implementation factors for local use with WHO's support, without deliberately assessing source recommendations content. Meanwhile, the "Capacity Building Model" focuses on regional capacity building, while adapting WHO or other sources of CGs. The capacity building is on evidence synthesis methods and frameworks, in order to support the local development of a national guideline informed by international guidelines (145).

2) Assessment of source materials

According to the variability of the adaptation practice, study II stratified the assessment of source materials into CG level, recommendation level, and research evidence level. This stratification aligns with the concept's evolution highlighted by the review of CG adaptation frameworks, which is from adapting the source CGs to adapting specific recommendations, stratifying with constructed evidence tables and evidence to decision factors (93). For example, ADAPTE focuses on the assessment at the CG level, evaluating the quality of source CGs or based on panel discussions to reduce the number of source CGs, and on the recommendation level, by looking at the coherence of evidence and recommendations, and on the applicability of recommendations (86). In contrast, in recently published CG adaptation frameworks that follow the GRADE approach and the GRADE EtD frameworks, the assessment of source materials focuses on the evidence level, including updating source evidence or supplementing new evidence (87, 91).

3) Formulation of recommendations

Since 2010, the formulation of recommendations varied among current CG adaptation frameworks, depending on whether they included the GRADE approach (86, 87, 91). Initially, the Decision and Selection Module of the ADAPTE framework, suggests reviewing the assessment results of CG quality, supporting evidence, and context differences from source recommendations, without mentioning the evidence to decision process and factors (86, 146). Four years later, the decision-making process for CG adaptation started combining with the GRADE approach regarding formulating recommendations and going from evidence to recommendations, in the SNAP-IT adaptation framework (91, 146, 147). Afterwards, the GRADE evidence to decision framework was developed, and building on this latter framework, the GRADE-ADOLOPMENT approach for adoption, adaptation and development *de novo* recommendations was inspired (35, 87).

In study II, we summarised the process of formulation of recommendations for adapted CGs, including 1) reviewing the source materials assessment, including recommendations content, supporting evidence, evidence to decision factors and the evidence interpretation from the source CG group(s), 2) deciding whether to adapt, adopt or develop *de novo* recommendations, and 3) formulating the adapted recommendations (125). As organisations keep adopting GRADE, there is a clear trend in the CG adaptation arena to incorporate the GRADE approach and, to a lesser extent, the GRADE EtD frameworks (35, 87).

However, the formulation of recommendations for adapted CGs remains suboptimal, as highlighted by a review of CG adaptation methods contained in CG development guidance (137). Only 10% of identified CG

adaptation methods considered the indirectness of source evidence, 29% assessed the baseline risk of the outcomes, and 27% addressed the consideration of equity (137).

5.2.2.4 Comparison between clinical guideline development and adaptation process

Methods for adapting CGs follow a somewhat similar process as methods for developing CGs, sharing steps, like: 1) planning and establishing a CG development group, selection of the CG scope, and management of conflict of interests, 2) defining health questions, 3) searching and selecting evidence/source CGs, 4) evidence synthesis and assessment, 5) formulation of recommendations, 6) external review, and 7) follow-up activities (i.e., publication and dissemination, implementation, and updating), (Figure 06).

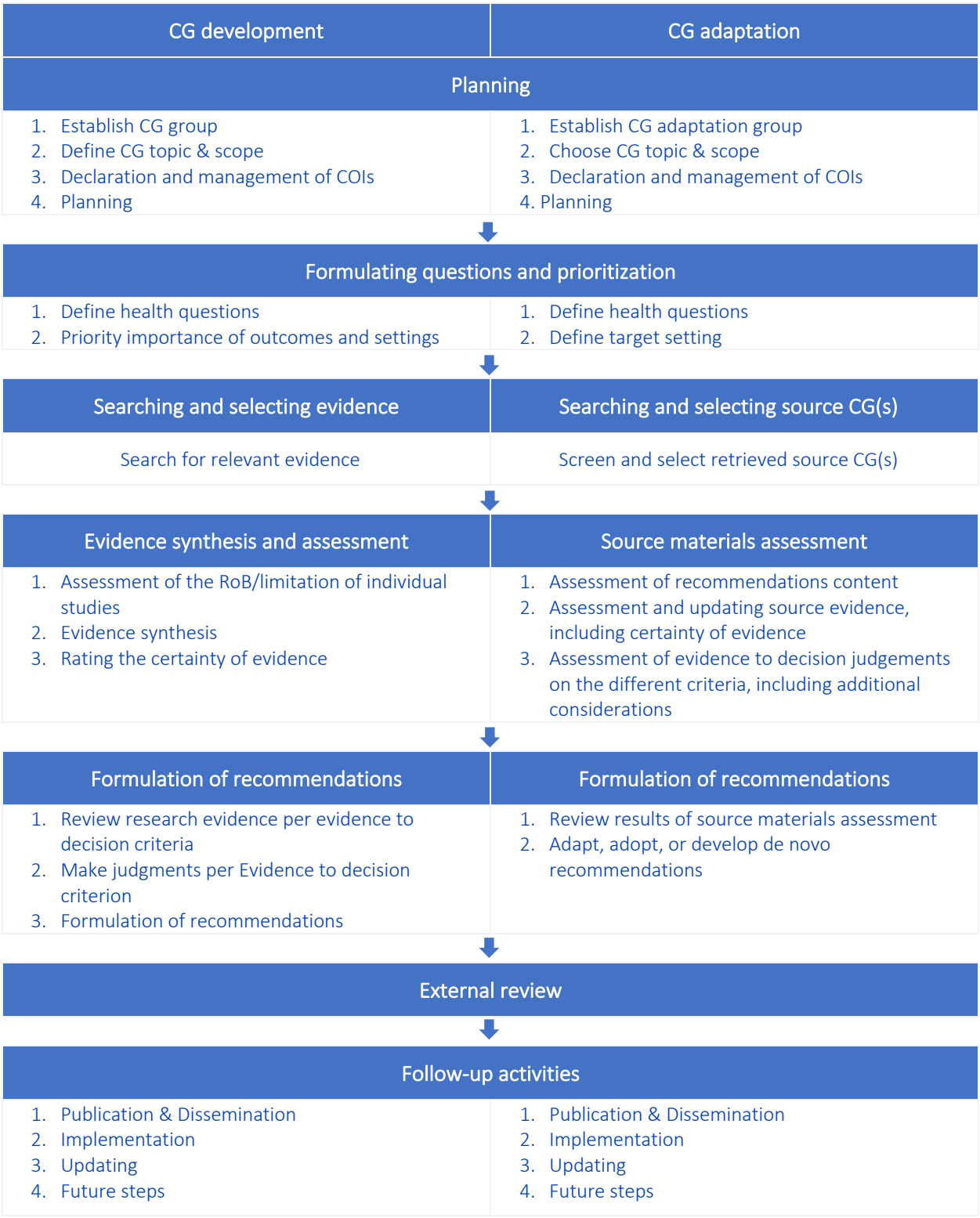

Figure 06. Clinical guideline development and adaptation steps

CG: clinical guideline; COI: conflict of interest; RoB: risk of bias.

However, specific steps in the CG adaptation process are different from CG development process, especially for the evidence synthesis and assessment, and formulation of recommendations (Figure 05). For CG development process, the evidence synthesis and assessment, focuses on the evidence synthesis per outcome and rating the certainty of evidence, for example, following the GRADE approach. In contrast, for CG adaptation the process requires assessing the recommendations content and source evidence synthesis, updating the evidence synthesis, ideally also based on evidence from the target context, and reviewing evidence to decision factors and judgements made by the source CG panel.

The decision-making process for formulating recommendations should consider all the most important aspects related to recommendations, including: the priority of the health problem, the balance between desirable and undesirable effects, the certainty of the evidence, the outcome importance, resources use, equity, acceptability, and feasibility (35). Given the necessity of considering the local context, the formulation of recommendations also requires the incorporation of local evidence or other contextualisation factors. Finally, each CG adaptation group must decide whether to adapt, adopt, or develop *de novo* recommendations. The current adaptation frameworks have not addressed well the decision-making process for the formulation of the adapted recommendations. Although the GRADE-ADOLOPMENT framework covers the essential aspects for healthcare decision-making (35, 87), this could apply to adapting those source CGs that followed the GRADE approach or using the GRADE EtD framework. For those source CGs that did not follow the GRADE approach, the CG adaptation decision-making process has not been as standardised yet.

5.2.2.5 Challenges of clinical guideline adaptation process

CG adaptation requires expertise in assessing and understanding CG development, as well as all the main aspects of adaptation (e.g., decision-making on whether to adapt, adopt, or develop *de novo* recommendations or how to deal with differences from source CGs). Consequently, the complexity of adaptation process challenges the CG adaptation groups. As some CG adaptation groups lack the expertise of advanced CG development and adaptation knowledge, they face challenges regarding understanding the rating system and decision-making process of source CGs (125). For example, in study II, one participant from a LMIC mentioned that CG developers in their setting do not know how to formulate clinical questions, synthesise and evaluate the evidence, or formulate recommendations based on the evidence (125). Moreover, solving the difference between the target adaptation setting and source CGs is also a big

challenge, as it requires additional expertise to contextualise recommendations based on the differences (125).

Other research studies have also identified similar challenges. For example, the GIN adaptation working group conducted an international survey regarding the potential need to update ADAPTE (148). The survey identified several specific areas that may need further guidance, including: selection of source CGs based on quality and currency assessment, deciding on the certainty of the evidence, and formulating adapted recommendations (unpublished data, GIN adaptation working group). Meanwhile, the same survey also collected additional comments which revealed specific challenges regarding the adaptation process, including when to define clinical questions for adapted CGs, and how to harmonise the different rating systems used by source CGs and adaptation settings (unpublished data, GIN adaptation working group).

5.2.3 Clinical guidelines and adapted clinical guidelines reporting

5.2.3.1 Clinical guidelines

Several reporting checklists are available for different types of CGs (Table 05). For example, the RIGHT statement (51) focuses on the presentation of evidence and recommendations, and the AGREE II reporting checklist (57) addresses mainly the methodological process. There is guidance for reporting the involvement of patients and the public – the GRIPP2 reporting checklist, deals with patient and public involvement, the methods used, outcome, process, and the impact of the stakeholders' engagement in the CG development process (149). Regarding updating – CheckUp, focuses on the methodological process for CG updating, and on the modifications made in updated recommendations (59). Meanwhile, the RIGHT-Ad@pt checklist was developed for the reporting of adapted CGs in healthcare, focusing on the reporting of the differences from source CGs, the CG adaptation process, and adapted recommendations with rationale for recommendations (124).

The development process of the RIGHT-Ad@pt checklist is similar to other reporting instruments for CGs, and aligns with the general guidance for developing reporting checklists (47). These steps include: generating an initial version through literature review and brainstorming, reaching consensus through a Delphi survey and/or face-to-face meetings, and validity testing through the external review process (47). In addition to Moher's guidance, and similarly to the development process of CheckUp (59), the development process of the RIGHT-Ad@pt checklist also includes an optimisation process of the checklist content for face validity and construct validity, through an initial assessment of real-life adapted CGs and

stakeholder interviews before initial consensus, and a final assessment of real-life adapted CGs after initial consensus (124).

The RIGHT-Ad@pt checklist has been developed as an extension of the RIGHT statement (51). The main differences, compared to the RIGHT statement, are the new section for the specific steps of CG adaptation ("Rigour of development"), and of contextualisation of the source CGs content to the target setting (the reporting of differences between adapted CGs and source CGs, and the methodological steps for adaptation process). RIGHT-Ad@pt suggests reporting differences on the brief description of the health problem(s), aim(s), and specific objectives, target population(s), end-users and settings, recommendations, and rationale/explanation for recommendations. In addition, the RIGHT-Ad@pt checklist includes a more specific methodological process for CG adaptation, including which adaptation framework/methodology was used, how the key questions were prioritised, how source CGs and recommendations were evaluated and selected, which methods were used for assessing the certainty of the body of evidence and strength of recommendations, and how consensus was reached (124).

Table 05. Reporting checklists for clinical guidelines

	AGREE II reporting checklist (57)	RIGHT statement(51)	GRIPP2(149)	CheckUp (59)
Objectives	To improve the quality of practice guideline reporting and aligns with AGREE II in its structure and content.	To support CG developers in the reporting, journal editors and peer reviewers to assess the reporting when considering CG for publication, and health care practitioners understand and implement a CG.	To guide the reporting of patient and public involvement (PPI), improve its quality, transparency, and consistency of PPI, and to involve patients in the development process of GRIPP2.	To evaluate the completeness of reporting in updated CGs, inform the reporting of updated CGs, and enhance its comprehensiveness and transparency.
Domains	1. Scope and Purpose. 2. Stakeholder Involvement. 3. Rigour of Development. 4. Clarity of Presentation. 5. Applicability. 6. Editorial Independence.	1.Basic information. 2.Background. 3.Evidence. 4.Recommendations. 5.Review and quality assurance. 6.Funding and declaration and management of interests. 7.Other information.	1: Abstract of paper. 2: Background to paper. 3: Aims of paper. 4: Methods of paper. 5: Capture or measurement of PPI impact. 6: Economic assessment. 7: Study results. 8: Discussion and conclusions.	1. The presentation of an updated guideline. 2. Editorial independence. 3. The methodology of the updating process.
Develop-ment methods	A method that follows the Moher guidance for the development of reporting checklist, which includes	A 4-step approach includes a literature review on reporting checklist for other study	By following the EQUATOR method for the development of reporting checklist, revising the	A multistep process includes an assessment of existing updated CGs, interviews with key

	reducing initial items by the working group and international experts, and conducting field testing and validity testing to generate final items.	designs (e.g., RCTs or SRs, etc.), a review of CG handbooks in terms of reporting contents, data extraction, and face-to-face meeting for the Delphi survey and to reach consensus.	original GRIPP checklist based on updating of SRs, three rounds of Delphi survey and a face-to-face meeting to reach consensus.	informants, three-round Delphi consensus survey, and external review processes with CG developers and users.
Number of items	23 items.	22 items.	34 items.	16 items.
Items about adapta-tion	None.	None.	None.	None.
Short version	No.	No.	Yes.	No.

AGREE: Appraisal of Guidelines, Research and Evaluation; CheckUp: Checklist for the Reporting of Updated Guidelines; – GRIPP2: Guidance for Reporting Involvement of Patients and the Public; RIGHT: Reporting Tool for Practice Guidelines in Health Care.

5.2.3.2 Adapted Clinical Guidelines

CG adaptation needs to address the differences in source CGs to achieve contextualization, ensuring the transparency of the CG adaptation process. For example, the ADAPTE framework suggests assessing the differences in PICO components, implementation barriers, and clinical practice, while the GRADE-ADOLOPMENT framework facilitates addressing the differences with respect to the evidence to decision factors, during the formulation of recommendations, and enables the presentation of modifications for each factor (86, 87). RIGHT-Ad@pt is a comprehensive reporting checklist for the adapted CGs, including the reporting of differences from source CGs, modifications in recommendations, and the rationale for recommendations regarding the criteria or factors that were considered. Moreover, the checklist suggests reporting the funding and COI management of both source CGs and adapted CGs to ensure the transparency and credibility of the adapted CGs (124).

The review from Wang et al. on the limitation and advantages of current adaptation framework, and our study II have summarised the main steps for CG adaptation, including prioritisation of key questions, the assessment and selection of source CGs, the assessment of recommendations and evidence, the formulation of recommendations, external review, and follow-up activities on updating, implementation, and future steps (93, 125). The RIGHT-Ad@pt, based on the findings of study II, checklist includes all the main steps, stratifying the reporting of the assessment and selection of source materials into: CG level (item 16), recommendation level (item 19), and evidence level (item 20, 21) (124, 125).

As discussed in study II, the decisions around the formulation of recommendations for adapted CGs remains challenging, highlighting the need for a transparent process (125). For example, as suggested in available frameworks, CG adaptation organisations may need to re-rate the certainty of the evidence or re-consider the criteria for decision-making on the strength of recommendations (86, 87). The RIGHT-Ad@pt checklist suggests explicitly reporting the methods used in this phase/stage to make the CG adaptation process as transparent and reliable as possible, regarding the certainty of the evidence, the strength of recommendations, the methods for reaching consensus (items 22 and 23), and the rationale for adapting or adopting recommendations (item 27) (124).

5.2.3.3 Reporting recommendations in adapted clinical guidelines

Currently, several studies have explored the optimal presentation for recommendations to improve its uptake. In 2015, a realistic review on the relation between the presentation of CGs and implementation, found two relevant areas: the CG content (i.e., stakeholder engagement, evidence synthesis, considered judgment and implementation factors), and its communication effectiveness (i.e., presentation format) (150). Based on these findings, the Guideline Implementability Decision Excellence Model (GUIDE-M) was developed to provide comprehensive guidance to improve CG implementation. The GUIDE-M includes key factors to be presented in CG that are related to the recommendations uptake, including reporting on the deliberations and contextualisation for end users (e.g., patients, providers, policy makers, society, and developers), language and format of recommendations (151). In 2017, a trial compared a digitally structured multi-layered presentation of CG recommendations with clinicians, showing that multi-layered presentation is preferable for guideline users. The multi-layered presentation format consisted of upfronted recommendations, as well as different layers of information regarding supporting evidence and the decision-making process (152).

The Checklist for the Reporting of Updated Guidelines (CheckUp) has been developed to assess the completeness of reporting of updated CGs, and to guide the reporting of updated recommendations (59). CheckUp suggests the reporting of updated recommendations and the justifications for updating to ensure the transparency and explicitness of updated recommendations (59). Similarly, the RIGHT-Ad@pt checklist suggests reporting the recommendations clearly, including information on the certainty of the evidence and the strength of recommendations, recommendations for relevant subgroups, and the rationale for the recommendation formulation. Most importantly, RIGHT-Ad@pt also distinguishes recommendations adapted based on modifications, adopted directly from source CGs, or developed *de novo* (124). Reporting

the abovementioned content may help standardise the reporting of recommendations of adapted CGs and contribute to the generation of evidence to explore the optimal presentation of adapted recommendations.

5.3 Strengths and limitations

The main strength of this thesis is that it is a compendium of rigorously executed and relevant studies, including: 1) the development of study protocols (115), 2) the publication in peer-reviewed journals, and 3) the participation of a multidisciplinary group of international researchers. The main limitation of the thesis is that the potential impact of the studies' findings on the methods for adapting CGs and the quality of adapted CGs has not been yet evaluated.

The specific strengths and limitations of each study included in the thesis are listed below (Table 06).

Table 06. Strengths and limitations of the thesis studies

Strengths	Limitations
Study I. "The development of clinical guidelines in China: insights from a national survey" (123)	
• We designed the study questionnaire following rigorous standards, and piloted it in national and international organisations. • We included 48 Chinese CG representatives from 13 clinical disciplines, and 13 provinces. • We conducted a comprehensive evaluation of CG development in a middle-income country, including adaptation and updating.	• We received a relatively low response rate. • We did not explore the CG development process that relied solely on experts' opinions.
Study II. "Current practices and challenges in adaptation of clinical guidelines: a qualitative study based on semi-structured interviews" (125)	
• We adopted a comprehensive recruitment strategy, to identify participants with CG adaptation expertise, ensuring representativeness. • We combined data from participants' views and experiences, and from published CG adaptation methods, to reduce participants' bias.	• The small sample size precluded exploring aspects like differences in country incomes. • We may have under-reported specific challenges from LMICs, as fewer participants were from LMICs.

• We applied a framework analysis based on published CG adaptation methods, to ensure findings' comprehensiveness. • We presented the qualitative results in friendly tabulated summaries.	
Study III. "A reporting tool for adapted guidelines in health care: the RIGHT-Ad@pt checklist" (124)	
• We published the study protocol in a peer-reviewed journal (115) • We developed RIGHT-Ad@pt, based on the strengths of the RIGHT statement. • The RIGHT-Ad@pt checklist was developed and approved by a wide range of stakeholders. • The checklist development process included usability testing with external reviewers, and assessments of published adapted guidelines, to enhance its validity.	• The RIGHT-Ad@pt checklist requires further validation in real-life use.

5.4 Implications

5.4.1 Implications for practice

- CG developers in China need to standardise methods for developing, adapting, and updating CGs to improve the trustworthiness of Chinese CGs. Future practices may include:
    - Implementation and standardisation of rigorous CG development processes, and adherence to reporting CGs' guidance.
    - Implementation and standardisation of rigorous CG adaptation processes, by adopting and validating optimal published CG adaptation methodologies, that are applicable to the national context.
    - Adequate stakeholder engagement to ensure that CG topics are relevant, adequately consider aspects such as acceptability and feasibility, and improve the implementation of recommendations.
    - Chinese medical associations and government should take the lead for CG development process in China, including implementation and monitoring, updating, as well as adaptation.
    - The provision of enough public funding for CG development organisations, to assure a more rigour and non-biased CG development process.
    - Implement structured and explicit COI declaration and management strategies, to improve editorial independence.

- CG adaptation groups may use the identified core steps and level of assessment of source materials, to streamline their processes, potentially improving the efficiency of the CG adaptation.

- The level of assessment of source materials (guidelines, recommendations, or evidence) allows CG adaptation groups to predefine the level of assessment, based on their available resources and skills, therefore, simplifying CG adaptation while remaining rigorous.

- Different audiences may use the RIGHT-Ad@pt checklist for different purposes:
    - CG developers can use the checklist, along with the user guide, to report their adapted CGs and inform their future adaptation process.
    - Journal editors and reviewers can use the checklist to ensure completeness and transparency of the reporting in the publication of adapted CGs.

- Clinicians could benefit from a more accurate reporting of adapted CGs based on the checklist, to identify adapted recommendations, and the justifications for any differences from source recommendations.
- Policymakers could use the checklist to evaluate the feasibility of adapted recommendations for local implementation, enhancing the applicability of CGs, and supporting health decision-making.

- The RIGHT-Ad@pt WG may explore strategies to improve the application of the checklist, including publication of an online version, development of an abridged version, and translation into other languages.
- The RIGHT-Ad@pt WG may surveil the evidence about adapting CG (e.g., methodological research and user feedback on the checklist) and update the checklist, as needed.

5.4.2 Implications for research

- In China, methodological research may focus on exploring efficient and rigorous CG adaptation processes, ensuring the trustworthiness of Chinese adapted CGs.
- The identified core steps and the three levels of assessment for CG adaptation needs formal assessment and validation, to be used as a CG adaptation framework.
- CG adaptation frameworks, processes, and methods, as well as stakeholders' inputs collected in this thesis, could be the base to develop rigorous international standards for adapting CGs, including guidance on making judgements and approaching the decision-making, and/or the development of a validated quality assessment tool for adapted CGs.
- The RIGHT-Ad@pt checklist requires further validation in real-life use, including a systematic assessment of the completeness of reporting of published adapted CGs.
- The potential influence of RIGHT-Ad@pt checklist should be explored, including the impact on the completeness of reporting and the quality of adapted CGs, as well as on the efficiency (e.g., time and resources needed) of CG adaptation.

6. CONCLUSIONS

6 Conclusions

- Methods for developing, adapting, and updating CGs in China are highly variable and informal; the CG development process is generally poorly managed and monitored, leading to the long-standing low quality of Chinese CGs (Study I).

- CG adaptation is being increasingly used in the CG arena, with numerous frameworks being developed, and some published; however, there is noticeable variability in the adaptation processes (Study II).

- RIGHT-Ad@pt, a checklist with seven sections and 34 items, is now available for informing developers on the reporting requirements of adapted CGs, addressing both the rigour of the adaptation process, and explicitness of adapted recommendations. (Study III).

- Aligning with the reporting content suggested by the RIGHT-Ad@pt checklist, ensures the transparency of the adaptation process and enhances the credibility of adapted CGs, benefiting relevant stakeholders, including developers, editors, clinicians, and policy makers (Study III).

- More methodological research is needed to optimise CG adaptation, including real-life implementation of RIGHT-Ad@pt, and to evaluate whether the publication of RIGHT-Ad@pt will have an influence on the reporting of adapted CGs. This research may also explore the potential effect of RIGHT-Ad@pt on the quality of adapted guidelines and on the efficiency of the adaptation process

7. REFERENCES

7 References

1. Institute of Medicine. Clinical practice guideline we can trust. Washington, DC: The National Academies Press, 2011.
2. Woolf SH. Practice guidelines: a new reality in medicine. I. Recent developments. Arch Intern Med. 1990;150(9):1811-8.136. Woolf SH. Practice guidelines: a new reality in medicine. I. Recent developments. Arch Intern Med. 1990;150(9):1811-8.
3. World Health Organization. WHO handbook for guideline development. WHO handbook for guideline development, 2014
4. Mullan F, Jacoby I. The town meeting for technology. The maturation of consensus conferences. JAMA. 1985;254(8):1068-72.
5. Woolf SH. Practice guidelines, a new reality in medicine. II. Methods of developing guidelines. Arch Intern Med. 1992;152(5):946-52.
6. Eccles M, Clapp Z, Grimshaw J, Adams PC, Higgins B, Purves I, Russell I. North of England evidence based guidelines development project: methods of guideline development. BMJ. 1996;312(7033):760-2.
7. Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. BMJ. 1999;318(7183):593-6.
8. Nathwani D. From evidence-based guideline methodology to quality of care standards. J Antimicrob Chemother. 2003;51(5):1103-7.
9. Evidence-Based Medicine Working Group. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA. 1992;268(17):2420-5. .
10. Weisz G, Cambrosio A, Keating P, Knaapen L, Schlich T, Tournay VJ. The emergence of clinical practice guidelines. Milbank Q. 2007;85(4):691-727.
11. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al. Going from evidence to recommendations. BMJ (Clinical research ed). 2008;336(7652):1049-51.
12. Atkins D, Eccles M, Flottorp S, Guyatt GH, Henry D, Hill S, et al. Systems for grading the quality of evidence and the strength of recommendations I: critical appraisal of existing approaches. The GRADE Working Group. BMC Health Serv Res 2004;4(1):38.
13. West S, King V, Carey TS, et al. Systems to Rate the Strength Of Scientific Evidence. Rockville (MD): Agency for Healthcare Research and Quality (US); 2002 Apr. (Evidence Reports/Technology Assessments, No. 47.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK33881/. Accessed in May 30, 2022.
14. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-6.
15. Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011;64(4):380-2.
16. Thornton J, Alderson P, Tan T, Turner C, Latchem S, Shaw E, et al. Introducing GRADE across the NICE clinical guideline program. J Clin Epidemiol. 2013;66(2):124-31.
17. Developing NICE guidelines: the manual. https://www.nice.org.uk/process/pmg20/chapter/reviewing-research-evidence#assessing-quality-of-evidence-critical-appraisal-analysis-and-certainty-in-the-findings. Accessed on January 18, 2022.
18. Qaseem A, Kansagara D, Lin JS, Mustafa RA, Wilt TJ; Clinical Guidelines Committee of the American College of Physicians, et al. The Development of Clinical Guidelines and Guidance Statements by the Clinical Guidelines Committee of the American College of Physicians: Update of Methods. Ann Intern Med. 2019;170(12):863-870.

