BMJ Open

Current practices and Challenges in ad@ptation of Clinical Guidelines: A qualitative study based on semi-structured interviews

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-053587
Article Type:	Original research
Date Submitted by the Author:	23-May-2021
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Keywords:	Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, QUALITATIVE RESEARCH, STATISTICS & RESEARCH METHODS

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Current practices and Challenges in ad@ptation of Clinical Guidelines: A qualitative study based on semi-structured interviews

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Abstract

Introduction

As an alternative to developing *de novo* clinical guidelines (CGs), adapting CGs reduces waste of resources and avoids duplication of efforts. Published adapted CGs are generally of low quality, poorly reported, and not based on published frameworks. Current practice of CGs adaptation is still not well known.

Methods

We conducted semi-structured interviews with CGs developers, who had adapted CGs within the last three years. We identified potential participants through published adapted CGs, recommendations from experts, and a review of the Guideline International Network Conference attendees' list. Data collection, on the reason for CGs adaptation and methodology, continued until sampling saturation was identified. We conducted a framework analysis for the CGs adaptation process, and thematic analysis for participants' views and experiences about adaptation process. We report the study following the COREQ checklist.

Results

We conducted ten interviews and identified nine adaptation methodologies. We identified reasons for CGs adaptation, including not only developing *de novo* CGs or implementing source CGs, but also harmonising and updating existing CGs. We identified the following core steps of adaptation process 1) selection of scope, 2) assessment of source materials (CGs, recommendations, and evidence level), 3) decision-making process, 4) external review and follow up process. Challenges on CGs adaptation include limitations from source CGs (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 CGs, with the emergence of different purposes. The identification of core steps and assessment levels could help CGs adaptation developers streamline their processes. More methodological research is needed to develop rigorous international standards for adapting CGs.

Keywords

Practice Guideline, adaptation, qualitative research, evidence-based practice.

Words count

Abstract	288/300
Manuscript	3946/5000

Abbreviations

AGREE II	Appraisal of Guidelines for Research & Evaluation II
CG	Clinical Guideline
EtD	Evidence to Decision
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
HIC	High Income Country
LMIC	Low-Middle Income Country
SR	Systematic Review

Strengths and limitations of this study

- Published adapted CGs are generally of low quality, poorly reported, and not based on published frameworks. Our study could help understand better the current practice of CGs adaptation and the challenges raised in this process, thus improving the adaptation process.
- To ensure participants' representativeness, we invited CGs adaptation experts through different ways, including adapted CGs, attendees from the G-I-N conference, and other 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 CGs adaptation in-depth and how the participants address specific issues.
- We did not conduct data analysis based on country income due to the small sample size and fewer participants from Low-Middle Income Countries (LMICs). Some specific challenges, such as particular contextualisation issues, would be more pronounced in LMICs, underreported in our study.

1. Introduction

Clinical guidelines (CGs) adaptation is an efficient methodology to develop contextualised recommendations (1, 2). CGs 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). CGs 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, CGs adaptation could also be used as an alternative method to develop *de novo* CGs, with the expectation to reduce the waste of resources and avoid duplication of efforts. However, this process should follow a similar and systematic approach as that of the source CGs to benefit from the quality of source CGs (3, 5, 6).

Currently, there is no single standard adaptation methodology (7, 8). One systematic review identified eight frameworks for CGs adaptation (1): ADAPTE (9), Adapted ADAPTE (10), Alberta Ambassador program adaptation phase (11), GRADE-ADOLOPMENT (4), Making GRADE the irresistible choice (MAGIC) (12), RAPADAPTE (13), Royal College of Nursing (RCN) (14), and (Systematic Guideline Review) SGR (15). Most of these frameworks are based on the ADAPTE tool, while some use the GRADE Evidence to Decision (EtD) frameworks (1, 4, 9). Comparison between frameworks showed similarities in the initial and final phase 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 CGs adaptation periodically emerge (16-18).

Despite this, published adapted CGs seldom used a published adaptation methodology and are still of suboptimal quality (19). A systematic survey that evaluated 72 published adapted CGs found that only 57 reported any detail of adaptation method, and only 23 used a published adaptation methodology. The proportion of published adapted CGs satisfying the steps of ADAPTE ranges from 4% and 100%. In addition, the mean score of adapted CGs assessed using 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 three years (7, 10, 21). Besides, most adaptation frameworks require methodology expertise; this might be a barrier for many CGs adaptation groups, especially those from low-middle income countries (LMICs). Although international collaboration and providing staff training could help, this should be based on a standardised adaptation process. Furthermore, most of the 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).

Besides, fundamental gaps between international recommendations and realistic best practice are being reported due to poorly CGs adaptation, which leaves health providers with non-useful guidance (22). There is an urgent need to explore the proper adaptation process and share the global adaptation experience. Therefore, we conducted a qualitative analysis based on semi-structured interviews to better understand the current practice of CGs adaptation and identify the challenges raised in this process, thus providing accordance for the improvement of the adaptation process.

2. 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 (23). We reported findings using the COREQ (Consolidated criteria for reporting qualitative research) checklist (24).

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".

2.1. Participants

We sampled a group of CG developers, who had been involved in CGs adaptation over the past three years using a snowball sampling method (25). We identified potential participants from 1) authors list of 16 published adapted CGs retrieved from a search of adapted CGs through PubMed (from 1992 to December of 2019) (Appendix 01) (26), 2) suggestions from the advisory group of the RIGHT-Ad@pt project, and 3) attendees of the Guideline International Network (G-I-N) conference 2019.

We contacted potential participants by e-mail with an invitation letter, including 1) an introduction of the RIGHT-Ad@pt project, 2) the eligibility criteria, 3) the