19. Qaseem A, Forland F, Macbeth F, Ollenschläger G, Phillips S, van der Wees P, et al. Guidelines International Network: toward international standards for clinical practice guidelines. Ann Intern Med. 2012;156(7):525-31.
20. Schünemann HJ, Wiercioch W, Etxeandia I, Falavigna M, Santesso N, Mustafa R, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. Cmaj. 2014;186(3):E123-42.
21. National Comprehensive Cancer Network. Development and Update of Guidelines. https://www.nccn.org/ guidelines/guidelines-process/development-and-update-of-guidelines. Accessed 20 May 2021.
22. Aplicación de las Recomendaciones de las Guías de Práctica Clínica a la Toma de Decisiones Compartida. Manual Metodológico. 19 abril 2022. https://doi.org/10.46995/man_9. Accessed in May 30, 2022.
23. Sonnad SS. Organizational tactics for the successful assimilation of medi- cal practice guidelines. Health Care Manage Rev. 1998;23(3):30–7.
24. Thomas J, Kneale D, McKenzie JE, Brennan SE, Bhaumik S. Chapter 2: Determining the scope of the review and the questions it will address. In: Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook.
25. Lefebvre C, Glanville J, Briscoe S, Featherstone R, Littlewood A, Marshall C, et al. Chapter 4: Searching for and selecting studies. In: Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook.
26. Munn Z, Stern C, Aromataris E, Lockwood C, Jordan Z. What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences. BMC Med Res Methodol. 2018 ;18(1):5.
27. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook.
28. Guyatt G, Oxman AD, Sultan S, Brozek J, Glasziou P, Alonso-Coello P, et al. GRADE guidelines: 11. Making an overall rating of confidence in effect estimates for a single outcome and for all outcomes. J Clin Epidemiol. 2013;66(2):151-7.
29. Guyatt GH, Oxman AD, Kunz R, Vist GE, Falck-Ytter Y, Schunemann HJ. What is "quality of evidence" and why is it important to clinicians? BMJ (Clinical research ed). 2008;336(7651):995-8.
30. Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, et al. GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). J Clin Epidemiol. 2011;64(4):407-15.
31. Guyatt GH, Oxman AD, Kunz R, Brozek J, Alonso-Coello P, Rind D, et al. GRADE guidelines 6. Rating the quality of evidence--imprecision. J Clin Epidemiol. 2011;64(12):1283-93.
32. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 7. Rating the quality of evidence--inconsistency. J Clin Epidemiol. 2011;64(12):1294-302.
33. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 8. Rating the quality of evidence--indirectness. J Clin Epidemiol. 2011;64(12):1303-10.
34. Guyatt GH, Oxman AD, Montori V, Vist G, Kunz R, Brozek J, et al. GRADE guidelines: 5. Rating the quality of evidence--publication bias. J Clin Epidemiol. 2011 Dec;64(12):1277-82.
35. 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.

36. AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. Qual Saf Health Care. 2003;12(1):18-23.
37. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al; AGREE Next Steps Consortium. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ. 2010;182(18):E839-42.
38. Jue JJ, Cunningham S, Lohr K, Shekelle P, Shiffman R, et al. Developing and Testing the Agency for Healthcare Research and Quality's National Guideline Clearinghouse Extent of Adherence to Trustworthy Standards (NEATS) Instrument. Ann Intern Med. 2019;170(7):480-487.
39. Guidelines and Measures Updates. Content last reviewed September 2018. Agency for Healthcare Research and Quality, Rockville, MD. https://www.ahrq.gov/gam/updates/index.html. Accessed in May 27, 2022.
40. Alonso-Coello P, Irfan A, Solà I, Gich I, Delgado-Noguera M, Rigau D, et al. The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. Qual Saf Health Care. 2010;19(6):e58.
41. Armstrong JJ, Goldfarb AM, Instrum RS, MacDermid JC. Improvement evident but still necessary in clinical practice guideline quality: a systematic review. J Clin Epidemiol. 2017;81:13-21.
42. Tejada S, Ramírez-Estrada S, Tejo AM, Forero CG, Pomares X, Gallego M, et al. Critical appraisal of international adult bronchiectasis guidelines using the AGREE II tool. Eur J Intern Med. 2022:S0953-6205(22)00035-8.
43. Montero-Odasso MM, Kamkar N, Pieruccini-Faria F, Osman A, Sarquis-Adamson Y, Close J, et al. Evaluation of Clinical Practice Guidelines on Fall Prevention and Management for Older Adults: A Systematic Review. JAMA Netw Open. 2021;4(12):e2138911.
44. Nuckols TK, Lim YW, Wynn BO, Mattke S, MacLean CH, Harber P, et al. Rigorous development does not ensure that guidelines are acceptable to a panel of knowledgeable providers. J Gen Intern Med. 2008;23(1):37-44.
45. Brouwers MC, Spithoff K, Kerkvliet K, Alonso-Coello P, Burgers J, et al. Development and Validation of a Tool to Assess the Quality of Clinical Practice Guideline Recommendations. JAMA Netw Open. 2020;3(5):e205535.
46. Florez ID, Brouwers MC, Kerkvliet K, Spithoff K, Alonso-Coello P, Burgers J, et al. Assessment of the quality of recommendations from 161 clinical practice guidelines using the Appraisal of Guidelines for Research and Evaluation-Recommendations Excellence (AGREE-REX) instrument shows there is room for improvement. Implement Sci. 2020;15(1):79.
47. Moher D, Schulz KF, Simera I, Altman DG. Guidance for developers of health research reporting guidelines. PLoS Med. 2010;7(2):e1000217.
48. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700.
49. Moher D. Reporting research results: a moral obligation for all researchers. Can J Anaesth. 2007;54(5):331-5.
50. The EQUATOR. Enhancing the QUAlity and Transparency Of health Research. https://www.equator-network.org/. Accessed in 1st June, 2022.
51. Chen Y, Yang K, Marušic A, Qaseem A, Meerpohl JJ, Flottorp S, et al. A Reporting Tool for Practice Guidelines in Health Care: The RIGHT Statement. Ann Intern Med. 2017;166(2):128-132.
52. RIGHT reporting for right decision: Translation. http://www.right-statement.org. Accessed in 1st June, 2022.
53. Xie R, Xia Y, Chen Y, Li H, Shang H, Kuang X, et al. The RIGHT Extension Statement for Traditional Chinese Medicine: Development, Recommendations, and Explanation. Pharmacol Res. 2020;160:105178.

54. Wang X, Chen Y, Akl EA, Tokalić R, Marušić A, Qaseem A, et al; RIGHT working group. The reporting checklist for public versions of guidelines: RIGHT-PVG. Implement Sci. 2021;16(1):10.
55. Tang C, Duan Y, Zhang Y, Zhang Y, Chen Z, Tang X, et al; RIGHT (Reporting Items for Practice Guidelines in Healthcare) for Acupuncture Working Group. RIGHT for acupuncture: An extension of the RIGHT statement for clinical practice guidelines on acupuncture. J Clin Epidemiol. 2021;139:330-339.
56. Luo X, Akl EA, Zhu Y, Lv M, Liu X, Song Y et al. Developing the RIGHT extension statement for practice guideline protocols: the RIGHT-P statement protocol [version 1; peer review: 1 approved with reservations]. F1000Research 2022, 11:275.
57. Brouwers MC, Kerkvliet K, Spithoff K, AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines BMJ 2016; 352 :i1152.
58. AGREE-REX Reporting Checklist. https://www.agreetrust.org/wp-content/uploads/2019/06/AGREE-REX-Reporting-Checklist.pdf. Accessed in May 22, 2022.
59. Vernooij RW, Alonso-Coello P, Brouwers M, Martinez Garcia L, CheckUp Panel. Reporting Items for Updated Clinical Guidelines: Checklist for the Reporting of Updated Guidelines (CheckUp). PLoS Med. 2017;14(1):e1002207.
60. Vernooij RWM, Martínez García L, Florez ID, Hidalgo Armas L, Poorthuis MHF, Brouwers M, Alonso-Coello P. Updated clinical guidelines experience major reporting limitations. Implement Sci. 2017;12(1):120.
61. Lalisang TJM, Usman N, Hendrawidjaya I, Handaya AY, Nasution S, et al. Clinical Practice Guidelines in Complicated Intra-Abdominal Infection 2018: An Indonesian Perspective. Surg Infect (Larchmt). 2019;20(1):83-90.
62. Yang Y, Lu J, Ma Y, Xi C, Kang J, Zhang Q, Jia X, Liu K, Du S, Kocher F, Seeber A, Gridelli C, Provencio M, Seki N, Tomita Y, Zhang X. Evaluation of the reporting quality of clinical practice guidelines on lung cancer using the RIGHT checklist. Transl Lung Cancer Res. 2021;10(6):2588-2602.
63. Han J, Tao M, Wu X, Li D, Ma Y, Dawood S, Steele CW, Tan KK, Wang Q. Reporting quality of practice guidelines on colorectal cancer: evaluation using the RIGHT reporting checklist. Ann Transl Med. 2021;9(14):1175.
64. Zhang S, Wu L, Wang Y, Zhou Q, Luo X, Mathew JL, et al. Methodological and reporting quality of pediatric clinical practice guidelines: a systematic review. Ann Transl Med. 2021;9(15):1258.
65. Maes-Carballo M, Mignini L, Martín-Díaz M, Bueno-Cavanillas A, Khan KS. Quality and reporting of clinical guidelines for breast cancer treatment: A systematic review. Breast. 2020;53:201-211.
66. Schünemann HJ, Fretheim A, Oxman AD, WHO Advisory Committee on Health Research. WHO Advisory Committee on health research. improving the use of research evidence in Guideline development: 1. guidelines for guidelines. Health Res Policy Syst 2006;4.
67. Bhaumik S. Use of evidence for clinical practice guideline development. Trop Parasitol 2017;7:65–71.
68. Olayemi E, Asare EV, Benneh-Akwasi Kuma AA. Guidelines in lower-middle income countries. British Journal of Haematology. 2017;177(6):846-54.
69. Fervers B, Burgers JS, Haugh MC, Latreille J, Mlika-Cabanne N, Paquet L, et al. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. Int J Qual Health Care 2006;18:167–76.
70. Bhaumik S, Jagadesh S, Ellatar M, et al. Clinical practice guidelines in India: quality appraisal and the use of evidence in their development. J Evid Based Med 2018;11:26–39.
71. Kredo T, Gerritsen A, van Heerden J, Conway S, Siegfried N. Clinical practice guidelines within the Southern African Development Community: a descriptive study of the quality of guideline development and concordance with best evidence for five priority diseases. Health Res Policy Syst. 2012;10:1.
72. Molino CG, Romano-Lieber NS, Ribeiro E, et al. Non-Communicable disease clinical practice guidelines in Brazil: a systematic assessment of methodological quality and transparency. PLoS One 2016;11:e0166367.

73. Chen YL, Yao L, Xiao XJ, Wang Q, Wang ZH, Liang FX, et al. Quality assessment of clinical guidelines in China: 1993 - 2010. Chin Med J (Engl). 2012;125(20):3660-4.
74. Chen Y, Wang C, Shang H, Yang K, Norris SL. Clinical practice guidelines in China. BMJ. 2018;360:j5158.
75. [Chinese guideline on menopause management and menopause hormone therapy (2018)]. Zhonghua Fu Chan Ke Za Zhi. 2018;53(11):729-39.
76. Jiang M, Liao LY, Liu XQ, He WQ, Guan WJ, Chen H, et al. Quality assessment of clinical practice guidelines for respiratory diseases in China: a systematic appraisal. Chest. 2015;148(3):759–66.
77. Deng W, Li L, Wang Z, Chang X, Li R, Fang Z, et al. Using AGREE II to evaluate the quality of traditional medicine clinical practice guidelines in China. J Evid Based Med. 2016;9(3):152-62.
78. Yao S, Wei D, Chen YL, Wang Q, Wang XQ, Zeng Z, et al. Quality assessment of clinical practice guidelines for integrative medicine in China: A systematic review. Chin J Integr Med. 2017;23(5):381-5.
79. Wu D, Jiang W, Yu L, Wang Y, Tao Y, Tang H, et al. Quality assessment of clinical practice guidelines for infectious diseases in China. J Evid Based Med. 2018;11(2):95-100.
80. Jiang L, Krumholz HM, Li X, Li J, Hu S. Achieving best outcomes for patients with cardiovascular disease in China by enhancing the quality of medical care and establishing a learning healthcare system. Lancet. 2015 Oct 10;386(10002):1493-505.
81. Lu J, Zhao W, Chen T, Xu Z, Sun X, Xie H, et al. Influence of guideline adherence and parameter control on the clinical outcomes in patients with diabetic nephropathy. BMJ Open Diabetes Res Care. 2020;8(1).
82. Jin Y, Li Z, Han F, Huang D, Huang Q, Cao Y, et al. Barriers and enablers for the implementation of clinical practice guidelines in China: a mixed-method study. BMJ Open. 2019;9(9):e026328.
83. Zeng L, Li Y, Zhang L, Liu G, Zhang Y, Zhen S, et al. Guideline use behaviours and needs of primary care practitioners in China: a cross-sectional survey. BMJ Open. 2017;7(9):e015379.
84. Lu S, Luo X, Ni X, Li H, Meng M, Cai Y, et al. Reporting quality evaluation of the stroke clinical practice guidelines: a systematic review. Syst Rev. 2021;10(1):262.
85. Han J, Tao M, Wu X, Li D, Ma Y, Dawood S, et al. Reporting quality of practice guidelines on colorectal cancer: evaluation using the RIGHT reporting checklist. Ann Transl Med. 2021;9(14):1175.
86. Fervers B, Burgers JS, Voellinger R, Brouwers M, Browman GP, Graham ID, et al. Guideline adaptation: an approach to enhance efficiency in guideline development and improve utilisation. BMJ Qual Saf. 2011;20(3):228-36.
87. Schünemann HJ, Wiercioch W, Brozek J, Etxeandia-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;81:101-110.
88. Burgers JS, Anzueto A, Black PN, Cruz AA, Fervers B, Graham ID, et al. Adaptation, evaluation, and updating of guidelines: article 14 in Integrating and coordinating efforts in COPD guideline development. An official ATS/ERS workshop report. Proc Am Thorac Soc. 2012;9(5):304-10.
89. Darzi A, Abou-Jaoude EA, Agarwal A, Lakis C, Wiercioch W, Santesso N, et al. A methodological survey identified eight proposed frameworks for the adaptation of health related guidelines. J Clin Epidemiol. 2017;86:3-10.
90. Okely AD, Ghersi D, Hesketh KD, Santos R, Loughran SP, Cliff DP, et al. A collaborative approach to adopting/adapting guidelines - The Australian 24-Hour Movement Guidelines for the early years (Birth to 5 years): an integration of physical activity, sedentary behavior, and sleep. BMC Public Health 2017;17(S5):869.
91. Kristiansen A, Brandt L, Agoritsas T, Akl EA, Berge E, Bondi J, et al. Adaptation of trustworthy guidelines developed using the GRADE methodology: a novel five-step process. Chest. 2014;146(3):727-34.
92. Harrison MB, Légaré F, Graham ID, Fervers B. Adapting clinical practice guidelines to local context and assessing barriers to their use. CMAJ. 2010;182(2):E78-84.

93. Wang Z, Norris SL, Bero L. The advantages and limitations of guideline adaptation frameworks. Implement Sci. 2018;13(1):72.
94. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. J Clin Epidemiol. 1993;46(12):1417-32.
95. Feder G, Eccles M, Grol R, Griffiths C, Grimshaw J. Clinical guidelines: using clinical guidelines. BMJ. 1999;318(7185):728-30.
96. Abdul-Khalek RA, Darzi AJ, Godah MW, Kilzar L, Lakis C, Agarwal A, et al. Methods used in adaptation of health-related guidelines: A systematic survey. J Glob Health. 2017;7(2):020412.
97. Amer YS, Elzalabany MM, Omar TI, Ibrahim AG, Dowidar NL. The 'Adapted ADAPTE': an approach to improve utilizatiutilisationDAPTE guideline adaptation resource toolkit in the Alexandria Center for Evidence-Based Clinical Practice Guidelines. J Eval Clin Pract. 2015;21(6):1095-106.
98. Amer YS, Wahabi HA, Abou Elkheir MM, et al. Adapting evidence- based clinical practice guidelines at university teaching hospitals: a model for the eastern Mediterranean region. J Eval Clin Pract 2019;25:550–60.
99. Rycroft-Malone J, Duff L. Developing clinical guidelines: issues and challenges. J Tissue Viability. 2000;10(4):144-9, 152-3.
100. Graham ID, Harrison MB, Brouwers M, Davies BL, Dunn S. Facilitating the use of evidence in practice: evaluating and adapting clinical practice guidelines for local use by health care organizatorganisationst Gynecol Neonatal Nurs. 2002;31(5):599-611.
101. Graham ID, Harrison MB. Evaluation and adaptation of clinical practice guidelines. Evid Based Nurs. 2005;8(3):68-72.
102. Muth C, Gensichen J, Beyer M, Hutchinson A, Gerlach FM. The systematic guideline review: method, rationale, and test on chronic heart failure. BMC Health Serv Res. 2009;9:74.
103. Harstall C, Taenzer P, Angus DK, Moga C, Schuller T, Scott NA. Creating a multidisciplinary low back pain guideline: anatomy of a guideline adaptation process. J Eval Clin Pract. 2011;17(4):693-704.
104. Chakraborty SP, Jones KM, Mazza D. Adapting lung cancer symptom investigation and referral guidelines for general practitioners in Australia: reflections on the utility of the ADAPTE framework. J Eval Clin Pract. 2014;20(2):129-35.
105. Graham I, Harrison M, Straus S, Tetroe J, Caswell W, Robinson N. Lost in translation: time for a map? Journal of Continuing Education in the Health Professions 2006; 26: 13–24.
106. Harrison MB, Graham ID, van den Hoek J, Dogherty EJ, Carley ME, Angus V. Guideline adaptation and implementation planning: a prospective observational study. Implement Sci. 2013;8:49.
107. Lockwood C, Stephenson M, Lizarondo L, van Den Hoek J, Harrison M. Evidence implementation: Development of an online methodology from the knowledge-to-action model of knowledge translation. Int J Nurs Pract. 2016;22(4):322-9.
108. Alper BS, Tristan M, Ramirez-Morera A, Vreugdenhil MM, Van Zuuren EJ, Fedorowicz Z. RAPADAPTE for rapid guideline development: high-quality clinical guidelines can be rapidly developed with limited resources. Int J Qual Health Care. 2016;28(3):268-74.
109. National Health and Medical Research Council (NHMRC). Guidelines for Guidelines. Adopt, adapt or start from scratch. https://www.nhmrc.gov.au/guidelinesforguidelines/plan/adopt-adapt-or-start-scratch. Accessed 8 March 2022.
110. Godah MW, Abdul Khalek RA, Kilzar L, Zeid H, Nahlawi A, Lopes LC, et al. A very low number of national adaptations of the World Health Organization guidelines for HIV and tuberculosis reported their processes. J Clin Epidemiol. 2016;80:50-56.
111. Maaløe N, Meguid T, Housseine N, Tersbøl BP, Nielsen KK, Bygbjerg IC, et al. Local adaption of intrapartum clinical guidelines, United Republic of Tanzania. Bull World Health Organ. 2019;97(5):365-370.

112. Maaløe N, Ørtved AMR, Sørensen JB, Sequeira Dmello B, van den Akker T, Kujabi ML, et al. The injustice of unfit clinical practice guidelines in low-resource realities. Lancet Glob Health. 2021;9(6):e875-e879.
113. Sharma D, Cotton M. A call for glocal guidelines for global health. Trop Doct. 2021;51(3):285-287.
114. Sarkis-Onofre R, Poletto-Neto V, Cenci MS, Moher D, Pereira-Cenci T. CONSORT endorsement improves the quality of reports of randomized clinical trials in dentistry. J Clin Epidemiol. 2020;122:20-26.
115. Song Y, Darzi A, Ballesteros M, Martínez García L, Alonso-Coello P, Arayssi T, et al. Extending the RIGHT statement for reporting adapted practice guidelines in healthcare: the RIGHT-Ad@pt Checklist protocol. BMJ Open. 2019;9(9):e031767.
116. Darzi A, Harfouche M, Arayssi T, Alemadi S, Alnaqbi KA, Badsha H, et al. Adaptation of the 2015 American College of Rheumatology treatment guideline for rheumatoid arthritis for the Eastern Mediterranean Region: an exemplar of the GRADE Adolopment. Health Qual Life Outcomes. 2017;15(1):183.
117. Dizon JM, Machingaidze S, Grimmer K. To adopt, to adapt, or to contextualise? The big question in clinical practice guideline development. BMC Res Notes. 2016;9(1):442.
118. Shah MA, Oliver TK, Peterson DE, Einhaus K, Schneider BJ, Denduluri N, et al. ASCO Clinical Practice Guideline Endorsements and Adaptations. J Clin Oncol. 2020;38(8):834-840.
119. CCO guideline endorsement protocol 2019. www.projectdev:cco endorsement_protocol - PEBC Toolkit. Accessed in December 9th, 2019.
120. Dynamed Evidence-Based Methodology. Accessed in December 1st, 2019. https://www.dynamed.com/home/editorial/evidence-based-methodology.
121. DELBI. German Instrument for Methodological Guideline. Appraisal.https://www.leitlinien.de/mdb/edocs/pdf/literatur/german-guideline-appraisal-instrument-delbi.pdf. Accessed in December 1st, 2019.
122. Mehndiratta A, Sharma S, Gupta NP, Sankar MJ, Cluzeau F. Adapting clinical guidelines in India-a pragmatic approach. BMJ. 2017;359:j5147.
123. Song Y, Li J, Chen Y, Guo R, Alonso-Coello P, Zhang Y. The development of clinical guidelines in China: insights from a national survey. Health Res Policy Syst. 2021;19(1):151.
124. Song Y, Alonso-Coello P, Ballesteros M, Cluzeau F, Vernooij RWM, Arayssi T, et al. A Reporting Tool for Adapted Guidelines in Health Care: The RIGHT-Ad@pt Checklist. Ann Intern Med. 2022;175(5):710-719.
125. Song Y, Ballesteros M, Li J, Martínez García L, Niño de Guzmán E, Vernooij RWM, et al. Current practices and challenges in adaptation of clinical guidelines: a qualitative study based on semistructured interviews. BMJ Open. 2021;11(12):e053587.
126. Zhou Q, Wang Z, Shi Q, Zhao S, Xun Y, Liu H, et al. Clinical Epidemiology in China series. Paper 4: The reporting and methodological quality of Chinese clinical practice guidelines published between 2014 and 2018: A systematic review. J Clin Epidemiol. 2021;140:189-199.
127. Zhou X, Xu S, Ren Q, Chen J. Quality and Specific Concerns of Clinical Guidelines for Integrated Chinese and Western Medicine: A Critical Appraisal. Evid Based Complement Alternat Med. 2020;2020:9254503.
128. Zhang R, Yan SY, Wang YY, Huang Q, Ren XY, Tan R, et al. Analysis of the Status and Trends of Chinese Clinical Practice Guideline Development Between 2010 and 2020: A Systematic Review. Front Med (Lausanne). 2021;8:758617.
129. Barker TH, Dias M, Stern C, Porritt K, Wiechula R, Aromataris E, et al. Guidelines rarely used GRADE and applied methods inconsistently: A methodological study of Australian guidelines. J Clin Epidemiol. 2021;130:125-134.
130. Gagliardi AR, Brouwers MC. Integrating guideline development and implementation: analysis of guideline development manual instructions for generating implementation advice. Implement Sci. 2012;7:67.

131. Martínez García L, Sanabria AJ, García Alvarez E, Trujillo-Martín MM, Etxeandia-Ikobaltzeta I, Kotzeva A, et al. The validity of recommendations from clinical guidelines: a survival analysis. CMAJ. 2014;186(16):1211-9.
132. Niño de Guzmán E, Song Y, Alonso-Coello P, Canelo-Aybar C, Neamtiu L, Parmelli E, et al. Healthcare providers' adherence to breast cancer guidelines in Europe: a systematic literature review. Breast Cancer Res Treat. 2020;181(3):499-518.
133. Villarreal-Garza C, Mesa-Chavez F, Ferrigno AS, De la Garza-Ramos C, Fonseca A, Villanueva-Tamez K, et al. Adjuvant endocrine therapy for premenopausal women with breast cancer: Patient adherence and physician prescribing practices in Mexico. Breast. 2021;59:8-15.
134. Zhong F, Liu C, Zhang X. Guideline adherence for the treatment of advanced schistosomiasis japonica in Hubei, China. Parasitol Res. 2014;113(12):4535-41.
135. Zuo K, Chu Y, Zhang Z, Luo X, Deng J, Chen F, et al. [A national investigation on the application of Chinese guideline for the diagnosis and treatment of chronic rhinosinusitis]. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2015;50(1):50-3.
136. Grimmer K, Louw Q, Dizon JM, Brown SM, Ernstzen D, Wiysonge CS. A South African experience in applying the Adopt-Contextualise-Adapt framework to stroke rehabilitation clinical practice guidelines. Health Res Policy Syst. 2019;17(1):56.
137. El-Khoury R, Noureldine M, Abboud W, Khabsa J, Schünemann H, Akl E. Methods of guideline adaptation: a review of guideline development guidance. In: Advances in Evidence Synthesis: special issue Cochrane Database of Systematic Reviews 2020;(9 Suppl 1).
138. Yao X, Xia J, Jin Y, Shen Q, Wang Q, Zhu Y, et al. Methodological approaches for developing, reporting, and assessing evidence-based clinical practice guidelines: a systematic survey. J Clin Epidemiol. 2022;146:77-85.
139. Choi SJ, Jeong WK, Jo AJ, Choi JA, Kim MJ, Lee M, et al. Method- ology for developing evidence-based clinical imaging guidelines: Joint recommendations by Korean Society of Radiology and National Evidence-based Healthcare Collaborating Agency. Korean J Radiol 2017;18(1):208e16.
140. Ayhan Baser D, Kahveci R, Baydar Artantas A, Yasar I_, Aksoy H, Koc EM, et al. Exploring guideline adaptation strategy for Turkey: is "ADAPTE" feasible or does it need adaptation as well? J Eval Clin Pract 2018;24:97e104.
141. Akbari EM, Mohammadi G, Vosoogh-Moghaddam A, Vosoogh- Moghaddam A, Rabanikhah F, Javadi H, et al. National health guide- lines in I.R of Iran, an innovative approach for developing countries. Iran J Cancer Prev 2015;8(2):77e83.
142. Salarvand S, Hemati S, Adibi P, Taleghani F, Saleki M. An innovative approach to clinical practice guideline adaptation in the nursing profes- sion in a developing country. Cancer Manag Res 2020;12:2255e64.
143. Irajpour A, Hashemi M, Taleghani F. Clinical practice guideline for end-of-life care in patients with cancer: a modified ADAPTE process. Support Care Cancer 2022;30(3):2497e505.
144. Leśniak W, Morbidoni L, Dicker D, Marín-León I; EFIM. Clinical practice guidelines adaptation for internists - An EFIM methodology. Eur J Intern Med. 2020;77:1-5.
145. Wang Z, Grundy Q, Parker L, Bero L. Variations in processes for guideline adaptation: a qualitative study of World Health Organization staff experiences in implementing guidelines. BMC Public Health. 2020;20(1):1758.
146. 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.
147. Andrews JC, Schünemann 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.

148. Guideline International Network. GIN ADAPTE survey 2019. https://connect.g-i-n.net/filerepository?parent=602e53477e1bec0007ee8a69. Accessed in May 29, 2022.
149. Staniszewska S, Brett J, Simera I, Seers K, Mockford C, Goodlad S, et al. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. BMJ. 2017;358:j3453.
150. Kastner M, Makarski J, Hayden L, Durocher L, Chatterjee A, Brouwers M, et al. Making sense of complex data: a mapping process for analyzing findings of a realist review on guideline implementability. BMC Med Res Methodol. 2013;13:112.
151. Brouwers M, Makarski J, Kastner M, Hayden L, Bhattacharyya O, the GUIDE-M Research Team. The Guideline Implementability Decision Excellence Model (GUIDE-M): a mixed methods approach to create an international resource to advance the practice guideline field. Implementation Science. 2015;10(1):36.
152. Brandt L, Vandvik PO, Alonso-Coello P, Akl EA, Thornton J, Rigua D, et al. Multilayered and digitally structured presentation formats of trustworthy recommendations: a combined survey and randomised trial. BMJ Open. 2017;7(2):e011569.

Appendix I

Protocol: "Extending the RIGHT statement for reporting adapted practice guidelines in healthcare: the RIGHT-Ad@pt Checklist protocol"

BMJ Open

Extending the RIGHT statement for reporting adapted practice guidelines in healthcare: the RIGHT-Ad@pt Checklist protocol

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ABSTRACT

Introduction The adaptation of guidelines is an increasingly used methodology for the efficient development of contextualised recommendations. Nevertheless, there is no specific reporting guidance. The essential Reporting Items of Practice Guidelines in Healthcare (RIGHT) statement could be useful for reporting adapted guidelines, but it does not address all the important aspects of the adaptation process. The objective of our project is to develop an extension of the RIGHT statement for the reporting of adapted guidelines (RIGHT-Ad@pt Checklist).

Methods and analysis To develop the RIGHT-Ad@pt Checklist, we will use a multistep process that includes: (1) establishment of a Working Group; (2) generation of an initial checklist based on the RIGHT statement; (3) optimisation of the checklist (an initial assessment of adapted guidelines, semistructured interviews, a Delphi consensus survey, an external review by guideline developers and users and a final assessment of adapted guidelines); and (4) approval of the final checklist. At each step of the process, we will calculate absolute frequencies and proportions, use content analysis to summarise and draw conclusions, discuss the results, draft a report and refine the checklist.

Ethics and dissemination We have obtained a waiver of approval from the Clinical Research Ethics Committee at the Hospital de la Santa Creu i Sant Pau (Barcelona, Spain). We will disseminate the RIGHT-Ad@pt Checklist by publishing into a peer-reviewed journal, presenting to relevant stakeholders and translating into different languages. We will continuously seek feedback from stakeholders, surveil new relevant evidence and, if necessary, update the checklist.

Strengths and limitations of this study

- There is no current tool for reporting adapted guidelines. The extension of the RIGHT statement for adapted practice guidelines (RIGHT-Ad@pt Checklist) will fill this gap and provide a clear guidance for the reporting of guideline adaptation.
- To develop the checklist, we will use the best available methodological research evidence, adopt a systematic and rigorous multistep process and collect and build on the views and experiences of international stakeholders including guideline methodologists, policymakers, journal editors and guideline users.
- The RIGHT-Ad@pt Checklist can be used within guideline adaptation to guide reporting, to improve the completeness of reporting, to evaluate publications and to inform implementation decisions of healthcare.
- We will not conduct a complete formal validation of the checklist since our current process will not include an assessment of neither construction nor criterion validity.

INTRODUCTION

The WHO defines guidelines as 'systematically developed evidence-based statements which assist providers, recipients and other stakeholders to make informed decisions about appropriate health interventions.' Guidelines have been increasingly used to provide guidance for policies or public health interventions, changes in resource availability or access to services based on evidence.[1] There is evidence that the methodological quality of guidelines has slowly improved over the last decades.[2–4] However, most guideline developers do not have enough resources for developing high-quality de novo guidelines.[5] Most low/middle-income countries still do not have formal organisations, technical capacity or collaborations to develop evidence-based guidelines.[6] When guidelines are developed in those settings, their quality is typically poor.[7–13] Adapting published high-quality evidence-informed guidelines becomes a more efficient option.[14–16]

Adaption of guidelines means the use of existing trustworthy guidelines, with (adapt) or without (adopt) modifications, to provide local, regional or national guidance.[15–17] Schünemann *et al* defined adapted recommendations as recommendations with: (1) potential change in the specific population, intervention, or comparator with respect to the original recommendations; (2) potential change in the certainty of the evidence; and (3) information on 'conditions', monitoring, implementation and implications for research.[16] Adopted recommendations were defined as recommendations with: (1) the same specific population, intervention and comparators as the original recommendations; (2) the same certainty of the evidence; and (3) information on implementation.[16] Adaptation of guidelines is an increasingly used methodology for the efficient development of contextualised recommendations that are relevant for diverse health systems.[16–18] Guideline adaptation takes into consideration local contextual factors such as language, availability and accessibility of services and resources, the healthcare setting and the relevant stakeholders' cultural and ethical values.[19] At the same time, it should be based on similar systematic and transparent approaches as the source guideline in order to benefit from its quality and validity.[20] However, adaptation is not always possible. For example, when a trustworthy guideline is not available, a de novo guideline development process needs to be considered.[16 21]

Despite the increasing need, there is no standard adaptation method implemented internationally.[21 22] A systematic review of the literature identified eight published frameworks for adaptation of clinical, public health or health system guidelines, concluding that the 'adaptation' phases of the processes were notably different.[23] Moreover, the process for adapting guidelines was usually poorly reported, including WHO guidelines.[24] For example, Godah *et al* systematically assessed the processes employed in the adaptation of WHO guidelines for HIV and tuberculosis. Out of 170 eligible adapted guidelines, only 32 (32/170, 19%) reported the methods used in the adaptation process.[24] Similarly, Abdul-Khalek *et al* assessed the methods used for adapting health-related guidelines published in peer-reviewed journals.[25] Out of the 72 included adapted guidelines, 57 reported some degree of detail about the adaptation method used, and only 23 (23/57, 40%) reported using a specific adaptation method. These findings call for a need to optimise the methods used in guideline adaptation, and to improve the reporting of the adaptation process in adapted guidelines.[24]

Guidelines for reporting health research have been developed to enhance the accurate, complete and transparent reporting of health research publications (http://www.equator-network.org/). Moher *et al* defined a reporting guideline as 'a checklist, flow diagram, or explicit text to guide authors in reporting a specific type of research, developed using explicit methodology.'[26] Its aim is to indicate the minimum reporting standards, for readers to comprehend the design, conduct, analysis and interpretation of a study, and to assess the validity of results.[26 27] A transparent reporting approach could help guideline developers frame the decision-making during the development process, and guideline users about the suitability for adapting, and consequently the adaptation process.

Currently, the main tools available for the reporting of guidelines development are: (1) the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument, including the AGREE Reporting Checklist[28]; and (2) the Reporting Items of Practice Guidelines in Healthcare (RIGHT) statement to improve the reporting of guidelines.[29] The RIGHT statement was formally developed as a reporting checklist for de novo guidelines.[29] Although it could be useful for the reporting of adapted guidelines,[30] it does not cover some of the steps that are specific to guidelines adaptation (eg, description of methods used to search and identify guidelines).[29] Therefore, to ensure rigour, transparency, clarity and reproducibility of reporting the adaptation process, we will develop an extension of the RIGHT statement for the reporting of adapted guidelines.

Objective

To develop the RIGHT-Ad@pt Checklist as an extension of the RIGHT statement tailored to adapted guidelines.

METHODS AND ANALYSIS

To develop the checklist, we will build on the RIGHT statement,[29] review methodology research evidence on guidelines adaptation[23–25] and adopt a multistep process we have successfully implemented in the development of similar tools.[31 32] Table 1 describes the multistep development process of the RIGHT-Ad@pt Checklist, which includes: (1) establishment of a Working Group; (2) generation of an initial checklist; (3) optimisation of the checklist (an initial assessment of adapted guidelines, semistructured interviews, a Delphi consensus survey, an external review by guideline developers and users and a final assessment of adapted guidelines); and (4) approval of the final checklist. Figure 1 illustrates the development process, and figure 2 presents the timeline.

Establishment of the RIGHT-Ad@pt Working Group

The RIGHT-Ad@pt Working Group will include: (1) a Coordination Team; (2) an Advisory Group; and (3) a Delphi Panel.[26 31 32]

Coordination Team

The Coordination Team (YS, MB, LMG, PAC, EAA) will lead and coordinate the RIGHT-Ad@pt development process and ensure its completion according to the established timeline. Specifically, the Coordination Team will be responsible for (1) generating the initial version of the checklist; (2) implementing each step of the process; and (3) reporting the findings of each step of the processes. We have collected

Table 1 Description of the multistep development process

			Optimisation of the checklist						Approval of the final checklist
	Establishment of the Working Group	**Generation of the initial checklist**	**Initial assessment of adapted guidelines**	**Semistructured interviews**	**Delphi consensus survey**	**External review by guideline developers**	**External review by guideline users**	**Final assessment of adapted guidelines**	
Main objective	To identify individuals who are relevant to participate in the project	To develop the initial version of the checklist	To assess the adequacy of each item of the checklist	To explore current practices in adaptation of guidelines	To define the list of items to be included in the checklist	To assess the usefulness of each item of the checklist	To assess the usefulness of each item of the checklist	To assess the adequacy of each item of the checklist	To approve the final version of the checklist
Study design	–	–	Methodological survey of adapted guidelines	Semistructured interviews	Delphi consensus survey	Survey	Semistructured interviews	Methodological survey of adapted guidelines	–
Participants	► Coordination Team ► Advisory Group ► Delphi Panel Members	► Coordination Team ► Advisory Group	Coordination Team (two reviewers)	Guideline developers	Delphi Panel Members	Guideline developers	Guideline users	Coordination Team (two reviewers)	► Coordination Team ► Advisory Group
Main outcome	–	–	Applicability rating of each item of the checklist	Participants' views and experiences with process for adapting guidelines	Items considered relevant to report the adaptation of guidelines	Usefulness rating of each item of the checklist	Participants' views and experiences with the checklist	Applicability rating of each item of the checklist	–
Study size	Convenience sample	–	Convenience sample of 10 adapted guidelines	Sampling saturation	20–30 participants from GIN Adaptation Guidelines Working Group, WHO and authors of adapted guidelines	GIN community	Sampling saturation	Convenience sample of 10 adapted guidelines	–

GIN, Guidelines International Network.

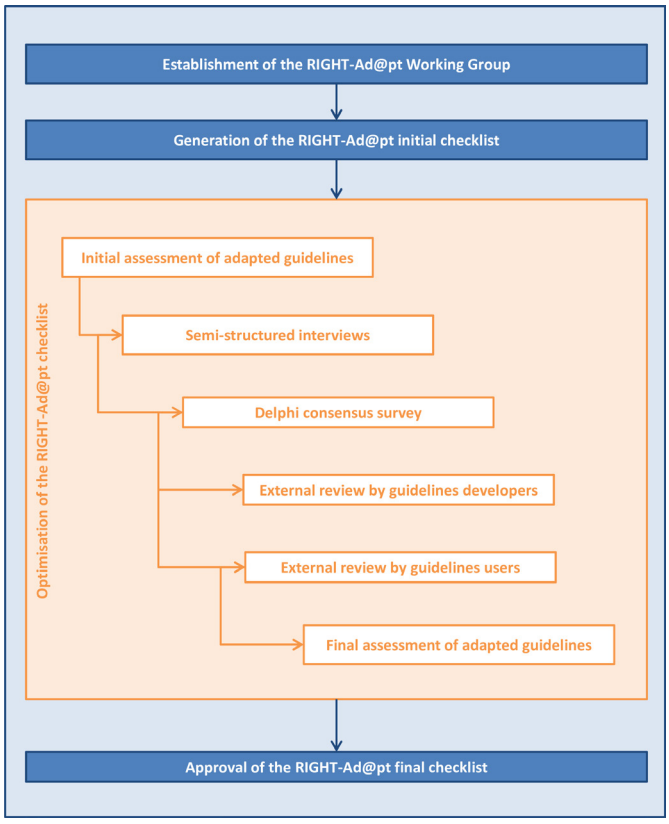

Figure 1 Multistep development process of RIGHT-Ad@pt. RIGHT, Reporting Items of Practice Guidelines in Healthcare.

the conflicts of interests (CoI) of all members of the Coordination Team (online supplementary file 1).

Advisory Group

The Advisory Group is a multidisciplinary group (8–10 people) including (1) guideline methodological experts (defined as having experience and expertise in guideline methods); (2) guideline developers (defined as having participated in guideline development groups and/or guideline adaptation groups at least once in the past year); (3) guideline users (defined as healthcare professionals that use guidelines on a regular basis); and (4) journal editors of guideline-related journals.[26] Members of the Advisory Group will review and provide expert advice during the different steps of the RIGHT-Ad@pt development process. The Advisory Group will approve the final checklist and accompanying guidance. We have collected the CoIs of all members of the Advisory Group (online supplementary file 1).

Delphi Panel

The Delphi Panel will be comprising 20–30 members, with profiles similar to those of the members of the Advisory Group (guideline methodological experts, guideline developers, guideline users and journal editors of guideline-related journals).[33 34] We will aim for country income, gender and profile representativeness of participants. We will identify participants from the Guidelines International Network (GIN) Adaptation Guidelines Working Group (http://www.g-i-n.net/working-groups/adaptation), WHO, authors of adapted guidelines[25] and expert colleagues. The panel's CoIs will be collected.

Generation of the initial checklist

The Coordination Team will generate the initial version of the checklist building on the RIGHT statement.[29] We will conduct this step via monthly face-to-face and online meetings within the Coordination Team. The Coordination Team will review the results, draft a report with a proposal of the initial version for the Advisory Group to review and produce a final version taken into consideration their feedback.

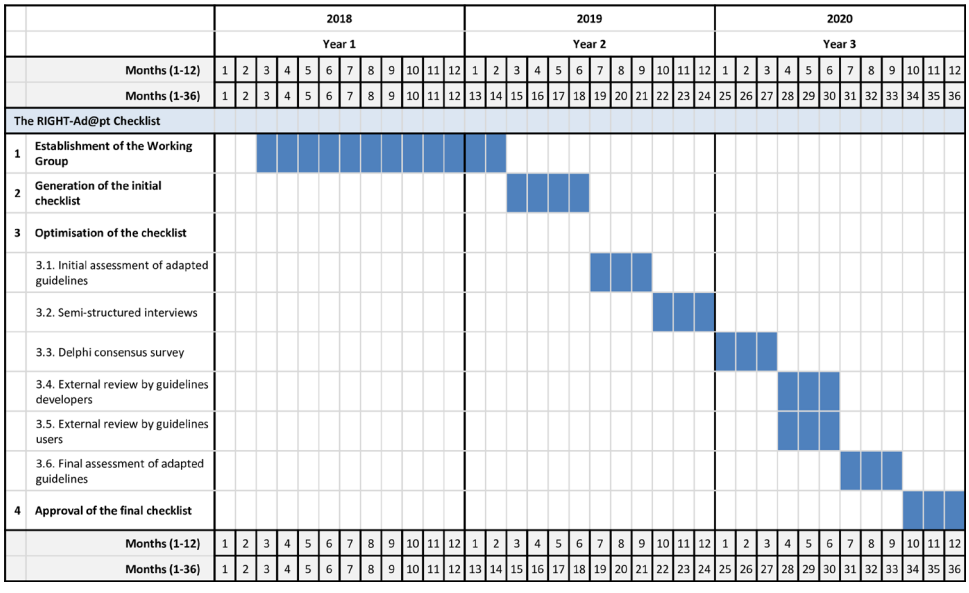

Figure 2 Timeline of RIGHT-Ad@pt. RIGHT, Reporting Items of Practice Guidelines in Healthcare.

Table 2 Research design steps relevant to the optimisation of the checklist and corresponding variables

	Initial assessment of adapted guidelines	Semistructured interviews	Delphi consensus survey	External review		Final assessment of adapted guidelines
				Guideline developers	Guideline users	
Response rate			X	X		
Characteristics of participants and workplaces		X	X	X	X	
Characteristics of adapted guidelines	X					X
Completeness of reporting	X					X
Participants' views and experiences		XX			XX	
Assessment of each item	XX (adequacy and suggestions)	X (understanding and suggestions)	XX (inclusion, understanding and suggestions)	XX (usefulness, understanding and suggestions)	X (understanding and suggestions)	XX (adequacy and suggestions)
Overall assessment of the checklist		X	X	X	X	

XX: main outcome; X: other outcomes.

Optimisation of the checklist

Initial assessment of adapted guidelines

We will survey published adapted guidelines using initial checklist. We will explore the adequacy of each item (defined as overall completeness of reporting as well as the quantity of example supporting the item[35]), and refine the checklist. We will also record the main characteristics of the adapted guidelines (eg, title, year or adaptation process), completeness of reporting process for adapting guidelines and suggestions to improve the checklist (table 2).

We will assess a convenience sample of 10 adapted guidelines available in English and published in the last 5 years.[36] We will also take into account country income level, type of organisation and region. Two reviewers from the Coordination Team will independently apply the initial version of the checklist to adapted guidelines. The two reviewers will resolve potential disagreements by discussion, and if necessary, by consulting a third reviewer.

For quantitative variables (characteristics of adapted guidelines, completeness of reporting and adequacy), we will calculate absolute frequencies and proportions. For qualitative variables (suggestions to improve the checklist), we will use content analysis to summarise and draw conclusions.[36] The Coordination Team will review the results, draft a report, review and agree on the relevant checklist modifications. If members of the Coordination Team do not reach consensus on specific items, they will consult the Advisory Group.

Semistructured interviews

We will survey guideline developers who were involved in guideline adaptation over the past 3 years. We will explore participants' views and experiences on guidelines adaptation, and refine the checklist. We will also record the characteristics of participants and their workplaces, participants' understanding of each item, suggestions to improve the checklist and participants' overall assessment of the checklist (table 2). Each interview will last approximately 1 hour and will be recorded and transcribed with participant's permission. The interview transcripts will be sent to interviewees for approval.

We will identify the participants with the support of the Advisory Group. We will contact via email and conduct online interviews. We will continue recruitment and collect data until information becomes repetitive and no new information emerges (sampling saturation).[37 38]

For quantitative variables (characteristics of participants and workplaces, participants' understanding of each item and participants' overall assessment of the checklist), we will calculate absolute frequencies and proportions. For qualitative variables (participants' views and experiences, and suggestions to improve the checklist), we will use content analysis to summarise and draw conclusions.[39] The Coordination Team will review the results, draft a report, review and agree on the relevant checklist modifications. If members of the Coordination Team do not reach consensus on specific items, they will consult the Advisory Group.

Delphi consensus survey

We will conduct a Delphi consensus survey to reach a consensus with the Delphi Panel about the included items in the checklist. We will also record response rate, characteristics of participants and workplaces, participants' understanding of each item, suggestions to improve the checklist and participants' overall assessment of the checklist (table 2).

Before the first Delphi round, we will provide the Delphi Panel Members with a brief background material on the topic. In the first Delphi round, we will ask participants to rate whether each item should be included in the checklist using a 7-point Likert scale (1=strongly disagree and 7=strongly agree).[31 32 40] We will calculate the median score for inclusion of each item and will classify them as (1) excluded (median score of 1–3 points); (2) review, modify and retest (median score of 4–5 points or with substantial comments); and (3) included (median score of 6–7 points and without substantial comments).[31 32] After each Delphi round, we will provide feedback to Delphi Panel Members (data reported will be anonymised). We will conduct additional Delphi rounds until consensus regarding items inclusion is reached (median score of 6–7) and no more relevant comments on the items are provided (two or three rounds, as needed). We will use online software to design the survey and collect responses (http://www.clinapsis.com/). We will not invite non-responders or partial responders (questionnaires with no response for more than 20% of the items) to subsequent Delphi rounds.

For quantitative variables (response rate, characteristics of participants and workplaces, inclusion score, participants' understanding of each item and participants' overall assessment of the checklist), we will calculate absolute frequencies and proportions. For qualitative data (suggestions to improve the checklist), we will use content analysis to summarise and draw conclusions.[39] We will not consider questionnaires with no response for more than 20% of the items. The Coordination Team will review the results of the Delphi consensus survey, draft a report with a proposal for the Advisory Group to review and produce a final version taken into consideration their feedback.

External review

External review by guideline developers

We will survey guideline developers who were involved in guideline adaptation over the past 3 years. We will explore usefulness of each item (defined as provision of enough and clear information in order to be used with effectiveness, efficiency and satisfaction to check the reporting of adapted guidelines[41]) using a 7-point Likert scale (1=strongly disagree and 7=strongly agree),[40] and refine the checklist. We will also record response rate, characteristics of participants and workplaces, participants' understanding of each item, suggestions to improve the checklist and participants' overall assessment of the checklist (table 2).

We will identify participants by contacting professionals associated with the GIN community (http://www.g-i-n.net) and WHO. We will use online software to design the survey and collect responses (http://www.clinapsis.com/).

For quantitative variables (response rate, characteristics of participants and workplaces, usefulness score, participants' understanding of each item and participants' overall assessment of the checklist), we will calculate absolute frequencies and proportions. For qualitative data (suggestions to improve the checklist), we will use content analysis to summarise and draw conclusions.[39] We will not consider questionnaires with no response for more than 20% of the items.

External review by guideline users

We will conduct external review semistructured interviews with guideline users who have used adapted guidelines over the past 3 years. We will explore participants' views and experiences using the checklist, and refine the checklist. We will also record the characteristics of participants and workplaces, participants' understanding of each item, suggestions to improve the checklist and participants' overall assessment of the checklist (table 2). Each interview will last approximately 1 hour and will be recorded and transcribed with participant's permission. The interview transcripts will be sent to interviewees for approval.

We will identify the participants with the support of the Advisory Group. We will contact via email and conduct online interviews. We will continue recruitment and collect data until information becomes repetitive and no new information emerges (sampling saturation).[37 38]

For quantitative variables (characteristics of participants and workplaces, usefulness score, participants' understanding of each item and participants' overall assessment of the checklist), we will calculate absolute frequencies and proportions. For qualitative data (participants' views and experiences, and suggestions to improve the checklist), we will use content analysis to summarise and draw conclusions.[39] The Coordination Team will review the results of the external review (guideline developers and users), draft a report with a proposal for the Advisory Group to review and produce a final version taken into consideration their feedback.

Final assessment of adapted guidelines

We will conduct a final assessment of the validity of each item in a set of adapted guidelines. We will also record the main characteristics of the adapted guidelines (eg, title, year or adaptation process), completeness of reporting process for adapting guidelines and suggestions to improve the checklist (table 2).

We will assess a convenience sample of 10 adapted guidelines available in English and published in the last 5 years.[36] We will also take into account country income level, type of organisation and region. Two reviewers from the Coordination Team will independently apply the final

version of the checklist to adapted guidelines. The two reviewers will resolve potential disagreements by discussion, and if necessary, by consulting a third reviewer.

For quantitative variables (characteristics of adapted guidelines, completeness of reporting and adequacy), we will calculate absolute frequencies and proportions. For qualitative variables (suggestions to improve the checklist), we will use content analysis to summarise and draw conclusions.[39] The Coordination Team will review the results, draft a report, review and agree on the relevant checklist modifications. If members of the Coordination Team do not reach consensus on specific items, they will consult the Advisory Group.

Approval of the final checklist

The Coordination Team will generate the final version of the checklist. The final checklist will highlight the changes from the RIGHT statement,[29] including (1) the items that remained unchanged, (2) the items that were modified, (3) the items that were added as part of the extension, and (4) the items that were omitted. All members of the Coordination Team and the Advisory Group will need to review and approve the final version of the checklist through consensus discussion.

Patient and public involvement

Patient and public will not be involved in the study.

DISCUSSION

Executive summary

The aim of this project is to develop the RIGHT-Ad@pt Checklist, as an extension of the RIGHT statement tailored for guideline adaptation, to improve the rigour and transparency of guideline adaptation reporting. To develop the checklist, we will build on the RIGHT statement, use the best available evidence from published methodological research on this topic and use a rigorous multistep process involving multiple stakeholders.

Our study in the context of previous research

Adaptation of high-quality guidelines is an alternative to developing de novo guidelines that saves both time and resources, and avoids duplication of effort. The ADAPTE framework is one of the earliest systematic approaches to adapt guidelines to local context.[15 42] Building on work done for WHO in 2006, the 'GRADE-ADOLOPMENT' framework proposed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Evidence to Decision frameworks for the adaptation, adoption and de novo development of guidelines.[16] Despite these advances, there is variability in the quality of reporting of adapted practice guidelines and no guidance for their reporting is available.[23 25] The proposed checklist might help with reducing the variability of adaptation process and improving the quality of reporting. The checklist is not intended to support guideline development, which will be done through an extension of the GIN-McMaster Guideline Development Checklist.[43]

Strengths and limitations

Our proposal has some limitations. For example, we will only include guidelines published in English in the assessment of adapted guidelines. The checklist will inform about the completeness of the reporting but not necessarily about the quality of the adaptation process. We will not conduct a complete formal validation of the checklist since our current process will not include an assessment of neither construction nor criterion validity[44]; however, our proposed approach will ensure both face and content validity.

Our proposal has several strengths. The development of the checklist will be comprehensive, including the use of previous methodological evidence[23–25 29 31 32] and the engagement of the multidisciplinary international guideline community. We will collect views and experiences from different stakeholders, including methodologists, guideline developers, guideline users and journal editors. We will also ensure the diversity of participants in terms of country level of income, gender and field of expertise. This will allow us to incorporate the different stakeholders' perspective about the adaptation of guidelines. We will address the risk of bias in each step of the development process. To minimise interviewer bias, semi-structured interviews will be conducted using an interview guide. To minimise selection bias, we will invite all GIN Adaptation Guidelines Working Group members as well as other stakeholders to join the Delphi Panel and to participate in the external review survey. To minimise non-response bias, we will make the survey available online for 4 weeks and we will send two reminders prior to the round closing date.

Implications for practice and research

RIGHT-Ad@pt will help improve the completeness when reporting adapted guidelines, therefore contribute to improve their quality, and facilitate their implementation. The checklist will allow the guideline developers to guide their reporting, journal editors to improve the reporting of published adapted guidelines, policymakers to inform on implementation decisions and guideline users to evaluate the completeness of the reporting within adapted guidelines. Future research should focus on the performance of a complete formal validation of the checklist and its assessment in a representative sample of contemporary adapted guidelines. Surveillance on the use of the checklist and assessment of its impact could also be a topic of research.

Ethics and dissemination

The protocol obtained a waiver of approval (did not involve patients, biological samples or clinical data) from the Clinical Research Ethics Committee at the Hospital de la Santa Creu i Sant Pau (Barcelona, Spain). Nevertheless,

we will request written informed consent from all participants and anonymise all data.

The dissemination activities will include: (1) publication of the RIGHT-Ad@pt Checklist in a peer-reviewed journal; (2) presentation of the project to relevant stakeholders (eg, via international conferences, electronic bulletins, related websites (http://www.right-statement.org/, http://www.equator-network.org/) and social media (eg, Twitter); and (3) translation of the checklist into different languages. The implementation activities will include: (1) engaging with journal editors to encourage the use of the checklist; and (2) evaluation of the impact of the checklist on the reporting of adapted guidelines. Finally, we will continuously seek feedback from stakeholders, surveil new relevant evidence and, if necessary, update the checklist.

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REFERENCES

1. World Health Organization. *WHO handbook for guideline development*. WHO handbook for guideline development, 2014.
2. Alonso-Coello P, Irfan A, Sola I, *et al*. The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. *BMJ Qual Saf* 2010;19:e58.
3. Armstrong JJ, Goldfarb AM, Instrum RS, *et al*. Improvement evident but still necessary in clinical practice guideline quality: a systematic review. *J Clin Epidemiol* 2017;81:13–21.
4. Institute of Medicine. *Clinical practice guideline we can trust*. Washington, DC: The National Academies Press, 2011.
5. Schünemann HJ, Fretheim A, Oxman AD. WHO Advisory Committee on health research. improving the use of research evidence in Guideline development: 1. guidelines for guidelines. *Health Res Policy Syst* 2006;4.
6. Bhaumik S. Use of evidence for clinical practice guideline development. *Trop Parasitol* 2017;7:65–71.
7. Bhaumik S, Jagadesh S, Ellatar M, *et al*. Clinical practice guidelines in India: quality appraisal and the use of evidence in their development. *J Evid Based Med* 2018;11:26–39.
8. Canelo-Aybar C, Balbin G, Perez-Gomez Á, *et al*. [Clinical practice guidelines in Peru: evaluation of its quality using the AGREE II instrument]. *Rev Peru Med Exp Salud Publica* 2016;33:732–8.
9. Kredo T, Gerritsen A, van Heerden J, *et al*. Clinical practice guidelines within the Southern African Development Community: a descriptive study of the quality of guideline development and concordance with best evidence for five priority diseases. *Health Res Policy Syst* 2012;10.
10. Machingaidze S, Zani B, Abrams A, *et al*. Series: clinical epidemiology in South Africa. paper 2: quality and reporting standards of South African primary care clinical practice guidelines. *J Clin Epidemiol* 2017;83:31–6.
11. Machingaidze S, Grimmer K, Louw Q, *et al*. Next generation clinical guidance for primary care in South Africa - credible, consistent and pragmatic. *PLoS One* 2018;13:e0195025.
12. Molino CG, Romano-Lieber NS, Ribeiro E, *et al*. Non-Communicable disease clinical practice guidelines in Brazil: a systematic assessment of methodological quality and transparency. *PLoS One* 2016;11:e0166367.
13. Talagala IA, Samarakoon Y, Senanayake S, *et al*. Sri Lankan clinical practice guidelines: a methodological quality assessment utilizing the agree II instrument. *J Eval Clin Pract* 2018.
14. Fervers B, Burgers JS, Haugh MC, *et al*. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. *Int J Qual Health Care* 2006;18:167–76.
15. Fervers B, Burgers JS, Voellinger R, *et al*. Guideline adaptation: an approach to enhance efficiency in guideline development and improve utilisation. *BMJ Qual Saf* 2011;20:228–36.
16. Schünemann HJ, Wiercioch W, Brozek J, *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.
17. Darzi A, Harfouche M, Arayssi T, *et al*. Adaptation of the 2015 American College of Rheumatology treatment guideline for rheumatoid arthritis for the Eastern Mediterranean Region: an exemplar of the GRADE Adolopment. *Health Qual Life Outcomes* 2017;15:183.
18. Okely AD, Ghersi D, Hesketh KD, *et al*. A collaborative approach to adopting/adapting guidelines - The Australian 24-Hour Movement Guidelines for the early years (Birth to 5 years): an integration of physical activity, sedentary behavior, and sleep. *BMC Public Health* 2017;17(S5):869.
19. Burgers JS, Anzueto A, Black PN, *et al*. Adaptation, evaluation, and updating of guidelines: article 14 in integrating and coordinating efforts in COPD Guideline development. An official ATS/ERS workshop report. *Proc Am Thorac Soc* 2012;9:304–10.
20. Kristiansen A, Brandt L, Agoritsas T, *et al*. Applying new strategies for the national adaptation, updating, and dissemination of trustworthy guidelines: results from the Norwegian adaptation of

the antithrombotic therapy and the prevention of thrombosis, 9th Ed: American College of chest physicians evidence-based clinical practice guidelines. *Chest* 2014;146:735–61.
21. Mehndiratta A, Sharma S, Prakash N, *et al*. Adapting clinical guidelines in India—a pragmatic approach. *BMJ* 2017;359.
22. Kredo T, Bernhardsson S, Machingaidze S, *et al*. Guide to clinical practice guidelines: the current state of play. *Int J Qual Health Care* 2016;28:122–8.
23. Darzi A, Abou-Jaoude EA, Agarwal A, *et al*. A methodological survey identified eight proposed frameworks for the adaptation of health related guidelines. *J Clin Epidemiol* 2017;86:3–10.
24. Godah MW, Abdul Khalek RA, Kilzar L, *et al*. A very low number of national adaptations of the World Health Organization guidelines for HIV and tuberculosis reported their processes. *J Clin Epidemiol* 2016;80:50–6.
25. Abdul–Khalek RA, Darzi AJ, Godah MW, *et al*. Methods used in adaptation of health–related guidelines: a systematic survey. *J Glob Health* 2017;7:020412.
26. Moher D, Schulz KF, Simera I, *et al*. Guidance for developers of health research reporting guidelines. *PLoS Med* 2010;7:e1000217.
27. Liberati A, Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6:e1000100.
28. Brouwers MC, Kerkvliet K, Spithoff K. Agree next steps Consortium. The agree reporting checklist: a tool to improve reporting of clinical practice guidelines. *BMJ* 2016;352.
29. Chen Y, Yang K, Marušic A, *et al*. A reporting tool for practice guidelines in health care: the right statement. *Ann Intern Med* 2017;166:128–32.
30. Tokalić R, Viđak M, Buljan I, *et al*. Reporting quality of European and Croatian health practice guidelines according to the RIGHT reporting checklist. *Implement Sci* 2018;13.
31. Vernooij RWM, Alonso-Coello P, Brouwers M, *et al*. Reporting items for updated clinical guidelines: checklist for the reporting of updated guidelines (CheckUp). *PLoS Med* 2017;14:1002207.
32. Martínez García L, Pardo-Hernandez H, Niño de Guzman E, *et al*. Development of a prioritisation tool for the updating of clinical guideline questions: the UpPriority tool protocol. *BMJ Open* 2017;7:e017226.
33. Akins RB, Tolson H, Cole BR. Stability of response characteristics of a Delphi panel: application of bootstrap data expansion. *BMC Med Res Methodol* 2005;5:37.
34. Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. *PLoS Med* 2011;8:e1000393.
35. Glenton C, Carlsen B, Lewin S, *et al*. Applying GRADE-CERQual to qualitative evidence synthesis findings—paper 5: how to assess adequacy of data. *Implement Sci* 2018;13(S1).
36. Arain M, Campbell MJ, Cooper CL, *et al*. What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC Med Res Methodol* 2010;10:67.
37. Grossoehme DH. Overview of qualitative research. *J Health Care Chaplain* 2014;20:109–22.
38. Guetterman TC. Descriptions of sampling practices within five approaches to qualitative research in education and the health sciences. *Forum Qual Soc Res* 2015;16.
39. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Med Res Methodol* 2008;8:45.
40. Likert R. A technique for the measurement of attitudes. In: *Archives of psychology*, 1932.
41. van der Weegen, Verwey R, Tange H, *et al*. Usability testing of a monitoring and feedback tool to stimulate physical activity. *Patient Prefer Adherence* 2014;8:311–22.
42. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 13. Applicability, transferability and adaptation. *Health Res Policy Syst* 2006;4.
43. Schünemann HJ, Wiercioch W, Etxeandia I, *et al*. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. *Can Med Assoc J* 2014;186:E123–42.
44. AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. *Qual Saf Health Care* 2003;12:18–23.

Appendix II

Modifications during the multi-step development process of the RIGHT-Ad@pt checklist

Step	Initial assessment of adapted guidelines	
From	RIGHT-Ad@pt checklist version 1 - initial version (7 sections, 26 topics, 40 items)	
To	RIGHT-Ad@pt checklist version 2 (7 sections, 28 topics, 36 items)	
		n
Major modifications		**21**
Improving items		8
	Inclusion of new content	
	1. We included "target country/region name" in "Publication" item	
	2. We included "health system" in "Focus" item	
	3. We included "note any differences compared to the source guideline(s)" in "Aim(s) and specific objectives" item	
	4. We included "note any differences compared to the source guideline(s)" in "Users" item	
	5. We included "criteria/factors to formulate the recommendations" in "Criteria/factors to formulate the recommendations" item	
	6. We included "applicability to different settings" in "Limitations" item	
	Deletion of some content	
	7. We deleted "target country/region name" of the "Developer" item	
	8. We deleted "difference from source guideline(s) and adapted guideline" of the "Summary" item	
Combining items		6
	1. We combined item 22 "New evidence, updated systematic reviews" and 23 "New evidence, other systematic reviews"	
	2. We combined item 22 "New evidence, updated systematic reviews" and 23 "New evidence, other systematic reviews" (we delated item 23)	
	3. We combined item 25 "Recommendations, list" and 27 "Recommendations, identification"	
	4. We combined item 25 "Recommendations, list" and 27 "Recommendations, identification" (we delated item 27)	
	5. We combined item 26 "The strength of recommendations and the certainty of the evidence" and 28 "Recommendations, differences from the source recommendations"	
	6. We combined item 26 "The strength of recommendations and the certainty of the evidence" and 28 "Recommendations, differences from the source recommendations" (we delated item 28)	
Deleting items		1
	1. We deleted item 17 "Development of key questions, selection and prioritization"	
Improving topics		2
	1. We modified "Evidence" topic into "Rigour of development" topic	
	2. We modified "Systematic reviews" topic into "Evidence synthesis" topic	
Including new topics		2
	1. We included "Source guideline(s)" topic	
	2. We included "Adaptation framework/methodology" topic	

Modification of the item sequence	2

1. We moved "Contributors" item from "Background" section to "Rigour of development" section
2. We moved "Decision-making processes" item from "Recommendations" section to "Rigour of development" section

Minor modifications	**8**

1. "Identification" item
2. "Contact information" item
3. "Basic epidemiology of the problem" item
4. “Population(s)” item
5. "PICOs" item
6. "Source guideline(s)" item
7. "Certainty of evidence" item
8. "Implementation" item

User guide

We drafted the initial version of the user guide

Step	**Semistructured interviews**
From	RIGHT-Ad@pt checklist version 2 (7 sections, 28 topics, 36 items)
To	RIGHT-Ad@pt checklist version 3 (7 sections, 26 topics, 35 items)
	n
Major modifications	**14**
Improving items	10

Inclusion of new content

1. We included "country" in "Developer" item
2. We included "key questions' prioritization and selection" in "Development of key questions" item
3. We included "the strength of recommendation" in "Certainty of evidence and the strength of recommendations" item
4. We included "the balance of benefits and harms" in "Criteria/factors to formulate the recommendations" item

Modification of the content

5. We modified "source guideline(s)/recommendation(s)" to "source guideline(s)" in "Source guideline(s)" item
6. We modified "source guideline(s)" to "recommendation(s) from the source guideline" in "Source recommendation(s)" item
7. We modified "adapted guideline" to "adapted recommendation(s)" in "Supporting evidence" item
8. We modified "source guideline(s)" to "source recommendation(s)" in "New evidence" item

Deletion of some content

9. We excluded "country" in "Publication" item
10. We delated "note any differences compared to the source guideline(s) if applicable" of the "Implementation" item

Combining items	2

1. We combined item 35 "Gaps in the evidence, suggestions for research" and item 36 "Limitations"
2. We combined item 35 "Gaps in the evidence, suggestions for research" and item 36 "Limitations" (we delated item 36)

Improving topics 1

1. We modified "Title" topic to "Title/Subtitle" topic

Deleting topics 1

1. We deleted "Cover page" topic

Minor modifications **3**

1. "Contact information" item
2. "Decision-making processes" item
3. "Conflicts of interest" item

User guide

We improved the content of the user guide

Step	**Delphi consensus survey, first round**
From	RIGHT-Ad@pt checklist version 3 (7 sections, 26 topics, 35 items)
To	RIGHT-Ad@pt checklist version 4.1 (7 sections, 28 topics, 35 items)
	n
Major modifications	**10**
Improving items	3

Inclusion of new content

1. We included “different criteria” in “Source recommendation(s)” item
2. We included “potential barriers and strategies” in “Implementation” item
3. We included “challenges of the adaptation process” in “Challenges, limitations, and suggestions for research” item

Improving topics 3

1. We modified “Key questions” topic to “Source guideline(s)” topic
2. We modified “Source guideline(s)/recommendation(s)” topic to “Source recommendation(s)” topic
3. We retrieved “Cover/first page” topic

Modification of the item sequence 3

1. We moved “Focus” item from “Cover/first page” topic to “Title/subtitle” topic
2. We moved “Publication” item from “Title/subtitle” topic to “Cover/first page” topic
3. We moved “Source guideline(s)” item above “Key questions” topic

Including response options 1

1. We included response options to assess the reporting of each item (“Yes”, “No”, “Unclear”, “Not Applicable”)

Minor modifications **13**

1. “Identification” item
2. “Contact information” item
3. “Basic epidemiology of the problem” item

4. “Population(s)” item
5. “Contributors” item
6. “Development of key questions” item
7. “Supporting evidence” item
8. “New evidence” item
9. “Certainty of evidence and the strength of recommendations” item
10. “Decision-making processes” item
11. “Recommendations for subgroups” item
12. “Access” item
13. “Update” item

User guide

- We improved the content of the user guide
-

Step	**Delphi consensus survey, second round**
From	RIGHT-Ad@pt checklist version 4.1 (7 sections, 28 topics, 35 items)
To	RIGHT-Ad@pt checklist version 4.2 (7 sections, 27 topics, 34 items)
	n
Major modifications	**3**
Improving items	2

Inclusion of new content

1. We included “date for literature search” in “Publication” item
2. We included “list of all the recommendations” in “Summary” item

Deleting items 1

1. We delated “Access” item

Minor modifications **11**

1. “Identification” item
2. “Focus” item
3. “Developer and country” item
4. “Basic epidemiology of the problem” item
5. “Framework adaptation process” item
6. “Source recommendation(s)” item
7. “Recommendations” item
8. “The strength of recommendations and the certainty of the evidence” item
9. “Recommendations for subgroups” item
10. “Criteria/factors to formulate the recommendations” item
11. “Quality assurance” item

User guide

We improved the content of the user guide

Step	**External review by guideline developers and users**
From	RIGHT-Ad@pt checklist version 4.2 (7 sections, 27 topics, 34 items)
To	RIGHT-Ad@pt checklist version 5 (7 sections, 27 topics, 34 items)
	n
Major modifications	**4**

Improving items	4

Inclusion of new content

1. We included “region” in “Developer and country” item
2. We included “a summary for the adapted guideline” in “Summary” item
3. We included “note any differences (if applicable) compared to the source recommendation(s)” in “Recommendations for subgroups” item

Modification of the content

4. We simplified the content of “New evidence” item

Minor modifications	**11**

1. “Basic epidemiology of the problem” item
2. “Aim(s) and specific objectives” item
3. “Population(s)” item
4. “Users” item
5. “Setting(s)” item
6. “Framework adaptation process” item
7. “Development of key questions” item
8. “The strength of recommendations and the certainty of the evidence” item
9. “Organisational approval” item
10. “Funding” item
11. “External review and quality assurance” topic

3. User guide

We improved the content of the user guide

Step	**Final assessment of adapted guidelines**
From	RIGHT-Ad@pt checklist version 5 (7 sections, 27 topics, 34 items)
To	RIGHT-Ad@pt checklist version 6 (7 sections, 27 topics, 34 items)
	n
Major modifications	**2**
Improving topics	1

1. We modified “Background” topic to “Scope” topic

Deleting response option	1

1. We deleted “Not Applicable” response option

Minor modifications	**11**

1. “Identification” item
2. “Publication” item
3. “Developer and country” item
4. “Summary” item
5. “Contact information” item
6. “Basic epidemiology of the problem” item
7. “Contributors” item
8. “Framework adaptation process” item
9. “Development of key questions” item
10. “New evidence” item
11. “Certainty of evidence and the strength of recommendations” item

User guide
We improved the content of the user guide

Step	**Approval of the final version of the checklist**
From	RIGHT-Ad@pt checklist version 6 (7 sections, 27 topics, 34 items)
To	RIGHT-Ad@pt checklist version 7 (7 sections, 27 topics, 34 items)
	n
Major modifications	**1**
Improving items	1
Inclusion of new content 1. We included "whether source authors were contacted" in "Publication of the source guideline(s)" item	
Minor modifications	**0**

User guide
We edited the final version of the user guide

Appendix III

RIGHT-Ad@pt User Guide

RIGHT-**Ad@pt**

A REPORTING TOOL FOR ADAPTED GUIDELINES IN HEALTH CARE: THE RIGHT-Ad@pt CHECKLIST [USER GUIDE]

October 2021

RIGHT-Ad@pt

A REPORTING TOOL FOR ADAPTED GUIDELINES IN HEALTH CARE: THE RIGHT-Ad@pt CHECKLIST

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1. SUMMARY

Background

The adaptation of guidelines is an increasingly used methodology for the efficient development of contextualised recommendations. Nevertheless, there is no specific reporting guidance. The essential Reporting Items of Practice Guidelines in Healthcare (RIGHT) statement may be useful for reporting adapted guidelines, but it fails to address all the important aspects of the adaptation process.

Objective

The objective of our project is to develop a reporting checklist for adapted guidelines.

Methods

To develop the RIGHT-Ad@pt Checklist, we have followed a multi-step process that included: (1) establishing a Working Group; (2) generating an initial checklist based on the RIGHT statement and methodological evidence on guideline adaptation; (3) optimising the checklist (an initial assessment of adapted guidelines, semi-structured interviews, a Delphi consensus survey, an external review by guideline developers and users and a final assessment of adapted guidelines); and (4) approval of the final checklist. At each step of the process, we calculated absolute frequencies and proportions, used content analysis for summarising and drawing conclusions, discussed the results, drafted a report and refined the checklist.

Results

The RIGHT-Ad@pt working group contains a Coordination Team, an Advisory Group, a Delphi panel. We generated the initial version of the RIGHT-Ad@pt (RIGHT-Ad@pt Version 01) based on 1) the existing checklist for both guideline assessment and reporting (the RIGHT statement, AGREE II instrument, CAN-Implement, and the CheckUP); 2) published adaptation frameworks

(ADAPTE, GRADE-ADOLOPMENT, and SNIP-II process); and 3) the experience of our working group members. We have optimised the RIGHT-Ad@pt checklist and updated the checklist into a new version after each step. We have: 1) assessed ten adapted guidelines (RIGHT-Ad@pt Version 02), 2) explored the current practice of guideline adaptation with semi-structured interviews (RIGHT-Ad@pt Version 03), 3) conducted a Delphi consensus survey (RIGHT-Ad@pt Version 04), 4) undertaken external reviews with guideline developers and users (RIGHT-Ad@pt Version 05), and 5)assessed a new set of adapted guidelines (RIGHT-Ad@pt Version 06). In addition, we also developed and improved the RIGHT-Ad@pt user guide along with the development process. Finally, the whole RIGHT-Ad@pt working group conducted a final approval discussion (RIGHT-Ad@pt Version 07) and approved it as the final version.

Conclusion

RIGHT-Ad@pt aims to improve completeness of reporting adapted guidelines, focusing on the standardisation, rigor, and transparency of the process and the clarify and explicitness of adapted recommendations

2. INTRODUCTION

Guidelines have been increasingly used to provide guidance for policies or public health interventions, changes in resource availability or access to services based on evidence(1). There is evidence that the methodological quality of guidelines has slowly improved over the last decades (2-4). However, most guideline developers do not have sufficient resources for developing high-quality de novo guidelines (5). Most low/middle-income countries still do not have formal organizations, technical capacity, well-established mechanisms of funding or collaborations to develop evidence-based guidelines (6). When guidelines are developed in those settings, their quality is typically poor (7-13). Adapting published high-quality evidence-informed guidelines becomes a more efficient option (14-16).

Adaptation of guidelines is an increasingly used methodology for the efficient development of contextualised recommendations that are relevant for diverse health systems (16-18). Adapted recommendations can be defined as recommendations with: (1) potential change in the specific population, intervention, or comparator with respect to the original recommendations; (2) potential change in the certainty of the evidence; and (3) information on 'conditions', monitoring, implementation and implications for research. Guideline adaptation takes into consideration local contextual factors such as language, availability and accessibility of services and resources, the healthcare setting and the relevant stakeholders' cultural and ethical values (19). At the same time, it should be based on similar systematic and transparent approaches to the source guideline in order to benefit from its quality and validity (20). However, adaptation is not always possible. For example, when a trustworthy guideline is not available, a de novo guideline development process needs to be considered (16).

Except for the increasing need, there are different adaptation methods implemented globally (21, 22). A systematic review of the literature identified eight published frameworks for adaptation of clinical, public health or health system guidelines, concluding that the 'adaptation' phases were notably different (23). Moreover, the process for adapting guidelines is usually

poorly reported (24, 25). These findings call for a need to optimise the methods used in guideline adaptation, and to improve the reporting of the adaptation process in adapted guidelines (24).

A transparent reporting approach could help both guideline developers and guideline users regarding the suitability **of the adaptation conducted** (26, 27). The RIGHT statement was developed as a reporting checklist for *de novo* guidelines (28). Although it could be of use for the reporting of adapted guidelines (29), it does not cover some of the steps that are specific to guidelines adaptation (e.g., description of methods used to search and identify guidelines). Therefore, to ensure rigor, transparency, clarity and reproducibility of reporting, we developed the RIGHT-Ad@pt checklist for the reporting of adapted guidelines.

The RIGHT-Ad@pt checklist contains seven domains and 34 items.

The domains are:

- Basic information
- Background
- Rigor of development
- Recommendations
- External review and quality assurance
- Funding, declaration and management of interest
- Other information

Each item contains:

- An explanation about “what to do” and “why this is important”
- Several examples extracted from published adapted guidelines
- Three options for users to check the reporting content (“Yes”, “No”, “ Unclear”) with justifications columns

3. APPLYING THE RIGHT-Ad@pt CHECKLIST

What is the RIGHT-Ad@pt checklist?

The RIGHT-Ad@pt checklist was developed as a reporting checklist to inform and assess the reporting of the adapted guidelines. The RIGHT-Ad@pt is not intended for use as an aide to the adaptation process or as a quality assessment tool, but users should pay attention to reporting requirements during the planning stage.

Who can apply the RIGHT-Ad@pt checklist?

The RIGHT-Ad@pt checklist could be used by

- Guideline developers to guide their reporting and inform their adaptation processes
- Journal editors to improve the reporting of published adapted guidelines
- Guideline users to evaluate the completeness of the reporting of adapted guidelines

How to apply the RIGHT-Ad@pt checklist?

The RIGHT-Ad@pt checklist should be used in conjunction with the entire User Guidance. Each judgement made by users should be clearly documented and reported.

We recommend the users select “yes” when the adapted guideline reports all the item contents suggested by RIGHT-Ad@pt; “No” when the adapted guideline does not report all the item contents; and “Unclear” when the reviewers can not judge the content reported by the adapted guideline. The “Notes” column could be used to justify users’ decisions if needed. The provided explanations describe what to report in certain circumstances and why this is important. The examples provided do not imply they represent good quality or high credibility of the adapted guidelines from which the examples were taken.

It is recommended that users of the checklist do not score each item or add them to create an overall score. Instead, we encourage users to interpret the reporting according to the responses and make an overall judgement.

Example for applying the RIGHT-Ad@pt checklist:

Items	Examples	Assessment	Page(s)	Note (s)
Item 3. Report the year of publication and the literature search date of the adapted guideline.	"Received: 13 July 2019 Revised: 4 October 2019 Accepted: 11 October 2019. Abstract - To adapt European Dermatology Forum (EDF) guidelines for AD to the Italian medical–legal context, the EDF guidelines were assessed independently by two independent Italian renowned experts in the field and further integrated with articles published and systematically reviewed before May 2019." (30)	**Yes**	P.1	
	"Received: 7 July 2019 Revised: 11 October 2019 Accepted: 15 January 2020". (31)	**No**	P.1	No literature search date was reported
Item 15. Report which framework or methodology was considered in the guideline adaptation process	"The EDF Consensus based guidelines (Ring et al., 2012a, 2012b; Wollenberg et al., 2018b; on which the present work is based) are an update of the 2012 guidelines (Ring et al., 2012b), integrated with evidence-based national guideline from Germany (Werfel et al., 2009), the Health Technology Report (Hoare, Li Wan Po, & Williams, 2000), as well as the position paper of the European Task Force on Atopic Dermatitis/European Academy of Dermatology and Venereology (Darsow et al., 2010). In 2015, during a meeting in Copenhagen, two authors were chosen to prepare the first draft of the guidelines; this draft was prepared on the basis of full articles only, published before March 2015. Eventual discrepancies were debated during the consensus process. Due to the consensus nature of the document, a systematic review of the literature was not performed to provide the first draft. The specifically appointed European Dermatology Forum (EDF) committee reviewed the first draft, hereby setting as target group dermatologists, pediatricians, allergists,	**Unclear**	P. 2	Neither a published or self-developed methodology, nor the adaptation process were reported.

	general practitioners as well as, more generally any physician involved in the management of AD." (30)			

4. RIGHT-AD@PT CHECKLIST

Section/Topic	No.	Item	Assessment	Page(s)	Note (s)
Basic information					
Title/Subtitle	1	Identify the report as an adaptation of practice guideline(s), that is include "guideline adaptation", "adapting", "adapted guideline/recommendation(s)", or similar terminology in the title/subtitle.	☐ Yes ☐ No ☐ Unclear		
	2	Describe the topic/focus/scope of the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
Cover/First page	3	Report the respective dates of publication and the literature search of the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
	4	Describe the developer and country/region of the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
Executive summary/Abstract	5	Provide a summary of the recommendations contained in the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
Abbreviations and acronyms	6	Define key terms and provide a list of abbreviations and acronyms (if applicable).	☐ Yes ☐ No ☐ Unclear		
Contact information of the guideline adaptation group	7	Report the contact information of the developer of the adapted guideline.	☐ Yes ☐ No ☐ Unclear		
Scope					
Source guideline (s)	8	Report the name and year of publication of the source guideline(s), provide the citation(s), and whether source authors were contacted.	☐ Yes ☐ No ☐ Unclear		
Brief description of the health problem(s)	9	Provide the basic epidemiological information about the problem (including	☐ Yes ☐ No		

		the associated burden), health systems relevant issues, and note any relevant differences compared to the source guideline(s).	☐ Unclear		
Aim(s) and specific objectives	10	Describe the aim(s) of the adapted guideline and specific objectives, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
Target population(s)	11	Describe the target population(s) and subgroup(s) (if applicable) to which the recommendation(s) is addressed in the adapted guideline, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
End-users and settings	12	Describe the intended target users of the adapted guideline, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
	13	Describe the setting(s) for which the adapted guideline is intended, and note any relevant differences compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
Rigor of development					
Guideline adaptation group	14	List all contributors to the guideline adaptation process and describe their selection process and responsibilities.	☐ Yes ☐ No ☐ Unclear		
Adaptation Framework/Methodology	15	Report which framework or methodology was used in the guideline adaptation process.	☐ Yes ☐ No ☐ Unclear		
Source guideline(s)	16	Describe how the specific source guideline(s) was(were) selected.	☐ Yes ☐ No ☐ Unclear		
Key questions	17	State the key questions of the adapted guideline using a structured format, such as PICO (population, intervention, comparator, and outcome), or another format as appropriate.	☐ Yes ☐ No ☐ Unclear		
	18	Describe how the key questions were developed/modified, and/or prioritised.	☐ Yes ☐ No ☐ Unclear		
Source recommendation(s)	19	Describe how the recommendation(s) from the source guideline(s) was(were) assessed with respect to the evidence	☐ Yes ☐ No ☐ Unclear		

		considered for the different criteria, the judgements and considerations made by the original panel.			
Evidence synthesis	20	Indicate whether the adapted recommendation(s) is/are based on existing evidence from the source guideline(s), and/or additional evidence.	☐ Yes ☐ No ☐ Unclear		
	21	If new research evidence was used, describe how it was identified and assessed.	☐ Yes ☐ No ☐ Unclear		
Assessment of the certainty of the body of evidence and strength of recommendation	22	Describe the approach used to assess the certainty/quality of the body/ies of evidence and the strength of recommendations in the adapted guideline and note any differences (if applicable) compared to the source guideline(s).	☐ Yes ☐ No ☐ Unclear		
Decision-making processes	23	Describe the processes used by the guideline adaptation group to make decisions, particularly the formulation of recommendations.	☐ Yes ☐ No ☐ Unclear		
Recommendations					
Recommendations	24	Report recommendations and indicate whether they were adapted, adopted, or *de novo.*	☐ Yes ☐ No ☐ Unclear		
	25	Indicate the direction and strength of the recommendations and the certainty/quality of the supporting evidence and note any differences compared to the source recommendations(s) (if applicable).	☐ Yes ☐ No ☐ Unclear		
	26	Present separate recommendations for important subgroups if the evidence suggests important differences in factors influencing recommendations and note any differences compared to the source recommendations(s) (If applicable).	☐ Yes ☐ No ☐ Unclear		
Rationale/explanation for recommendations	27	Describe the criteria/factors that were considered to formulate the recommendations or note any relevant differences compared to the source guideline(s) (if applicable).	☐ Yes ☐ No ☐ Unclear		
External review and quality assurance					
External review	28	Indicate whether the adapted guideline underwent an independent external review. If yes, describe the process.	☐ Yes ☐ No ☐ Unclear		

Organizational approval	29	Indicate whether the adapted guideline obtained organizational approval. If yes, describe the process.	☐ Yes ☐ No ☐ Unclear		
Funding, declaration and management of interest					
Funding source(s) and funder role(s)	30	Report all sources of funding for the adapted guideline and source guideline(s), and the role of the funders.	☐ Yes ☐ No ☐ Unclear		
Declaration and management of interests	31	Report all conflicts of interest of the adapted and the source guideline(s) panels, and how they were evaluated and managed.	☐ Yes ☐ No ☐ Unclear		
Other information					
Implementation	32	Describe the potential barriers and strategies for implementing the recommendations (if applicable).	☐ Yes ☐ No ☐ Unclear		
Update	33	Briefly describe the strategy for updating the adapted guideline (if applicable).	☐ Yes ☐ No ☐ Unclear		
Limitations and suggestions for further research	34	Describe the challenges of the adaptation process, the limitations of the evidence, and provide suggestions for future research.	☐ Yes ☐ No ☐ Unclear		

5. GLOSSARY AND ABBREVIATION

Key Definitions

Practice guideline

The WHO defines guidelines as "systematically developed evidence-based statements which assist providers, recipients and other stakeholders to make informed decisions about appropriate health interventions" (1).

Guideline adaptation (GA)

Adaption of guideline means the use of existing trustworthy guidelines, with (adapt), without (adopt) modifications, or including additional *de novo* recommendations, to provide local, regional or national guidance (15, 16, 23).

Adopted recommendations

Are recommendations with:

1) a same specific population, intervention, or comparator as the original recommendations,

2) a same the certainty of the evidence, and

3) information on implementation (16).

Adapted recommendations

Are recommendations with:

1) a change in the specific population, intervention, or comparator from the original recommendations,

2) a change in the certainty of the evidence, or

3) a change in the strength of recommendations by including additional information regarding the conditions, monitoring, implementation, and implications for research (16).

Abbreviations

ACP	American College of Physicians
AGREE	Appraisal Of Guidelines For Research & Evaluation II
AMSTAR	A measurement tool to assess the methodological quality of systematic reviews
ASCO	American Society of Clinical Oncology
ASH	American Society of Hematology
CCO	Cancer Care Ontario
CHEST	American College of Chest Physicians
COI	Conflicts of Interest
CPG	Clinical Practice Guideline
EtD	Evidence to Decision
GA	Guideline Adaptation
GIN	Guideline-International-Network
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
GRADE-ADOLOPMENT	GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations
LMIC	Low-middle income country
NHMRC	National Health and Medical Research Council
RCT	Randomised Controlled Trial
RIGHT	Reporting Tool for Practice Guidelines in Health Care

6. ITEMS, EXPLANATIONS, AND EXAMPLES

Basic Information

Title/Subtitle

1. Identify the report as an adaptation of practice guideline(s), that is include "guideline adaptation", "adapting", "adapted guideline/recommendation(s)", or similar terminology in the title/subtitle

What to do

Identify the report by using terms like "guideline adaptation", "adapting", "adapted guideline", or similar in the title/subtitle (i.e., adapted for...; adaptation of xx guideline), to help guideline users easily identify whether a guideline is total *de novo* or majorly/mostly an adapted guideline.

Why is this important?

Guideline adaptation could be a part of the *de novo* guideline development process, as well as guideline updating. However, unlike the *de novo* process, guideline adaptations are based on existing guidelines, using a specific methodology (e.g., ADAPTE or GRADE-ADOLOPMENT), and conducting adapted recommendations for local, regional, or national context (15). Reporting whether the guideline is an adaptation helps users distinguish the types of guidelines, and therefore understand its development process.

Example(s)

1. "Cancer pain management in adults: Evidence-based clinical practice guidelines **adapted for** use in Australia" (32)

2. "Interventions to Address Sexual Problems in People With Cancer: American Society of Clinical Oncology Clinical Practice Guideline **Adaptation of Cancer Care Ontario Guideline**" (33).

2. Describe the topic/focus/scope of the adapted guideline

What to do

Report the adapted guideline health topic/focus/scope in the title/subtitle. Health topic means the relevant health problem, condition, or disease. The focus/scope may be a combination of any or all of the following aspects: prevention, screening, and diagnosis, treatment, or management. Additionally, the perspective of population or individual patient might be taken into account along with the adaptation process and therefore should be reported.

Why is this important?

Guidelines may vary according to different scopes. Reporting the primary focus of adapted guidelines in the title is not only important for readers to quickly identify the relevance, but could also serve as a filter when searching for the relevant information.

Example(s)

1. "**Cancer pain management in adults:** Evidence-based clinical practice guidelines adapted for use in Australia". (32)

2. "**Interventions to Address Sexual Problems in People With Cancer**: American Society of Clinical Oncology Clinical Practice Guideline Adaptation of Cancer Care Ontario Guideline". (33)

Cover/first page

3. Report the the respective dates of publication and the literature search of the adapted guideline

What to do

Report the year of publication, as well as the last literature search date in the first page/cover page of the adapted guideline. Literature search could be specific for the source guideline(s) or the additional evidence.

If the adapted guideline is an updated version, specify what edition or version it is (e.g., 1st, 2nd, 3rd edition/version) to distinguish it from the original (34).

Why is this important?

The year of publication is an indicator as to whether the reader needs to look elsewhere for a valid and up-to-date guideline. As the speed of evidence updating increases (35, 36), readers need to quickly identify the year when the adapted guideline was published.

Example(s)

1. This is an adapted guideline **published in 2020; (last literature search until 2020 July)** (illustrative example).

4. Describe the developer and country/region of the adapted guideline

What to do

Describe the developer of the adapted guideline, as well as the country/region. Guidelines are developed by government bodies, professional societies, academic institutions, or healthcare systems (e.g., big hospital trusts), or other organizations.

Why is this important?

Since guideline adaptation is a modification of the source guideline for implementation in another setting (15), reporting the target country in the title/subtitle or cover page/first page would provide the users with an indication for selecting suitable adaptation products. It could also provide adaptation users with an overview of the quality of the adaptation process since guideline developers and methodologists are more likely to trust guidelines published by well-credentialed guideline development groups (22, 37).

Example(s)

1. "Interventions to Address Sexual Problems in People With Cancer: **American Society of Clinical Oncology Clinical Practice Guideline Adaptation** of Cancer Care Ontario Guideline" (33).

2. "**African Head and Neck Society** Clinical Practice guidelines for thyroid nodules and cancer **in developing countries and limited resource settings**" (31)

3. "Selection of Optimal Adjuvant Chemotherapy Regimens for Human Epidermal Growth Factor Receptor 2 (HER2) –Negative and Adjuvant Targeted Therapy for HER2-Positive Breast Cancers: **An American Society of Clinical Oncology Guideline Adaptation** of the Cancer Care Ontario Clinical Practice Guideline" (38).

Executive summary

5. Provide a summary of the recommendations contained in the adapted guideline.

What to do

Provide a summary of the recommendations contained in the adapted guideline before the main text. A table or bullet list format could help users have an overview of the recommendations and find out quickly if there are recommendations that meet their conditions. In the case there are

more than one recommendations under different recommendation sections, provide the list of the key recommendations.

In addition, a good summary should include key points for implementation regarding different specific audiences.

Why is this important?

A well-structured summary, including recommendations and modifications, will help readers locate the recommendations quickly and facilitate their implementation (28).

Example(s):

1. "Overview

   This guideline covers when to offer caesarean section, procedural aspects of the operation and care after caesarean section. It aims to improve the consistency and quality of care for women who are considering a caesarean section or have had a caesarean section in the past and are now pregnant again.

   Recommendations

   This guideline includes recommendations on (with a hyperlink to the recommendations):
   when to offer planned caesarean section
   when a caesarean section may be required during birth
   procedural aspects of caesarean section
   care of the baby and mother after caesarean section
   recovery after caesarean section
   subsequent pregnancy and childbirth after caesarean section

   Who is it for?

   Healthcare professionals
   Commissioners and providers
   Public health and trust managers
   Pregnant women, their families, birth supporters and other carers"(39)

2. "We applied a novel presentation format to 333 recommendations from 11 of the 15 Management chapters in AT9 and condensed and restructured them into 249 recommendations in a multi-layered format. We added additional relevant information, such as 29 best practice statements about new oral anticoagulants and practical information sections for 121 recommendations. Common reasons for modifications included feasibility of the recommendations in a national context, disagreement with applied baseline risk estimates, and re-evaluation of the balance between the benefits and harms of interventions in relation to assumed typical patient preferences and values. The adapted guideline was published and disseminated online in November 2013."(20)

3. "These Clinical Practice Guidelines and Principles of Care for people with dementia **are written primarily for health and aged care staff (doctors, nurses, allied health and care workers) who work with people with dementia in community, residential and hospital settings.** Health and aged care staff should apply the recommendations in their workplaces while also responding to the needs and preferences of the person with dementia and their carer(s) and family. **The following key points are addressed within the recommendations.** Examples from the whole list of key points:
   - The symptoms of dementia should be investigated the first time they are reported and not dismissed as a 'normal part of ageing'.
   - Health and aged care professionals should talk to the person with dementia and their carer(s) and family about the symptoms of dementia, treatments and services. Written information (such as brochures) should also be provided." (40)

Abbreviations and acronyms

6. Define key terms and provide a list of abbreviations and acronyms (if applicable)

What to do

Report the definition of the key terms as well as the explanations of the acronyms and abbreviations in the adapted guideline or its appendix. An additional link to the abbreviations might be helpful.

In the case that GA groups used a different evidence rating system, report the definition of the levels of evidence and grades. If a translation was conducted, report the definitions used in a particular country or institution.

Why is this important?

Since key terms, abbreviations and acronyms used in across the CPGs might be based on different meanings, it is essential to provide an accurate definition of them to ensure the understandability and implementability of the recommendations of the adapted guideline.

Example(s)

1. "**Keywords:** clinical practice guidelines; complicated intra-abdominal infection" (41).

2. "**ABBREVIATIONS:** AT9 = Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines; DECIDE = Developing and Evaluating Communication Strategies to Support Informed Decisions and Practice Based on Evidence; GRADE = Grading of Recommendations Assessment, Development, and Evaluation; LMWH = low-molecular-weight heparin" (20).

Contact information of the guideline adaptation group

7. Report the contact information of the developer of the adapted guideline

What to do

Report the contact information of those who have a central role in the adaptation project as well as the adaptation organization, for users to enquire or make suggestions. The information should include their affiliation, name, e-mail address, or credentials like the official website (if applicable).

Why is this important?

Reporting the contact information helps users of the adapted guideline communicate their questions, suggestions, or comments to the GA groups. The contact information is particularly useful when reading or implementing adapted guidelines, or for regular monitoring and updating.

Example(s)

1. **Correspond to:** Pablo Alonso-Coello, PhD, MD, Iberoamerican Cochrane Center - Biomedical Research Institute Sant Pau (IIB Sant Pau), Barcelona, Spain; Email: PAlonso@santpau.cat.

Scope

Source guideline (s)

8. Report the name and year of publication of the source guideline(s), provide the citation(s), and whether source authors were contacted.

What to do

Report the name, month (if applicable) and year of the source guideline(s) and provide their citation reference(s). Indicate whether source authors were contacted for permission (if required) or for additional information. If there is no need to contact source authors since the reporting of source guideline(s) are complete, provide one sentence to clarify this.

If only evidence from the source guideline was used — for example, only systematic reviews from source guideline(s) were considered —, then the name and year of those systematic reviews should be reported, and citation(s) provided.

Why is this important?

Reporting source guideline(s) ensures transparency and reproducibility of the adaptation process. It also provides the information for stakeholders to access source guideline(s) and check whether these are up to date.

Example(s)

1. "The STG on Diabetic foot management was developed by a team of experts and relevant stakeholders. The recommendations in the STG were adopted/ adapted from **four source guidelines which are International Working Group on the Diabetic Foot (IWGDF) 2015 - Prevention and Management of Foot, 2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections (IDSA 2012), and the National Institute for Health and Care Excellence (NICE) guidelines- Diabetic foot problems: prevention and management (NG19) (26th August, 2015) on diabetic foot, and Problems in Diabetes Guidance Documents and Recommendations NICE guideline- Lower limb peripheral arterial disease: diagnosis and management (NICE clinical guideline 147) on PAD (Peripheral Arterial Disease) November 2014.** Available from and full reference below: http://www.iwgdf.org/files/2015/; http://www.idsociety.org; https://www.nice.org.uk/guidance/NG19; https://www.nice.org.uk/guidance/cg147." (42)

2. "The Cognitive Decline Partnership Centre's Clinical practice guidelines and principles of care for people with dementia (Guidelines) was approved by the National Health and Medical Research Council (NHMRC) in February 2016. The Guidelines were developed by **adapting the UK's guidelines for dementia*** by a committee of experts in dementia, including carers of people with dementia and a GP. The Guidelines were released for public consultation and were reviewed by many medical colleges, including The Royal Australian College of General Practitioners (RACGP).
*National Institute for Health and Care Excellence. Dementia: Supporting people with dementia and their carers in health and social care. London: NICE, 2006." (40)

3. "The following guidelines met all criteria and were considered for adaptation:
   - **Scottish Intercollegiate Guidelines Network. Control of pain in adults with cancer. A national clinical guideline [Version amended 18 July 2011] Edinburgh: SIGN; 2008.**
   - **National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology. Adult cancer pain. Version 1.2012: NCCN; 2012.**" (32)

Brief description of the health problem(s)

9. Provide the basic epidemiological information about the problem (including the associated burden), health systems relevant issues, and note any relevant differences compared to the source guideline(s)

What to do

Report basic epidemiological parameters such as prevalence or incidence, morbidity, mortality and describe the problem arising. Sources (e.g., WHO statistics, etc.) of this information should be reported if applicable.

Highlight any differences in the epidemiological information of the issue specific to the setting, compared to that of the source guideline(s), such as funding and system constraints linked to applicability and feasibility of source guidelines to the local setting.

Several frameworks or websites for health policies/systems/services—such as the EPOC taxonomy (43), the Health systems Evidence database, or Global Burden of Disease—, might be helpful to guide the identification of the current key elements that would need to be reported.

Why is this important?

The epidemiological information provides stakeholders with the essential background of the guideline, justifies and highlights the needs for guideline adaptation, therefore contextualises better the health issue addressed in the adapted guideline.

Example(s)

1. "In 2018, there were an estimated 18.1 million new cases of cancer and 9.6 million cancer deaths worldwide.1 Of these, breast cancer accounted for >2.1 million new cases (11.6% of all cancers) and >626 000 deaths (6.6% of all cancer deaths) and was the leading cause of cancer death in women. The most important risk factors for breast cancer include sex, age, genetic predisposition (around 10% of cases), exposure to estrogens, low parity, a Western style diet, obesity and alcohol consumption. **In contrast to a relatively small increase in the incidence of breast cancer in Western countries, in Asia the incidence is increasing rapidly with an estimated >900 000 new cases reported for the whole of Asia for 2018 (43.6% of new breast cancer cases worldwide) and >300 000 breast cancer deaths (49.6% of breast cancer deaths worldwide)." (44)**

2. "Psoriatic arthritis (PsA) is a spondyloarthritis that affects up to a third of patients with psoriasis, a common in- flammatory skin disease affecting 1–3% of the population. The heterogeneous disease manifestations make management of PsA a challenge. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and the European League Against Rheumatism (EULAR) have updated their respective recommendations for the management of PsA. These recommendations are based on systematic reviews of literature and provide evidence-based recommenda- tions for the management of PsA. **However, they are primarily based on studies**

conducted in resource replete countries of Europe and North America; therefore, they may not be applicable to PsA patients in resource-poor countries in the Americas excluding Canada and the USA- (henceforth termed 'the Americas') and Africa."(45)

3. "The South African (SA) burden of disease has changed significantly over the last ten years. There is an increasing focus on the need for rehabilitation for chronic conditions and disability, as more lives are saved from communicable diseases. The shift in SA from communicable disease mortality to communicable and non-communicable disease morbidity, has put the spotlight firmly on the need for evidence-informed rehabilitation, to ensure that resources are wisely allocated to achieve best health and cost outcomes for people living with chronic disability and health problems.

   Stroke is a leading cause of disability worldwide. Over the past 40 years, the rate of stroke in places such as Southern India and rural SA has approximately doubled, whereas rates in more economically developed nations have decreased. The most striking problem is that disability and mortality rates arising from stroke are at least tenfold greater in medically underserved regions versus high-income countries (HICs). The causes of these disparities are explained by lack of access to early stroke screening, basic medical management, post-stroke rehabilitation, and secondary stroke prevention. The WHO initiated public health programmes to address stroke management in underserved regions." (46)

4. "Methods to detect recurrence—such as testing for serum cancer antigen 125 (CA125), which has been found to predict recurrence several months before physical symptoms are identified; examinations; and imaging tests—can vary from one centre to another, and there is currently no guidance within Ontario about appropriate tests, intervals, or models of follow-up care. To fill that gap in the disease management pathway for patients in Ontario, we created this evidence-based guideline." (47)

Aim(s) and specific objectives

10. Describe the aim(s) of the adapted guideline and specific objectives, and note any relevant differences compared to the source guideline(s)

What to do

Describe the general purpose of the adapted guideline, for example, 1) to implement trustworthy guidelines in the local setting (21, 41); 2) to develop a guideline *de novo* based on other source guideline(s) (48, 49); 3) to reconcile controversies of existing guidelines (50) or 4) to update their own recommendations (51), etc.; as well as specific objectives.

Objectives are more specific and might reflect the PICO elements of the key questions (28), such as improvements in health indicators (e.g., mortality and disease prevalence), quality of life, health systems performance, or treatment cost-effectiveness. To ensure transparency, differences in objectives compared to the source guideline(s) should also be reported.

Why is this important?

Since guideline adaptation is an alternative to developing *de novo* guidelines or for improving guideline implementation (14), reporting the aim and specific objective of the adapted guideline will help users have an overview of its trustworthiness as well as its key points of implementation.

Example(s)

1. "The aim of this study was to adapt the international clinical practice guidelines recommendations for people living with dementia (PLWD) to fit the general hospital setting in the Austrian context. Furthermore, a goal of the adaption was to identify recommendations which are applicable in the healthcare setting and, specifically, to the work performed by nurses." (52)

2. "Recommended strategies vary for breast cancer screening in average-risk women. Ages to start and discontinue mammography, screening intervals, the role of imaging methods other than mammography, and the role of clinical breast examination (CBE) have been points of disagreement among guideline developers.

   The goal of this American College of Physicians (ACP) guidance statement is to critically review selected guidelines from around the world and their included evidence to assist clinicians in making decisions about breast cancer screening in asymptomatic women with average risk for breast cancer. Included screening methods are CBE and breast imaging (that is, mammography, ultrasonography, magnetic resonance imaging (MRI), and digital breast tomosynthesis. This guidance statement does not address breast self-examination because no evaluated guideline recommends it for screening." (53)

3. "SCOPE AND OBJECTIVE OF THE GUIDELINE.

   a) To increase detection of hypertension in adults in India using a systematic, primary care led approach based on standardised measurements of BP and their follow up.

   b) To provide guidance on assessment of persons with hypertension appropriate to different levels of care in India.

   c) To provide a structured, simplified and standardised treatment guideline for hypertension in adults in India, along with implementation tools (quick reference guide, quality standards, patient information leaflets)

   d) To provide guidance on availability of a core list of medications in the public health system for treatment of hypertension.

   e) To outline research issues related to hypertension in India." (54)

Target population(s)

11. Describe the target population(s) and subgroup(s) (if applicable) to which the recommendation (s) is addressed in the adapted guideline and note any relevant differences compared to the source guideline(s)

What to do:

Describe the target population to which the recommendation(s) is addressed in the adapted guideline, and whether it matches that in the source guideline(s) (55). The description should include age, gender(s), diagnosis and comorbidities, and geographical location and/or ethnic group, if applicable.

If there are any discrepancies regarding the target population, report the differences compared to the source guideline(s), the rationale for using a guideline whose population of interest is different, and how those differences were addressed.

If there are specific subgroup populations to be considered for the target setting, report the target subgroup population in this section.

Why is this important?

The target population and the differences with the source guideline(s) provide stakeholders with information to understand potential modifications of the source recommendations and distinguish to what extend the adapted guideline is trustworthy and applicable. In addition, it provides considerations for implementing the guideline adaptation product.

Example(s)

1. "**Target Population:** Female patients who are being considered for, or who are receiving, systemic therapy after definitive surgery for early invasive breast cancer, defined largely as invasive cancer stages I to IIA (T1N0-1, T2N0)." (38)

2. "**The target population** for this guidance statement **is women with average risk for breast cancer**. The target audience is all clinicians. Age is the single most important risk factor for breast cancer. **Included guidelines generally define average-risk women as** those who do not have a personal history of breast cancer or a previous diagnosis of a high-risk breast lesion, are not at high risk for breast cancer due to genetic mutations known to increase that risk (such as BRCA1/2 gene mutation or another familial breast cancer syndrome), and were not exposed to radiation therapy to the chest in childhood. However**, definitions of average risk vary among guidelines**. In addition, although risk factors (including early menarche, ...etc.) may put a woman at greater risk for breast cancer than women without these factors, **the evaluated guidelines generally include women with these factors**

under the umbrella of average risk. Therefore, our guidance statement applies to these women. Guidelines vary somewhat in target populations and screening methods addressed. Both the U.S. Preventive Services Task Force and the World Health Organization (WHO) include women with dense breasts and those with a single family member with breast cancer in their guideline's target population. The Canadian Task Force on Preventive Health Care guideline also includes women with dense breasts; however, it explicitly mentions that women with a first-degree relative with breast cancer are considered to be at increased risk and are thus excluded from the guideline."(53)

End-users and settings

12. Describe the intended target users of the adapted guideline, and note any relevant differences compared to the source guideline (s)

What to do

Report who the target users of the adapted guideline are, for example, primary care providers, clinical specialists (including sub-speciality), patients/carers, public health practitioners, programme managers, or policymakers.

If the target users of the adapted guideline differ from those in the source guideline(s), indicate similarities and/or differences between them in the background section and provide rationale.

Why is this important?

How the adapted guideline is reported will influence its value and usefulness (56). Previous surveys found that the applicability of published adapted guidelines is often weak (25). Specifying the target users of the adapted guideline in the background and justifying the discrepancy compared to the source guideline(s) will facilitate its implementation.

Example(s)

1. "**Target Audience Health care practitioners**, such as oncologists, urologists, gynaecologists, primary care providers, surgeons, nurses, physiotherapists, social workers, counselors, psychologists, psychiatrists, and sex therapists/counsellors, and advanced practice providers, such as physician assistants and nurse practitioners." (33)

2. "**These Clinical Practice Guidelines and Principles** of Care for people with dementia **are written primarily for health and aged care staff** (doctors, nurses, allied health and care workers) who work with people with dementia in community, residential and hospital settings." (40)

3. "**This guideline is intended to be relevant to hospital staff** caring for patients with diabetic foot problems in referral centres, non-specialized carers who provide secondary and primary care, prevention podiatrists and patient and their care givers." (42)

4. "**This guideline is intended for use by Canadian health care providers** in diverse clinical or treatment settings. **This guideline is also intended for researchers and decision makers** with an interest in understanding the key elements to a comprehensive smoking cessation system in Canada." (57)

13. Describe the setting(s) for which the adapted guideline is intended, and note any relevant differences compared to the source guideline(s)

What to do

Report the setting(s) for which the adapted guideline is intended. For example: community, primary, secondary, tertiary, or several of these healthcare levels, or out-patient, in-patient facilities.

If there are any differences in the setting between the source and the adapted guidelines, report the differences and explain the rationale of using them with their potential impact on evidence synthesis that will be used from the source guideline(s).

Why is this important?

Guideline adaptation aims to provide local, regional, or national guidance based on existing trustworthy guidelines, with (adapt) or without (adopt) modifications; applicable to a specific context. For example, the point estimate and confidence intervals of the data in the source guideline may not be the same, so the GA group might need to modify the recommendations to avoid over or underestimating. Therefore, it is important to report differences between the source and the adaptation regarding the target setting to provide a contextual background to the decisions and adapted /adopted recommendations.

Example(s)

1. "**Rehabilitation is currently not included in any national South Africa CPG**. This lack of local guidance perhaps underpins evidence that stroke care varies across the country, and that many stroke sufferers do not have access to rehabilitation. These shortcomings are in accordance with the WHO report, which estimated that in LMICs, only 26% to 55 % of people receive the rehabilitation they need. This World Health Survey revealed that people with disabilities were more than twice as likely to the SA healthcare system for the growing number of people in need of post-stroke rehabilitation." (46)

Rigor of development

Guideline adaptation groups

14. List all contributors to the guideline adaptation process, and describe their selection process and responsibilities

What to do

Report the names of all contributors to the guideline adaptation process and their role; for example: members of the steering group, guideline adaptation panel, external reviewer, systematic review team, methodologist, and guideline users. Their selection process, including whether there is a training process or not, should also be provided to ensure the credibility of guideline adaptation process.

Additionally, all members of the working group should declare any financial and intellectual conflict of interest in the following section (see item 31).

Ideally, GA groups should include key stakeholders affected by the guideline (e.g., clinicians, patients, caregivers, or the public, and policy makers) (55). A summary of the contributors could be included as an appendix or cited from guideline manual of the GA group/organization, if applicable.

Why is this important?

Numerous stakeholders are currently involved in the development and use of guidelines (4). They can contribute to and provide comments on the clinical guideline at various stages of the guideline development. Hence reporting this aspect is essential for transparency.

Example(s)

1. "**Forming a treatment guideline committee:** The development committee consisted of a chairman (Dr. Wie, the Catholic University College of Medicine) and five committee members recommended by the Korean Society for Chemotherapy and the Korean Society of Infectious Diseases, one committee member recommended by the Korean Association of Urogenital Tract Infection and Inflammation, two committee members recommended by the Korean Urological Association, and two committee members recommended by the Korean Society of Nephrology." (58)

2. "The Guideline Development Group (GDG) was formed in 2009 by the CAN-ADAPTT Coordinating Team and the GDG Chair, Dr. Selby. There are seven members of the GDG ranging from family physician to public health researcher to physician specialists (see page ii for a list of GDG members).

Each GDG member was a Section Lead for one of the sections listed on page 3. GDG Members were identified by the Chair to include experts in each topic area while ensuring a multi-disciplinary and nationally representative committee.

1) GUIDELINE DEVELOPMENT GROUP COMMITTEE:

The Guideline Development Group (GDG) was directly responsible for the review of existing guidelines and evidence and the development of summary statements for the CAN-ADAPTT Clinical Practice Guideline.

Dr. xx, MBBS, CCFP, FCFP, MHSc, Dip ABAM
Principal Investigator, CAN-ADAPTT
Chair, CAN-ADAPTT Guideline Development Group
Section Co-Lead: Mental Health and/or Other Addiction(s)
Clinical Director, Addictions Program
Head, Nicotine Dependence Clinic, Centre for Addiction and Mental Health
Associate Professor, Departments of Family and Community Medicine, Psychiatry and Dalla Lana School of Public Health University of Toronto, Toronto, Ontario
Etc.

2) CAN-ADAPTT COORDINATING TEAM

Dr. xxx, BSc
Former Network Manager, CAN-ADAPTT
Centre for Addiction and Mental Health, Toronto, Ontario…" (57)

3. "We asked relevant medical specialty societies to nominate candidate panellists. **We recruited 42 content experts, 11 of whom were designated as chapter editors and took primary responsibility for completing the adapted chapters.** Each panellist reported time spent on the adaptation work." (20)

Adaptation framework/methodology

15. Report which framework or methodology was used considered in the guideline adaptation process

What to do

Provide the adaptation framework(s)/method(s) followed, briefly describe the approach and provide key citations (if applicable). Ideally, GA groups could use one of the published adaptation processes (e.g., ADAPTE process (55), CAN-IMPLEMENT (59)), GRADE-ADOLOPMENT (16), SNAP-IT (20)), adapt/deviate from these methods with justification (e.g.,
Adapted ADAPTE (60), RAPADAPTE (61)), or use self-established adaptation methodologies (e.g., American Society of Clinical Oncology (ASCO) endorsement/adaptation methodology) (49).

In the case that an informal adaptation process (e.g., simple adoption without a properly reported methodology) was used, this should be stated. If applicable, report any software used in the adaptation process (e.g., GRADEProGDT, MAGIC etc.).

Why is this important?

This will provide users with initial information on the methodological foundation of the adapted guideline, as well as ensure transparency and trustworthiness of the adaptation process.

Example(s)

1. "This guideline adaptation **was informed by the ADAPTE methodology**, which was used as an alternative to de novo guideline development for this guideline." (38, 62).
2. "Adaptation of the 2015 American College of Rheumatology treatment guideline for rheumatoid arthritis for the Eastern Mediterranean Region: an exemplar of the **GRADE Adolopment**" (17)
3. "Adapting AT9 to a Norwegian setting represented an opportunity to apply and evaluate the feasibility of our proposed **adaptation process (MAGIC)**." (20)
4. "After reviewing the existing guidelines in other countries, the Korean CPG on invasive diagnostic testing (https://www.guideline.or.kr/evaluation/sub2.php) was developed using the adaptation process." (63)

Source guideline(s)

16. Describe how the source guideline(s) was(were) selected

What to do

Report the selection process of the source guideline(s) by providing the eligibility criteria (like good quality, trustworthiness, most up-to-date, and context applicability with respect to population, interventions, etc.), search strategy, database(s) used, and screening methods. If specific source guideline(s) were selected without searching, provide the reason for the usage of those specific source guideline(s).

If multiple source guidelines are included, report the reason(s). The prioritisation process might be based on the criteria for selecting guidelines or other approaches (64, 65).

Several tools and websites are available for the GA groups, such as the AGREE II (66) to assess the quality, the NEATS instrument to assess trustworthiness (67), or ECRI guideline trust website that provides guideline quality assessment. For updated guidelines, CheckUp can be used to assess the reporting of updated guidelines (34). Some organizations might use their own criteria too (55, 68).

Why is this important?

Since the quality and trustworthiness of the adapted guideline depends on the source guideline(s), reporting this process is essential.

Example(s)

1. "Systematic search and critical appraisal of guidelines

   To assess and utilize existing guidelines during the development of the present guideline, well-established guideline registers and the websites of large periodontal societies were electronically searched for potentially applicable guideline texts:

   • Guideline International Network (GIN)
   • Guidelinecentral.com
   • The National Institute for Health and Clinical Excellence (NICE)
   • Canadian Health Technology Assessment (CADTH)
   • European Federation for Periodontology (EFP)
   • American Academy of Periodontology (AAP)
   • American Dental Association (ADA)

   to be potentially relevant, scored highest in the critical appraisal using AGREE II and was, therefore, used to inform the guideline development process.

   Table: Results of the guideline search (examples)

Database	Identified	potentially relevant guidelines
GIN International Guidelines Library	Comprehensive periodontal therapy: a statement by the American Academy of Periodontology [citation]	8 years old, recommendations not based on systematic evaluation of evidence, **not applicable**
	DG PARO S3 guideline (Register Number 083-029) - Adjuvant systemic administration of antibiotics for subgingival instrumentation in the context of systematic periodontitis treatment [citation]	Very recent, high methodological standard, very similar outcome measures, – **relevant**

   GIN: Guideline International Network"(69)

2. "**Existing guidelines were identified via the reference lists of previous reviews and searches of online databases and clearing houses and were screened according to eight criteria:**

   - Primary focus on adults with chronic cancer pain
   - Relevance across tumour types and stages inclusion of recommendations for assessment and/or management
   - Of pain by means of either pharmacological or non-pharmacological intervention
   - Capacity to inform pain assessment and management across disciplines and settings
   - Published in the previous 3 years (i.e. 2008 or later)

- National or international (i.e., not centre-specific)
- Available in English
- Independently rated as 'recommended' or 'strongly recommended' by two members of the Working Party based on criteria of the Appraisal of Guidelines Research & Evaluation (AGREE) Instrument" (32)

3. "We selected AT9 because it is an authoritative international CPG that, at the time we began, was current (published in February 2012). Furthermore, AT9 is the largest CPG to rigorously apply the GRADE methodology, providing authoritative assessments of confidence in evidence and explicit rationales for the strength of its recommendations. Finally, AT9 informs practice in a wide variety of clinical contexts (e.g., hematology, surgery, cardiology, obstetrics)." (20)

4. "Prior to being engaged in the CAN-ADAPTT Project, the Guidelines Advisory Committee had conducted, in November 2006, a full review of CPGs in the area of smoking cessation published in the English language. In December 2008, a new systematic search was conducted for the CAN-ADAPTT Project, to identify CPGs published since the previous review. This search used the same terms as November 2006, such as smoking, tobacco, or nicotine. The search was conducted in Ovid MEDLINE, Ovid Embase, guideline repositories such as National Guideline Clearinghouse, renowned developers with a history of developing high quality guidelines, as well as websites of national and international specialty societies.

   The 14 guidelines identified in both reviews were evaluated by four independent reviewers using the AGREE Instrument. In addition to the AGREE Instrument, 8 additional questions were included as part of the appraisal. CAN-ADAPTT considered only those guidelines that scored highly in multiple AGREE domains, particularly in the areas of Rigor of Development and Editorial Independence, as well as guidelines that were 'strongly recommended' by reviewers as being applicable to the Canadian context.

   Six guidelines met our criteria and were selected for use in developing the dynamic CAN-ADAPTT CPG [Appendix E]. This process has been developed and was recommended by the Guidelines Advisory Committee (GAC)." (57)

Key questions

17. State the key questions of the adapted guideline using a structured format, such as PICO (population, intervention, comparator, and outcome), or another format as appropriate

What to do

For each key question, justify any changes in the PICO element compared to the source guideline(s). PICO (population, intervention, comparison, and outcomes) is the recommended and standardised framework that should be followed when reporting evidence search in guideline development (70-72).

Depending on the scope of the adapted guideline, other formats may be used as appropriate, such as the PICOTS (population, intervention, comparison, outcomes, timeframe of the outcome of interest, and healthcare setting), the PIPOH (Population, Intervention/diagnostic, Professionals, Outcomes, Healthcare settings) for guideline adaptation (55), or the PIRD (Population, Index Test, Reference Test, Diagnosis of Interest) for diagnostic questions (73).

Why is this important?

A set of clear and focused key questions are important considerations for GA groups to complete the adaptation process while identifying which questions are not applicable to the target context (55).

Example(s)

1. **PICO 1:** Which anti-viral therapy is the preferred treatment option for persons with chronic Hepatitis C infection?
    - **Population:** Adults and Children with chronic HCV infection
    - **Intervention:** combination of direct-acting anti-viral therapy with or without ribavirin therapy
    - **Comparison:** pegylated interferon and ribavirin therapy with or without DAA or other DAA
    - **Outcomes:** Rate of SVR, decompensated liver disease, hepatocellular carcinoma, all-cause mortality, and treatment-related adverse events leading to discontinuation of therapy, Quality of life, resource use, cost-effectiveness. (74)

18. Describe how the key questions were developed/modified and/or prioritised

What to do

Briefly describe the process used to develop and/or identify the key questions. Some GA groups develop their key questions upfront, and some others use the source guideline(s) to identify, prioritise, and develop/adapt them. An online survey might be useful to facilitate the prioritisation process for considering whether the key questions are relevant or not (16).

The source guideline(s) might not include a question of interest to the group conducting the adaptation. In that case, *de novo* questions need to be created (16, 48, 51). GA groups should

report the key questions in an inclusive way and highlight which questions in the adapted guideline were developed *de novo,* and provide the rationale. A summary of this process could be included as an appendix.

Why is this important?

Reporting the process for identifying key questions could highlight the different importance and relevance of each question for the target context, ensure the transparency of the rigorous development of adaptation, and allow adaptation users to differentiate the reason behind each question.

Example(s)

1. "This guideline was designed to answer a series of practical questions (Chapter 11) about how to treat people with borderline personality disorder (BPD), how to support families and carers of people with BPD, and how the configuration of health services can best meet the needs of people with BPD. Special needs of Aboriginal and Torres Strait Islander people with BPD were also considered.

   Clinical questions appropriate for literature searching, including twenty-one clinical questions adapted from the source guideline (UK national BPD clinical practice guideline) and five new clinical questions, were formulated using the PICO structure (population, intervention/indicator, control/comparator, outcome), with the assistance of the methodologist.

   Chapter 11: clinical questions (Examples):

   The clinical questions on which the recommendations are based are listed below.

   Italics indicates a new question formulated by the Committee. All other clinical questions were

   previously addressed in the UK national BPD clinical practice guideline.

   Additional literature searches were conducted to identify studies involving Aboriginal and Torres Strait Islander people with BPD, and for evidence on cost-effectiveness of BPD management strategies.

   11.1 Identifying and assessing BPD

   1. What can help clinicians identify features of BPD in young people?

   2. Are there tools/assessments that could be used?

   11.2 Managing risk factors and preventing BPD

   3. What are the risk factors for BPD? (New clinical questions)

   4. What preventative interventions are available to reduce the incidence of BPD?

   (as a primary or secondary outcome) (New clinical questions), etc." (76)]

2. "The broad Cancer Care Ontario (CCO) guideline addressed the overarching question, What is the optimal adjuvant systemic therapy for female patients with early operable breast cancer when patient and disease factors are considered? The specific subset of recommendations from that guideline being considered in this ASCO adaptation addressed the optimal use of cytotoxic chemotherapy and HER2-directed therapy. **CCO recommendations relating to the role of the patient and disease factors in selecting adjuvant therapy for women with early breast cancer and relating to the use of adjuvant endocrine therapy are the subject of a separate ASCO guideline endorsement and guideline, respectively**." (38)

3. "**For each selected guideline, we used a formal process to prioritize approximately 3 - 10 key clinical questions for inclusion during wave 1 and 10 - 5 questions during wave 2, based on the questions addressed in existing evidence syntheses.** Guideline panel members completed online surveys to rate the relative importance of clinical questions for the Saudi Arabia health care setting. We used a 9-point Likert scale (1-least important; 9-most important). Panellists were asked to consider the patient's perspective, the availability of the interventions, and legal issues (e.g., intervention not available in KSA), but not to exclude questions for resource considerations (e.g., potential financial barriers for implementation of the proposed interventions). Mean and median importance ratings of questions guided inclusion in the guideline. To ensure that guidelines comprehensively addressed the topic with a complete set of recommendations, questions deemed complementary to those rated as important (e.g., questions that together addressed a complete diagnostic strategy) were also included. The selected questions were sent to panelists for approval, with opportunity for further input before finalization." (16)

Source recommendations(s)

19. Describe how recommendation(s) from the source guideline(s) was(were) assessed with respect to the evidence considered for the different criteria, the judgements and considerations made by the original panel

What to do

Describe the process followed to assess the source recommendation(s), and report the review of the different criteria (e.g., effects, resources, values, and preferences), including the supportive evidence and the judgments made by the original panel. If there are other relevant considerations, such as implementation or monitoring, these should also be similarly assessed and reported. A summary of the process could be included as an appendix.

If several recommendations for the same question are available from the selected source guidelines, some GA groups may find it useful to map recommendations using a table (55).

For groups of source guideline(s) using GRADE, the use of Evidence to Decision frameworks can help structure the process (16) (77).

More recent tools have been developed that are available to assess, and might be used; such as, the TRANSFER approach to assessing the transferability of systematic reviews (78), or the AGREE-REX tool to assess the clinical credibility and implementability of recommendations (79).

Why is this important?

For guideline adaptation, only relying on the source guideline(s) is not sufficient. GA groups need to assess each recommendation in order to decide whether they should be adapted or adopted.

Example(s)

1. "The content review is completed by an ad hoc panel convened by ASCO that includes representatives of several disciplines. …

   On the basis of a preliminary content review of the draft CCO guideline by two members of ASCO's Breast Cancer Advisory Group, the CCO recommendations on the selection of optimal adjuvant chemotherapy regimens and the selection of adjuvant targeted therapy for HER2-positive cancers were selected as a possible adaptation opportunity. The Advisory Group subsequently ranked the adaptation of the CCO recommendations on chemotherapy and targeted therapy as one of its top three priorities for breast cancer guideline development.

   On the basis of the content review of the CCO guideline, the ASCO Panel agreed that, in general, the recommendations were clear and thorough and were based on the most relevant scientific evidence, and they presented options that will be acceptable to patients. However, for some topics addressed in the CCO guideline, the ASCO Panel formulated a set of adapted recommendations on the basis of local context and practice beliefs of the Panel members: "Selection of Optimal Adjuvant Chemotherapy Regimens for Human Epidermal Growth Factor Receptor 2 (HER2) –Negative and Adjuvant Targeted Therapy for HER2-Positive Breast Cancers: An American Society of Clinical Oncology Guideline Adaptation of the Cancer Care Ontario Clinical Practice Guideline" (38)

2. "In addition to our review of each guideline, we examined the evidence supporting the 4 that scored highest (ACS, CTFPHC, USPSTF, and WHO). We also considered recommendations for adoption or adaptation from these 4 guidelines when developing our own guidance.

   Several factors were important in considering guideline quality. The ACS, CTFPHC, USPSTF, and WHO guidelines best articulated benefits, harms, and strength of the evidence and how these link to recommendations. The lower-scoring guidelines often inadequately described how they considered these factors in developing the recommendations, or they relied on lower-quality evidence. The guidelines varied in the studies they reported, weighting of observational or modelling studies

relative to randomized controlled trials (RCTs), and emphasis on relative versus absolute effects. The guidelines rarely addressed the small absolute effect on breast cancer mortality; the long lead time to any reduction in this mortality, especially in women with estimated life expectancy less than 15 to 20 years; and the low incidence of breast cancer for women younger than 60 years." (53)

Evidence synthesis

20. Indicate whether the adapted recommendation(s) is/are based on existing evidence from the source guideline(s), and/or additional evidence

What to do

Explicitly indicate whether the research evidence comes from the source guideline(s) or not, and provide the citation(s)it. GA groups could review and adapt recommendations based on the research evidence considered in the source guideline(s) (e.g., systematic reviews, cost-effective studies), or on other existing research evidence (e.g., local data, or primary studies for target context).

Why is this important?

Reporting this information provides users with all the evidence used in the adaptation process and helps the GA panels justify any modifications/differences in the adapted recommendations.

Example(s)

1. "The located meta-analyses, systematic reviews, and randomized controlled trials **were used as a supplementary evidence** base for the recommendations and are cited where appropriate in the text." (62)

2. "For each topic, **the Committee considered evidence identified in the systematic literature review undertaken for this guideline,** as well as earlier evidence presented in the UK national borderline personality disorder (BPD) clinical practice guideline." (76)
3. "**In addition, we searched the literature for studies and data relevant to patients' values and preferences and economic data** ... **we solicited panellists for additional studies on baseline risks and economic data**." (17)

4. "**A search for new evidence was conducted by ASCO guidelines staff to identify relevant randomized controlled trials, systematic reviews, and meta-analyses published since the CCO guideline was completed.**" (38)

21. If new research evidence was used, describe how it was identified and assessed.

What to do

Report the process of identifying new research evidence in addition to the source evidence, by providing the search strategies, the eligibility criteria, and describing how the risk of bias/methodological limitations were assessed (e.g., AMSTAR II for systematic reviews (80), Cochrane risk of bias for RCT (81), Newcastle-Ottawa Scale (NOS) or ROBINS-I tool for non-randomised studies (82, 83).

If the GA group updated the search of the source evidence, indicate any changes that were made (e.g., changes in eligibility criteria, additional outcomes, etc.).

Additional evidence could be synthesised with the evidence used in the source guideline(s) or reported separately in a subsection along with each recommendation. A summary of the identification process could be included as an appendix.

Why is this important?

Reporting the process of identifying other research evidence will increase the trustworthiness of the adapted guideline and ensure its reproducibility.

Example(s)

1. "The updated search was guided by the "signals" approach that is designed to identify only new, potentially practice-changing data—signals—that might translate into revised practice recommendations. The approach relies on targeted routine literature searching and the expertise of ASCO Expert Panel members to help identify potential signals. **The Methodology Supplement (available at www.asco.org/survivorshipguidelines) provides additional information about the signals approach.** The updated search yielded 159 records. A review of these results plus studies identified by searching reference lists and known seminal papers resulted in 19 new, recommendation changing studies being included. **Table 2** summarizes the number and types of studies included per sexual dysfunction condition." (33)

Table 2. Symptoms and Interventions for Sexual Dysfunction (adapted from CCO guideline) (Example)

Symptom	Possible Intervention	Evidence
For women with cancer		
Difficulty with sexual response, such as desire, arousal, or orgasm	Psychosocial counselling, psychosexual counselling Regular stimulation (including	Two systematic reviews[14,15] Two RCTs [56,57] Three other [58-60]

	masturbation) Flibanerin for premenopausal women	

2. "**Figure 1 depicts the process of searching and using the identified evidence for the recommendation questions selected by the panel**. We ran two searches for systematic reviews and primary studies respectively. **We searched Medline, Embase, Cochrane and Epistemonikos electronic databases from the last search date of the source guideline in September 2014, till February 2016. We used the same search terms as the source guideline search; we only added study design filters for primary studies and systematic reviews respectively. The search terms included both medical subject headings (MeSH) and text words.**

We used standards systematic review methodology including duplicate and independent approach to title and abstract screening, full-text screening, and data abstraction. We conducted calibration exercises, used standardized and pilot tested forms, and relied on a third reviewer to resolve disagreements.

When evaluating the potential use of identified systematic review, we considered the following three characteristics as important:

- Relevance (directness): we assessed the relevance of identified systematic reviews by matching their PICO to the PICO of the guideline questions. The minimum requirement was for the Population, Intervention and Control elements to match to a reasonable degree, i.e., not to have serious indirectness for more than one of the three elements.
- Quality (risk of bias): we assessed the risk of bias of relevant systematic reviews using AMSTAR (80). If we identified more than one relevant systematic review we prioritized the one with the highest quality.
- Being Up to date: we assessed whether the systematic review judged to be relevant and of highest quality was up to date. In case we had identified more than one systematic review, the judgment of relative up-to-dateness would have considered whether the systematic reviews included all relevant studies. When we identified new primary studies, we integrated the findings in the chosen systematic review.

When we identified no usable systematic review (based on the three above criteria), we updated the systematic review conducted by the source guideline-working group using the results of the search for primary studies." (17)

3. **"Search for Systematic Reviews and Primary Studies: A search of MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews for systematic reviews or primary literature that had been published between January 2010 and March 2015** used search terms related to ovarian cancer and to asymptomatic detection of recurrence and follow-up adopted from Cancer Australia's systematic

review. **Systematic reviews found to be directly relevant to the present guideline were assessed using the AMSTAR tool. The Clinicaltrials.gov database was also searched** for in-progress randomized controlled trials (RCTs)." (47)

Assessment of the certainty of the body of evidence and strength of recommendations

22. Describe the approach used to assess the certainty/quality of the body (ies) of evidence and the strength of recommendations in the adapted guideline and note any differences compared to the source guideline(s)

What to do

Report the approach used to assess the certainty of the body of evidence and the strength of recommendations, such as the GRADE rating system, Oxford Centre for Evidence-based Medicine (84), the GRADE-CERQual for qualitative evidence (85), or self-established rating system. If the adapted guideline used the same approach as source CGs, the authors should indicate this.

If the rating system used is different to that of the source guideline(s), explain why (e.g., source guideline(s) lacks a rating process, or it is not appropriate), and how GA groups moved from the ratings of the source guideline(s) to the ratings with the new system. A summary of the differences could be included as an appendix.

Why is this important?

The certainty (or quality) of evidence indicates the extent to which we can be confident that an estimate of effect is correct, while the strength of recommendation indicates to what extend we can be confident that the recommendation will do more good than harm (86, 87). Rating the certainty of evidence and strength of recommendations is essential for guideline development and adaptation processes.

Example(s)

1. "**An adapted version of the 'Infectious Diseases Society of America-United States Public Health Service Grading System' was used to define the level of evidence and strength (grade) of each recommendation (Table 1).**" (44)

Table 1. Voting on levels of agreement and definition of levels of evidence and grades of recommendation used by the panel of Asian experts in evaluating the ESMO consensus guidelines for the diagnosis, treatment and follow-up of patients of Asian ethnicity with early breast cancer

Level of evidence

I	Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity
II	Small randomised trials or large randomised trials with a suspicion of bias (low methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without control group, case reports, experts' opinions
Grades of recommendation	
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk of the disadvantages (adverse events, costs, etc.), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

2. "**The panel rated the certainty of evidence supporting each recommendation according to the GRADE methodology, as "high," "moderate," "low," or "very low". The panel graded the strength of each recommendation as either strong or conditional (also known as or called weak).** The factors considered when grading the strength of recommendation were as follows: priority of the problem, benefits and harms of the option, certainty of the evidence, values and preferences, resource use, feasibility, acceptability, and equity." (88)

3. "**The grades range from very low to high and were assigned using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Table 5).**" (40)

Table 5. Definitions of GRADE ratings of the quality of the evidence

GRADE of quality of the evidence	Description
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

Decision-making processes

23. Describe the processes used by the guideline adaptation group to make decisions; particularly the formulation of recommendations

What to do

Report the decision-making process and the methods used to achieve consensus (such as iterative discussions, a Delphi approach, the nominal group technique, or a consensus development conference). The participants and the definition of consensus should also be reported. If consensus is not reached, GA groups should report how the discrepancies were solved, for example, by vote.

Why is this important?

Decisions should be made following an explicit and rigorous process of negotiation. This process allows GA group members to explicitly express their expectations through a respectful and productive process, therefore helping to avoid potential decision-making biases and produce a higher-quality, more credible guideline (89).

Example(s)

1. "**Where there was full agreement between all voting parties that a recommendation could be adapted for use in their country, no further discussion was required. Where there was an absence of full agreement, however, a modified Delphi process was used during the final voting process at the face- to-face working meeting** in Seoul, to develop each of the disputed recommendations towards a consensus. **The Asian experts were asked to vote, based on the evidence available, on a scale of A to E (Table 1)**." (44)

Table 1. Voting on levels of agreement and definition of levels of evidence and grades of recommendation used by the panel of Asian experts in evaluating the ESMO consensus guidelines for the diagnosis, treatment and follow-up of patients of Asian ethnicity with early breast cancer

Voting on level of agreement	
A	Accept completely
B	Accept with some reservation
C	Accept with major reservation
D	Reject with some reservation
E	Reject completely

2. "**During a 2-day in-person meeting, followed by online communication and conference calls, the panel developed clinical recommendations based on the evidence summarized in the EtD tables**. For

each recommendation, the panel took a population perspective and came to consensus on the following: the certainty in the evidence, the balance of benefits and harms of the compared management options, and the assumptions about the values and preferences associated with the decision. The guideline panel also explicitly took into account the extent of resource use associated with alternative management options. The panel agreed on the recommendations (including direction and strength), remarks, and qualifications by consensus or, in rare instances, **by voting (an 80% majority was required for a strong recommendation**), based on the balance of all desirable and undesirable consequences. The final guidelines, including recommendations, were reviewed and approved by all members of the panel." (90)

3. "A content expert (rheumatologist) and a guideline methodologist co-chaired the final panel meeting. **They facilitated and steered the discussion, reflected on and summarized the panellists viewpoints, raised issues/concerns that could inform the decision-making process; and attempted to achieve consensus whenever possible.** The methodologist co-chair did not vote while the content co-chair did." (17)

Recommendations

Recommendations

24. Report recommendations and indicate whether they were adapted, adopted, or de novo

What to do

List all the recommendations in a clear and accurate way, and be explicit about whether the recommendations were adapted, adopted, or developed *de novo*.

If multiple source guidelines were considered, report the name and publication year of the source guideline(s) on which the recommendations were based.

Why is this important?

Clear and accurate recommendations are more likely to promote the implementation by guideline users (4). GA groups may modify (adapt), use verbatim (adopt) recommendation(s) from the source guideline(s), or develop a *de novo* clinical question when lacking appropriate source recommendation(s) (16). Reporting of all the recommendations and stating where they come from also ensures transparency of the adapted guideline.

Example(s)

1. "**Recommendations (example):**

Instruct a high-risk patient with diabetes to monitor foot skin temperature at home to prevent a first or recurrent plantar foot ulcer. This aims at identifying the early signs of inflammation, followed by action taken by the patient and care provider to resolve the cause of inflammation. (Weak; Moderate) **International Working Group on the Diabetic Foot (IWGDF) 2015 (Adopted)**" (42)

2. "**RECOMMENDATIONS (example):**

Screening ***(Modified from pan-Canadian guideline and NCCN Guideline for Cancer-Related Fatigue)***:

- All Health care providers should routinely screen for the presence of fatigue from the point of diagnosis onward, including after completion of primary treatment.
- All patients should be screened for fatigue as clinically indi- cated and at least annually.

Laboratory Evaluation ***(NCCN Guideline for Survivorship verbatim)***:

- Consider performing laboratory evaluation based on presence of other symptoms, onset, and severity of fatigue.
- Complete blood cell count with differential: compare end-of- treatment hemoglobin/hematocrit with current values; assess other cell lines (WBC and platelets).
- Comprehensive metabolic panel: assess electrolytes; assess hepatic and renal function." (62)

3. "**Recommendation (example)**

G1 – Assessment of Capacity and Consent	
G 1.2 **N C**	G 1.2 A formal evaluation of the capacity of the person with traumatic brain injury should be conducted, if needed, by an appropriately qualified professional. Periodic re-evaluation should be conducted as indicated clinically. (INESSS-ONF, 2015)

***N:** New recommendations formulated by the expert panel have been identified with the letter "N" and referenced as INESSS-ONF, 2015.

INESSS-ONF Level of Evidence

C: Recommendation supported primarily by expert opinion based on their experience, though uncontrolled

case series without comparison groups that support the recommendations are also classified here."(91)

25. Indicate the direction and strength of the recommendations and the certainty/quality of the supporting evidence and note any differences (if applicable) compared to the source recommendation(s)

What to do

Report the strength of the recommendations and the certainty of the evidence together with the recommendations.

If the strength of the recommendations and/or the certainty/quality of the evidence is graded or rated differently, differences should be reported. A summary of the differences could be included as an appendix. Using a table format or software might be helpful. If there is no difference between source recommendations and adapted ones, the authors should indicate this.

Why is this important?

It could help users identify differences between the adapted guideline and the source guideline(s), and to what extent they could trust the recommendations.

Example(s)

1. **"Recommendation (example):**
   4.8.8 Consider Achilles tendon lengthening, joint arthroplasty, single or pan metatarsal head resection or osteotomy to prevent a recurrent foot ulcer when conservative treatment fails in a high-risk patient with diabetes and a plantar foot ulcer**. (weak; low)** International Working Group on the Diabetic Foot (IWGDF) 2015 (Adopted)" (42)

2. "**Change in the certainty of evidence and the strength of recommendation:** After we formulated the eight final recommendations, we compared the certainty and strength of each of the adoloped recommendations to corresponding recommendations from the source guideline. **The certainty of the evidence of three of the eight recommendations changed: one from moderate to very low and two from low to very low. The factors that justified a very low certainty of the evidence in these three recommendations were: serious risk of bias and very serious imprecision. The strength of five out of the eight recommendations changed from strong to conditional. The factors that justified the conditional strength of these 5 recommendations were the following: cost (n = 5), impact on health equities (n = 4), the balance of benefits and harms (n = 1) and acceptability (n = 1)."**(17)

3. "Tests for women with high mammographic breast density **(example from *de novo* guideline)**
   In the context of an organised screening programme:
   - for asymptomatic women
   - with high mammographic breast density

   The ECIBC's Guidelines Development Group (GDG) **suggests:**
   - **screening with** either digital breast tomosynthesis (DBT) or digital mammography **(conditional recommendation, very low certainty of the evidence)**
   - **not implementing** tailored screening with both DBT and digital mammography **(conditional recommendation, very low certainty of the evidence)**
   - **not implementing** tailored screening with magnetic resonance imaging (MRI)

(conditional recommendation, very low certainty of the evidence)" (92)

26. Present separate recommendations for important subgroups if the evidence suggests important differences in factors influencing recommendations and note any differences (if applicable) compared to the source recommendation(s)

What to do

The same as for *de novo* guidelines: present recommendations separately for relevant subgroups (i.e., age, sex, ethnicity, and others).

If there is new research evidence suggests additional important subgroups in factors of influencing adaptation of recommendations — particularly the balance between the benefits and harms across subgroups, report the additional subgroups and note the difference compared to the source recommendation(s), including the corresponding research evidence and summary of findings. Whether the subgroup was predefined should also be indicated.

Why is this important?

Due to different reasons (e.g., baseline risk, value assigned to the outcomes, costs of resources, or equity), source recommendations for subpopulations might differ. In addition, subgroups relevant for GA groups might differ from the ones considered in the source guideline(s). Subgroups considered by the source guideline panel might or might not be relevant for the target context. Subgroups not considered by the source guideline(s) can be relevant in the context of the adapted guideline and should be reported as such.

Example(s)

1. See **Table 7**

Table 7. Final Recommendations for Selection of Optimal Adjuvant Chemotherapy Regimens for HER2-Negative and Adjuvant Targeted Therapy for HER2-Positive Breast Cancers: ASCO Guideline Adaptation of the CCO Clinical Practice Guide (examples)

Original CCO Guideline Clinical Topic	ASCO Final Recommendations* Recommendations for HER2-Negative Breast Cancer	Rationale for ASCO Adaptation
Capecitabine in patients age 65 years or older (CCO recommendation 11)	**In patients age 65 years or older, capecitabine is not recommended as an adjuvant chemotherapy option** in lieu of standard regimens such as	**The ASCO Panel modified the CCO recommendation to reflect that patients in**

	doxorubicincyclo phosphamide or cyclophosphamide methotrexate-fluorouracil (oral cyclophosphamide)	the clinical trial reported by Muss et al were age 65 years or older.

"*Recommendations designated by an asterisk are taken verbatim from the CCO guideline. Otherwise, recommendations have been substantively adapted or reworded for clarity by the ASCO Panel." (38)

2. "Recommendations (example):

   Women aged less than 20 years: For women younger than 20 years of age, we recommend not routinely screening for cervical cancer (Strong recommendation; high-quality evidence). Our recommendation is based on a very low incidence of and mortality due to cervical cancer in this age group, no studies addressing effectiveness for this age group, and evidence of minor harms to about 10% of women who undergo screening and more serious harms for some women who go on to further treatment. A strong recommendation against screening reflects our judgment that the potential harms of screening for women in this age group outweigh the benefits." (93)

Rationale/explanation for recommendations

27. Describe the criteria/factors that were considered to formulate the recommendations or note any relevant differences compared to the source guideline(s) (if applicable)

What to do

Report the criteria considered when formulating the recommendations if this information is not available in the source guideline(s), or note any relevant differences compared to the source guideline(s) (if any), and provide the corresponding justifications. The criteria can include the magnitude of the problem, the magnitude of the desirable and undesirable effects, the certainty of the evidence of effects, how people value the outcomes, balance of effects, economic considerations, impact on equity, acceptability, or feasibility.

Why is this important?

Strength of recommendations—and even direction—may change depending on the considered criteria (94, 95). Explicit reporting of the criteria considered by GA groups is crucial to understanding the formulated recommendations and any potential discrepancies with respect to the source guideline(s).

Example(s)

1. "**Strong recommendation:** It is recommended that soap and water should be used for hand hygiene when hands are visibly soiled.
   - **Benefits and harms (Substantial net benefits of the recommended alternative):** The benefits of using soap on visibly soiled hands clearly outweighs any undesirable effects. Plain soap can loosen and remove transient flora. If visible soiling is not removed, the effect of any alcohol-based hand rub is minimised, and effective hand hygiene is threatened.
   - **Certainty of the Evidence (High):** The evidence supporting the recommendation is from experimental, clinical or epidemiological studies and these were judged as either being well designed and/or based on a strong theoretical rationale.
   - **Preference and values (No substantial variability expected):** It is expected that all patients and staff of Australian healthcare facilities would highly value minimising infections during any episode of care. This would include maximising the potential effects of all types of hand hygiene.
   - **Resources and other considerations (no important issues with the recommended alternative):** Appropriate hand hygiene practices have an extremely high clinical impact across Australia's healthcare system. Practices are easy and feasible to implement. To maximise effectiveness, most healthcare facilities use a wide range of promotional and educational campaigns/signage." (96)

2. See **Table 8**.

"Table 8. Adapted – adopted recommendations (examples)" (42)

MoHFW guideline	Adopted/ Adapted	Original Guideline	Remarks
4.7.2 Refer the person with suspected Charcot's foot early (within one week) to the multidisciplinary foot care service Diabetic Foot care centre to confirm the diagnosis and offer non-weight-bearing treatment until definitive treatment can be started.	**Adapted**	NICE 2015 Guidelines on Diabetic Foot (NG19) says - Refer the person urgently (within 24 hours) to the multidisciplinary foot care service to confirm the diagnosis and offer non-weightbearing treatment until definitive treatment can be started.	**Urgently (within 24 hours) may not be possible in Indian context. So the word early (within one week) is used.** Diabetic Foot care centre: **In India, since there are no minimum standards of services offered to the diabetic foot patients**, in our recommendations we have used this term to denote this facility, which may exist at the General Practitioner's office, Primary health centre, Secondary care centre or at a tertiary care centre. Preferably, the diabetic

			foot care centre should consist of at least a surgeon, a physician, and an orthotist.

3. **"The panels often made modifications because of the feasibility of applying the recommendation in a Norwegian setting. Interventions excluded across chapters because they are not readily available in Norway were cilostazol, triflusal, and intermittent pneumatic compression devices;** For most recommendations, **low-dose unfractionated heparin was excluded in preference for the commonly used subcutaneous low-molecular-weight heparin (LMWH),** the latter in general having a slightly better risk-benefit profile and not requiring regular blood monitoring. Based on an absolute risk reduction of 17 per 1,000 pregnancies, the panel believed that most women would prefer thromboprophylaxis and, thus, concluded with a weak recommendation in favor of antepartum and postpartum prophylaxis." (20)

External review and quality assurance

External review

28. Indicate whether the adapted guideline underwent an independent external review. If yes, describe the process

What to do

Describe the external review process explicitly and in detail, including how the comments were compiled for discussion and how the modifications were determined if needed. External reviewers may include different types of professionals or relevant stakeholders (e.g., users, clinical experts, or allied organizations, etc.). They should be appropriately chosen, and complete details of the external reviewers, including full name, affiliation, location, discipline, and management of conflict of interest should be reported.

The external review process should preferably include a review of the clinical content and of the methodology process of the adapted guideline. In the absence of an external review process, a statement would be required.

Why is this important?

Considering representative experts and perspectives in the guideline group are limited, the current guideline development process undergoes an external review process to ensure its

comprehensiveness and quality (4). Reporting this information enhances the transparency and trustworthiness of the adapted guideline.

Example(s)

1. "This report was externally reviewed by the Association of Indonesian Digestive Surgeons (IKABDI) and one expert from the Ethics Committee of the Faculty of Medicine, Universitas Indonesia". (41)

2. "External Review:
   Based on survey results, the guideline was revised by members of the executive and sent to three expert reviewers outside the province for further review. Comments provided by the external reviewers were minor and general in nature (for example, "Good work by the group. Many comments are quite minor and intended to prompt consideration, nothing else"). Thus, the guideline, with minor changes, was published on the Alberta Health Services Web site." (75)

Organizational approval

29. Indicate whether the adapted guideline obtained organizational approval. If yes, describe the process

What to do

Indicate if the adapted guideline obtained organizational approval (from organization that adapted guidelines and/or from organization/s that developed source guideline(s)) and describe the process, such as: whether they submitted their guidelines and whether the guideline was approved.

Why is this important?

Formal support by professional organization(s) is helpful for a wide implementation of the guideline adaptation, and enhances approval by organization's members (55, 97). Sometimes guidelines developed by large organizations are more likely with better quality (37). For some guideline developers, it is often necessary to obtain organizational approval. This type of approval can increase the guideline´s credibility, acceptability, adoption, and implementation. Many countries are conducting quality assurance of guidelines and approving implementation processes, like Ireland (98) and Germany (48).

Example(s)

1. "The guidelines (recommendations) on pages 7-20 were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 1 February 2016 under section 14A of the National Health and Medical Research Council Act 1992. In approving the guidelines

(recommendations), NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. This approval is valid for a period of five years." (52)

2. "**On 30 July 2018, the ASH Guideline Oversight Subcommittee and the ASH Committee on Quality approved that the defined guideline development process was followed, and on 3 August 2018, the officers of the ASH Executive Committee approved submission of the guidelines for publication under the imprimatur of ASH**." (90)

Funding, declaration and management of interest

Funding source(s) and funder role(s)

30. Report all sources of funding for the adapted guideline and source guideline(s), and the role of the funders

What to do

Report all sources of funding for both the adapted guideline and the source guideline(s), and whether it will interact with the adaptation development process or not, as well as how this may have affected the content of the guideline. The funding source for adapted guideline(s) should be differentiated from those for source guidelines(s). If there was no funding (i.e. self-funded guideline group), this should be explicitly stated as well.

Why is this important?

Since guideline adaptation is a methodology for providing guidance based on existing guideline(s), it inherits the merits of the source guideline(s) while retaining the potential bias. In order to help adaptation users evaluate the potential impact of funding, the funding sources, as well as the role of the funders, need to be declared for both adapted and source guideline(s).

Example(s)

1. **"FUNDING/SUPPORT:** Innlandet Hospital Trust, the Southern and Eastern Norway Regional Health Authority, and the Norwegian Research Council have provided research grants. The Norwegian Medical Association has provided grants to support completion of the adaptation process.
   Role of sponsors: The sponsors had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript." (20)

2. **"Funding:** The development and publication of this guideline by the National Health and Medical Research Council (NHMRC) was funded by the Australian Government Department of Health and Ageing. **The involvement of the Department of Health and Ageing was limited to determining the scope of the guideline, and it had no involvement in the committee process of assessing evidence**

and formulating recommendations. At the first committee meeting in February 2011, the borderline personality disorder (BPD) Guideline Development Committee agreed on the scope and target audience for the guideline and developed the clinical questions that the guideline would address." (76)

Declaration and management of interests

31. Report all conflicts of interest of the adapted and the source guideline(s) panels, and how they were evaluated and managed

What to do

Report any sources of conflicts of interest (COI) (e.g., financial or intellectual, etc), as well as how the COIs were evaluated and managed, for both the adapted and source guideline(s), including the exclusion process of specific members with a conflict of interest from the voting panel. The COIs from adapted guideline(s) should be differentiated from those from source guidelines(s). Ideally, the COI could be managed according to an established method, like the Guideline-International-Network (GIN) principles for COI management (99) or American College of Physicians (ACP) methods (100), or other methods as appropriate.

If the information of the COI management from source guideline(s) is unavailable, a statement should be included. The full declarations of all the members could be included as an appendix.

Why is this important?

COI is an important potential source of bias in the development of clinical practice guidelines. It may influence the decision making or recommendation formulating process and should be clearly declared (99, 101). Considering that the quality of an adapted guideline relies on the source guideline(s), reporting COIs and their management for both source and adapted guideline(s) is crucial for users to detect potential bias and assess the quality of the adapted guidelines.

Example(s)

1. "**Conflicting interest statements and management**
   Working Party members were asked to declare any interests relevant to the guideline development, prior to commencement. Members were asked to update their information if they became aware of any changes to their interests.
   All declarations were added to a register of interests as listed in the table of "The Australian Adult Cancer Pain Management Guideline Working Party". The register was made available to the Working Party throughout the development of the guideline, allowing members to take any potential conflicts

of interest into consideration during discussions, decision making and formulation of recommendations.
The guidelines have now entered the updating phase. Guideline Working Party members are responsible to update their conflict of interest statements if a new interest arises." (32)

2. "**All members of the Panel completed ASCO's disclosure form**, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline." (38)
3. "**Financial/non-financial disclosures:** The authors have reported to CHEST the following conflicts of interest: Drs Akl, Guyatt, and Vandvik participated in the writing of the American College of Chest Physicians original guideline (Antithrombotic Therapy and Prevention of Thrombosis, 9th ed)." (20).

Other information

Implementation

32. Describe the potential barriers and strategies for implementing the recommendations (if applicable)

What to do

Report potential barriers and facilitators that may need to be taken into account when implementing the adapted guideline, as well as the resources needed (e.g., guideline summary documents, or links to the "how-to manual", etc.). In the case that recommendations against intervention/management have been widely used, de-implemeting plan should be considered and reported. There are several tools that might be useful to assess the barriers and facilitators for implementation, e.g., GLIA (102), EPOC(43), or Cochrane equity methods.

The implementation plan should emphasise the new and changed recommendations in the adapted version, and the improvements based on the success of the implementation plan from the source guideline. A statement may be made about the differences in the methodology of the implementation plans/strategies between the source and adapted guidelines (34).

Ideally, GA groups should provide details about potential implementation tools (e.g. clinical algorithms, integrated care pathway, medication table(s), performance/ quality measures, patient education information, online resources, mobile apps, etc.). Where an implementation plan was not developed/funded, this should be clearly stated.

Why is this important?

An implementation plan helps health-related practice guidelines maintain their effect (103) while helping policy-makers facilitate optimal health care measurement (104). Provide advice and/or additional materials, such as adapted guideline summary documents, that could support correct implementation (105).

Example(s)

1. "September 28, 2017: New content has been added to the sections on "Tools and resources" as well as on "Key indicators". The "Tools and resources" tab offers suggestions of tools and resources that can be used to support the implementation of the recommendations in each section of the guidelines. The "Key indicators" tab proposes examples of indicators that can be used to monitor the implementation of specific recommendations in each section of the guidelines. Downloadable PDF document with all Key indicators and Tools and resources are also available.—
   Tools and r Tools and Resources
   - Complete list of suggestions of tools and resources
   - Length of Stay (LOS) - Reference table (to support recommendations C 2.1, C 2.2. and C 3.1)
     - Ontario data
     - Quebec data
   - Medication Algorithm (to be used by physicians making decisions regarding Pharmacological Management of Agitation and Aggression following TBI) (pertinent to Section R10, P 1.1 and I 2.2)
   - Indications of use (Health Canada) and insurance coverage (for Quebec only) for the Pharmacological Management of TBI related Impairments (pertinent to multiple sections)" (91)

2. "DISSEMINATION AND IMPLEMENTATION
   Four regional coordinators representing Western Canada, Ontario, Quebec and Atlantic Canada provided information on the CAN-ADAPTT initiative, and collaborated with regional providers, researchers, policy makers and other stakeholders on guideline dissemination strategies. The guideline was disseminated to regional provider networks, at conferences and workshops, integrated into existing educational efforts, and summary articles were published in newsletters and journals.
   CAN-ADAPTT members were encouraged to disseminate the guideline by e-mail, and to discuss the guideline with colleagues. Members have also been incorporating the guideline into training or educational sessions.
   National and professional organizations have been promoting the guideline primarily through passive dissemination such as publishing articles in newsletters, and providing links to the CAN-ADAPTT Guideline on their websites.
   The CAN-ADAPTT website provides a virtual networking space where CAN-ADAPTT members are invited to comment on the guideline, suggest smoking cessation tools and resources and identify additional research gaps. Any member can post to an existing subject thread or create a new discussion topic." (57)

3. "Practice point (PP): **Consultation with culturally and linguistically diverse (CALD) community representatives who have appropriate knowledge and skills should occur in the development, implementation and review of any dementia initiative for CALD communities**." (52)

Update

33. Briefly describe the strategy for updating the adapted guideline (if applicable)

What to do

Report if there is a plan regarding the forthcoming updates of the adapted guideline.

If yes, describe the specific time frame with rationale and methodology that will be using for updating. If specific cases occur that trigger an update before the established time frame, such as the updating of source guideline(s), these should be reported as well.

If updating is not applicable, provide justification, for example, lacking funding support.

Why is this important?:

Guideline updating requires a three-stage process: identifying new evidence, determining whether that new evidence warrants an update, and updating the recommendations (34). Updating is a crucial process for maintaining the validity of recommendations and, by stating when updates are planned, users will be informed about a period of time during which the adapted guideline remains credible.

Example(s)

1. "**Updating the guideline:** This guideline will be updated each year from 2013 to include recommendations added to new editions of the source guidelines or any new guidelines that meet criteria for quality and applicability". (32)

2. "Practice guidelines developed by the Alberta Provincial Head and Neck Tumour Team **are reviewed on an annual basis**—or earlier, if critical new evidence or contextual information is brought to the attention of executive members of the team." (75)

3. "**An update of this guideline was not scheduled or required by our funder**, Health Canada. Funding support of CAN-ADAPTT continues until March 2012. Dr. Peter Selby will seek funding opportunities to continue the work of CAN-ADAPTT including an update to the guideline." (57)

4. "**Future Updates:** We plan to dynamically update the recommendations at least every 3 months by the same team that produced the adapted guideline". (20)

Limitations and suggestions for further research

34. Describe the challenges of the adaptation process, the limitations of the evidence, and provide suggestions for future research

What to do

The GA groups should report the limitations of the evidence. For example, poor reporting and low quality of source guideline(s), the discrepancies between source guidelines, COIs of source(s) and adapted guidelines panels. In addition, suggestions for future research should be provided. In case there are limitations related to the adaptation methodology, the GA groups should report and highlight how these limitation(s) could impact the validity of the recommendations.

Why is this important?

Guideline adaptation faces many limitations when put into practice (104). Acknowledging these limitations increases the trustworthiness of the guideline adaptation and provides suggestions to help guideline adaptation developers to highlight future research needs (106), especially for their target users and settings.

Example(s)

1. "CLARIFICATION AND LIMITATIONS
   Most research in the area of smoking cessation has examined cigarette use; it is important to note this limitation when using this guideline with smokeless tobacco users. More research is needed on smokeless tobacco products and the people who use smokeless tobacco to understand the impact of smoking cessation interventions." (57)

2. "The evidence supporting cardiac rehabilitation in heart failure (HF) are concrete. **However, further studies should assess which type(s) of multidisciplinary rehabilitation programs are beneficial under current Korean circumstances.** Regarding the surgical treatments of HF, the use of mechanical circulatory support (MCS) is expected to increase in Korea. Korean data about the indication and management of MCS are needed" (107)

6. REFERENCES

1. World Health Organisation. WHO handbook for guideline development. 2014.
2. Alonso-Coello P, Irfan A, Solà I, Gich I, Delgado-Noguera M, Rigau D, et al. The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. Qual Saf Health Care. 2010;19(6):e58.
3. Armstrong JJ, Goldfarb AM, Instrum RS, MacDermid JC. Improvement evident but still necessary in clinical practice guideline quality: a systematic review. J Clin Epidemiol. 2017;81:13-21.
4. IOM. Institute of Medicine. Clinical practice guideline we can trust. Washington, DC The National Academies Press. 2011.
5. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 1. Guidelines for guidelines. Health Res Policy Syst. 2006;4:13.
6. Bhaumik S. Use of evidence for clinical practice guideline development. Trop Parasitol. 2017;7(2):65-71.
7. Bhaumik S, Jagadesh S, Ellatar M, Kohli N, Riedha M, Moi M. Clinical practice guidelines in India: Quality appraisal and the use of evidence in their development. J Evid Based Med. 2018;11(1):26-39.
8. Canelo-Aybar C, Balbin G, Perez-Gomez Á, Florez ID. [Clinical practice guidelines in Peru: evaluation of its quality using the AGREE II instrument]. Rev Peru Med Exp Salud Publica. 2016;33(4):732-8.
9. Kredo T, Gerritsen A, van Heerden J, Conway S, Siegfried N. Clinical practice guidelines within the Southern African Development Community: a descriptive study of the quality of guideline development and concordance with best evidence for five priority diseases. Health Res Policy Syst. 2012;10:1.
10. Machingaidze S, Zani B, Abrams A, Durao S, Louw Q, Kredo T, et al. Series: Clinical Epidemiology in South Africa. Paper 2: Quality and reporting standards of South African primary care clinical practice guidelines. J Clin Epidemiol. 2017;83:31-6.
11. Machingaidze S, Grimmer K, Louw Q, Kredo T, Young T, Volmink J. Next generation clinical guidance for primary care in South Africa - credible, consistent and pragmatic. PLoS One. 2018;13(3):e0195025.
12. Molino CG, Romano-Lieber NS, Ribeiro E, de Melo DO. Non-Communicable Disease Clinical Practice Guidelines in Brazil: A Systematic Assessment of Methodological Quality and Transparency. PLoS One. 2016;11(11):e0166367.
13. Talagala IA, Samarakoon Y, Senanayake S, Abeysena C. Sri Lankan clinical practice guidelines: A methodological quality assessment utilizing the AGREE II instrument. J Eval Clin Pract. 2019;25(4):630-6.

14. Fervers B, Burgers JS, Haugh MC, Latreille J, Mlika-Cabanne N, Paquet L, et al. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. Int J Qual Health Care. 2006;18(3):167-76.
15. Fervers B, Burgers JS, Voellinger R, Brouwers M, Browman GP, Graham ID, et al. Guideline adaptation: an approach to enhance efficiency in guideline development and improve utilisation. BMJ Qual Saf. 2011;20(3):228-36.
16. Schunemann HJ, Wiercioch W, Brozek J, Etxeandia-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.
17. Darzi A, Harfouche M, Arayssi T, Alemadi S, Alnaqbi KA, Badsha H, et al. Adaptation of the 2015 American College of Rheumatology treatment guideline for rheumatoid arthritis for the Eastern Mediterranean Region: an exemplar of the GRADE Adolopment. Health Qual Life Outcomes. 2017;15(1):183.
18. Okely AD, Ghersi D, Hesketh KD, Santos R, Loughran SP, Cliff DP, et al. A collaborative approach to adopting/adapting guidelines - The Australian 24-Hour Movement Guidelines for the early years (Birth to 5 years): an integration of physical activity, sedentary behavior, and sleep. BMC Public Health. 2017;17(Suppl 5):869.
19. Burgers JS, Anzueto A, Black PN, Cruz AA, Fervers B, Graham ID, et al. Adaptation, evaluation, and updating of guidelines: article 14 in Integrating and coordinating efforts in COPD guideline development. An official ATS/ERS workshop report. Proc Am Thorac Soc. 2012;9(5):304-10.
20. Kristiansen A, Brandt L, Agoritsas T, Akl EA, Berge E, Flem Jacobsen A, et al. Applying new strategies for the national adaptation, updating, and dissemination of trustworthy guidelines: results from the Norwegian adaptation of the Antithrombotic Therapy and the Prevention of Thrombosis, 9th Ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2014;146(3):735-61.
21. Mehndiratta A, Sharma S, Gupta NP, Sankar MJ, Cluzeau F. Adapting clinical guidelines in India-a pragmatic approach. BMJ. 2017;359:j5147.
22. Kredo T, Bernhardsson S, Machingaidze S, Young T, Louw Q, Ochodo E, et al. Guide to clinical practice guidelines: the current state of play. Int J Qual Health Care. 2016;28(1):122-8.
23. Darzi A, Abou-Jaoude EA, Agarwal A, Lakis C, Wiercioch W, Santesso N, et al. A methodological survey identified eight proposed frameworks for the adaptation of health related guidelines. J Clin Epidemiol. 2017;86:3-10.
24. Godah MW, Abdul Khalek RA, Kilzar L, Zeid H, Nahlawi A, Lopes LC, et al. A very low number of national adaptations of the World Health Organization guidelines for HIV and tuberculosis reported their processes. J Clin Epidemiol. 2016;80:50-6.
25. Abdul-Khalek RA, Darzi AJ, Godah MW, Kilzar L, Lakis C, Agarwal A, et al. Methods used in adaptation of health-related guidelines: A systematic survey. J Glob Health. 2017;7(2):020412.
26. Moher D, Schulz KF, Simera I, Altman DG. Guidance for developers of health research reporting guidelines. PLoS Med. 2010;7(2):e1000217.
27. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6(7):e1000100.

28. Chen Y, Yang K, Marušic A, Qaseem A, Meerpohl JJ, Flottorp S, et al. A Reporting Tool for Practice Guidelines in Health Care: The RIGHT Statement. Ann Intern Med. 2017;166(2):128-32.
29. Tokalić R, Viđak M, Buljan I, Marušić A. Reporting quality of European and Croatian health practice guidelines according to the RIGHT reporting checklist. Implement Sci. 2018;13(1):135.
30. Damiani G, Calzavara-Pinton P, Stingeni L, Hansel K, Cusano F; "Skin Allergy" Group of SIDeMaST; etal. Italian guidelines for therapy of atopic dermatitis-Adapted from consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis). Dermatol Ther. 2019;32(6):e13121.
31. Zafereo M, Yu J, Onakoya PA, Aswani J, Baidoo K, Bogale M, et al. African Head and Neck Society Clinical Practice guidelines for thyroid nodules and cancer in developing countries and limited resource settings. Head Neck. 2020;42(8):1746-1756.
32. Australian Adult Cancer Pain Management Guideline Working Party. Cancer pain management in adults. Sydney: Cancer Council Australia. Available at http://wiki.cancer.org.au/australia/ Guidelines:Cancer_pain_management. Accessed August 1, 2021.
33. Carter J, Lacchetti C, Andersen BL, Barton DL, Bolte S, Damast S, et al. Interventions to Address Sexual Problems in People With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Adaptation of Cancer Care Ontario Guideline. J Clin Oncol. 2018;36(5):492-511.
34. Vernooij RW, Alonso-Coello P, Brouwers M, Martínez García L. Reporting Items for Updated Clinical Guidelines: Checklist for the Reporting of Updated Guidelines (CheckUp). PLoS Med. 2017;14(1):e1002207.
35. Shekelle PG, Ortiz E, Rhodes S, Morton SC, Eccles MP, Grimshaw JM, et al. Validity of the Agency for Healthcare Research and Quality clinical practice guidelines: how quickly do guidelines become outdated? Jama. 2001;286(12):1461-7.
36. Martínez García L, Sanabria AJ, García Alvarez E, Trujillo-Martín MM, Etxeandia-Ikobaltzeta I, Kotzeva A, et al. The validity of recommendations from clinical guidelines: a survival analysis. Cmaj. 2014;186(16):1211-9.
37. Molino CdGRC, Leite-Santos NC, Gabriel FC, Wainberg SK, Vasconcelos LPd, Mantovani-Silva RA, et al. Factors Associated With High-Quality Guidelines for the Pharmacologic Management of Chronic Diseases in Primary Care: A Systematic Review. JAMA Intern Med. 2019;179(4):553-60.
38. Denduluri N, Somerfield MR, Eisen A, Holloway JN, Hurria A, King TA, et al. Selection of Optimal Adjuvant Chemotherapy Regimens for Human Epidermal Growth Factor Receptor 2 (HER2) -Negative and Adjuvant Targeted Therapy for HER2-Positive Breast Cancers: An American Society of Clinical Oncology Guideline Adaptation of the Cancer Care Ontario Clinical Practice Guideline. J Clin Oncol. 2016;34(20):2416-27.
39. NICE. Fertility, pregnancy and childbirth - Intrapartum care - Caesarean section. 2019.
40. Guideline Adaptation Committee. Clinical Practice Guidelines and Principles of Care for People with Dementia. Sydney. Guideline Adaptation Committee; 2016.
41. Lalisang TJM, Usman N, Hendrawidjaya I, Handaya AY, Nasution S, Saunar RY, et al. Clinical Practice Guidelines in Complicated Intra-Abdominal Infection 2018: An Indonesian Perspective. Surg Infect (Larchmt). 2019;20(1):83-90.
42. STANDARD TREATMENT GUIDELINES. The Diabetic foot-Prevention and management in India.2016.

43. Effective Practice and Organisation of Care (EPOC). The EPOC taxonomy of health systems interventions. EPOC Resources for review authors. Oslo: Norwegian Knowledge Centre for the Health Services;
2016. epoc.cochrane.org/epoc-taxonomy. Accessed June 30, 2020.
44. Park YH, Senkus-Konefka E, Im SA, Pentheroudakis G, Saji S, Gupta S, et al. Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with early breast cancer: a KSMO-ESMO initiative endorsed by CSCO, ISMPO, JSMO, MOS, SSO and TOS. Ann Oncol. 2020;31(4):451-469.
45. Elmamoun M, Eraso M, Anderson M, Maharaj A, Coates L, Chandran V; et al. International league of associations for rheumatology recommendations for the management of psoriatic arthritis in resource-poor settings. Clin Rheumatol. 2020;39(6):1839-1850.
46. SOUTH AFRICANCONTEXTUALISED STROKE REHABILITATION GUIDELINE (SA-CSRG). January 2019.
47. Le T, Kennedy EB, Dodge J, Elit L. Follow-up of patients who are clinically disease-free after primary treatment for fallopian tube, primary peritoneal, or epithelial ovarian cancer: a Program in Evidence-Based Care guideline adaptation. Curr Oncol. 2016;23(5):343-50.
48. DELBI. German Instrument for Methodological Guideline Appraisal. https://www.leitlinien.de/mdb/edocs/pdf/literatur/german-guideline-appraisal-instrument-delbi.pdf. Accessed February 01, 2020.
49. Shah MA, Oliver TK, Peterson DE, Einhaus K, Schneider BJ, Denduluri N, et al. ASCO Clinical Practice Guideline Endorsements and Adaptations. J Clin Oncol. 2020;38(8):834-40.
50. Qaseem A, Kansagara D, Lin JS, Mustafa RA, Wilt TJ. The Development of Clinical Guidelines and Guidance Statements by the Clinical Guidelines Committee of the American College of Physicians: Update of Methods. Ann Intern Med. 2019;170(12):863-70.
51. Dynamed Evidence-Based Methodology. https://www.dynamed.com/home/editorial/evidence-based-methodology. Accessed February 01, 2020.
52. Mack S, Hahn S, Palli C, Findling T, Lohrmann C. Adaptation of Clinical Practice Guideline Recommendations in Hospitals for People Living With Dementia and Their Caregivers. Worldviews Evid Based Nurs. 2019;16(1):36-42.
53. Qaseem A, Lin JS, Mustafa RA, Horwitch CA, Wilt TJ. Screening for Breast Cancer in Average-Risk Women: A Guidance Statement From the American College of Physicians. Ann Intern Med. 2019;170(8):547-60.
54. Ministry of Health & Family Welfare Government of India. Screening, Diagnosis, Assessment, and Management of Primary Hypertension in Adults in India. 2016.
55. The ADAPTE Collaboration(2009).The ADAPTE Process: Resource Toolkit for Guideline Adaptation. Version 2.0 Available from: http://www.g-i-n.net. 2010.
56. Fearns N, Graham K, Johnston G, Service D. Improving the user experience of patient versions of clinical guidelines: user testing of a Scottish Intercollegiate Guideline Network (SIGN) patient version. BMC Health Serv Res. 2016;16:37.
57. CAN-ADAPTT. Canadian Smoking Cessation Clinical Practice Guideline. Toronto, Canada: Canadian Action Network for the Advancement, Dissemination and Adoption of Practice-informed Tobacco Treatment, Centre for Addiction and Mental Health. 2011.

58. Kang CI, Kim J, Park DW, Kim BN, Ha US, Lee SJ, et al. Clinical Practice Guidelines for the Antibiotic Treatment of Community-Acquired Urinary Tract Infections. Infect Chemother. 2018;50(1):67-100.
59. Harrison MB, Graham ID, van den Hoek J, Dogherty EJ, Carley ME, Angus V. Guideline adaptation and implementation planning: a prospective observational study. Implement Sci. 2013;8:49.
60. Amer YS, Elzalabany MM, Omar TI, Ibrahim AG, Dowidar NL. The 'Adapted ADAPTE': an approach to improve utilization of the ADAPTE guideline adaptation resource toolkit in the Alexandria Center for Evidence-Based Clinical Practice Guidelines. J Eval Clin Pract. 2015;21(6):1095-106.
61. Alper BS, Tristan M, Ramirez-Morera A, Vreugdenhil MM, Van Zuuren EJ, Fedorowicz Z. RAPADAPTE for rapid guideline development: high-quality clinical guidelines can be rapidly developed with limited resources. Int J Qual Health Care. 2016;28(3):268-74.
62. Bower JE, Bak K, Berger A, Breitbart W, Escalante CP, Ganz PA, et al. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical oncology clinical practice guideline adaptation. J Clin Oncol. 2014;32(17):1840-50.
63. Lee JY, Kwon JY, Na S, Choe SA, Seol HJ, Kim M, et al. Clinical Practice Guidelines for Prenatal Aneuploidy Screening and Diagnostic Testing from Korean Society of Maternal-Fetal Medicine: (2) Invasive Diagnostic Testing for Fetal Chromosomal Abnormalities. J Korean Med Sci. 2021; 25;36(4):e26.
64. El-Harakeh A, Lotfi T, Ahmad A, Morsi RZ, Fadlallah R, Bou-Karroum L, et al. The implementation of prioritization exercises in the development and update of health practice guidelines: A scoping review. PLoS One. 2020;15(3):e0229249.
65. El-Harakeh A, Morsi RZ, Fadlallah R, Bou-Karroum L, Lotfi T, Akl EA. Prioritization approaches in the development of health practice guidelines: a systematic review. BMC Health Serv Res. 2019;19(1):692.
66. AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. Qual Saf Health Care 2003;12:18-23.
67. Jue JJ, Cunningham S, Lohr K, Shekelle P, Shiffman R, Robbins C, et al. Developing and Testing the Agency for Healthcare Research and Quality's National Guideline Clearinghouse Extent of Adherence to Trustworthy Standards (NEATS) Instrument. Ann Intern Med. 2019;170(7):480-7.
68. CCO Guideline Endorsement Protocol: projectdev:cco_endorsement_protocol - PEBC Toolkit. Accessed December 24, 2019.
69. West N, Chapple I, Claydon N, D'Aiuto F, Donos N, Ide M, et al. BSP implementation of European S3 - level evidence-based treatment guidelines for stage I-III periodontitis in UK clinical practice. J Dent. 2021;106:103562.
70. World Health Organization. (2012). Annex 1. PICO questions. World Health Organization. https://apps.who.int/iris/handle/10665/75716.
71. Schünemann HJ, Cook D, Guyatt G. Methodology for antithrombotic and thrombolytic therapy guideline development: American College of Chest Physicians Evidence-based Clinical Practice Guidelines (8th Edition). Chest. 2008;133(6 Suppl):113s-22s.
72. https://www.cochranelibrary.com/about/pico-search. Accessed February 01, 2020.

73. Munn Z, Stern C, Aromataris E, Lockwood C, Jordan Z. What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences. BMC Med Res Methodol. 2018;18(1):5.
74. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO.
75. Harris JR, Lau H, Surgeoner BV, Chua N, Dobrovolsky W, Dort JC, et al. Health care delivery for head-and-neck cancer patients in Alberta: a practice guideline. Curr Oncol. 2014;21(5):e704-14.
76. NHMRC. National Health and Medical Research Council. Clinical Practice Guideline for the Management of Borderline Personality Disorder. Melbourne: National Health and Medical Research Council; 2012.
77. 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.
78. Munthe-Kaas H, Nøkleby H, Lewin S, Glenton C. The TRANSFER Approach for assessing the transferability of systematic review findings. BMC Med Res Methodol. 2020;20(1):11.
79. Brouwers MC, Spithoff K, Kerkvliet K, Alonso-Coello P, Burgers J, Cluzeau F, et al. Development and Validation of a Tool to Assess the Quality of Clinical Practice Guideline Recommendations. JAMA Netw Open. 2020;3(5):e205535.
80. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. Bmj. 2017;358:j4008.
81. Higgins JPT AD, Sterne JAC. Chapter 8: assessing risk of bias in included studies. In: Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions version 5.1.0 (updated March 2011). The Cochrane Collaboration. 2011.
82. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Oxford; 2000.
83. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355.
84. OCEBM. https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence. Accessed February 01, 2021
85. Lewin S, Glenton C, Munthe-Kaas H, Carlsen B, Colvin CJ, Gülmezoglu M, et al. Using qualitative evidence in decision making for health and social interventions: an approach to assess confidence in findings from qualitative evidence syntheses (GRADE-CERQual). PLoS Med. 2015;12(10):e1001895.
86. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. Bmj. 2004;328(7454):1490.
87. Hultcrantz M, Rind D, Akl EA, Treweek S, Mustafa RA, Iorio A, et al. The GRADE Working Group clarifies the construct of certainty of evidence. J Clin Epidemiol. 2017;87:4-13.
88. Arayssi T, Harfouche M, Darzi A, Al Emadi S, A. Alnaqbi K, Badsha H, et al. Recommendations for the management of rheumatoid arthritis in the Eastern Mediterranean region: an adolopment of the 2015 American College of Rheumatology guidelines. Clinical Rheumatology. 2018;37(11):2947-59.

89. WHO handbook for guideline development – 2nd ed. 16. Decision-making for guideline development at WHO. 2014.
90. Schünemann 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.
91. (INESSS-ONF Guideline) Clinical Practice Guideline for the rehabilitation of adults with moderate to severe TBI. 2016.
92. ECIBC. European Commission Initiative on Breast Cancer. Accessed February 01, 2021.
93. Dickinson J, Tsakonas E, Conner Gorber S, Lewin G, Shaw E, Singh H, et al. Recommendations on screening for cervical cancer. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2013;185(1):35-45.
94. Guyatt GH, Akl EA, Crowther M, Schünemann HJ, Gutterman DD, Lewis SZ. Introduction to the ninth edition: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):48s-52s.
95. Andrews JC, Schünemann 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.
96. National Health and Medical Research Council (NHMRC). Australian Guidelines for the Prevention and Control of Infection in Healthcare, Canberra: National Health and Medical Research Council. 2019.
97. Grol R, Dalhuijsen J, Thomas S, Veld C, Rutten G, Mokkink H. Attributes of clinical guidelines that influence use of guidelines in general practice: observational study. Bmj. 1998;317(7162):858-61.
98. Draft National Quality Assurance Criteria for Clinical Guidelines. Health Information and Quality Authority; https://www.hiqa.ie/sites/default/files/2017-01/Draft-National-Quality-Assurance-Criteria.pdf. 2011.
99. Schünemann HJ, Al-Ansary LA, Forland F, Kersten S, Komulainen J, Kopp IB, et al. Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines. Ann Intern Med. 2015;163(7):548-53.
100. Qaseem A, Wilt TJ. Disclosure of Interests and Management of Conflicts of Interest in Clinical Guidelines and Guidance Statements: Methods From the Clinical Guidelines Committee of the American College of Physicians. Ann Intern Med. 2019;171(5):354-61.
101. Thompson DF. Understanding financial conflicts of interest. N Engl J Med. 1993;329(8):573-6.
102. Shiffman RN, Dixon J, Brandt C, Essaihi A, Hsiao A, Michel G, et al. The GuideLine Implementability Appraisal (GLIA): development of an instrument to identify obstacles to guideline implementation. BMC Medical Informatics and Decision Making. 2005;5(1):23.
103. Steinhoff MC, Abd el Khalek MK, Khallaf N, Hamza HS, el Ayadi A, Orabi A, et al. Effectiveness of clinical guidelines for the presumptive treatment of streptococcal pharyngitis in Egyptian children. Lancet. 1997;350(9082):918-21.
104. Wang Z, Norris SL, Bero L. The advantages and limitations of guideline adaptation frameworks. Implement Sci. 2018;13(1):72.

105. Brouwers MC, Kerkvliet K, Spithoff K. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. Bmj. 2016;352:i1152.
106. Rosenfeld RM, Shiffman RN. Clinical practice guideline development manual: a quality-driven approach for translating evidence into action. Otolaryngol Head Neck Surg. 2009;140(6 Suppl 1):S1-43.
107. Kim MS, Lee JH, Kim EJ, Park DG, Park SJ, Park JJ, et al. Korean Guidelines for Diagnosis and Management of Chronic Heart Failure. Korean Circ J. 2017;47(5):555-643.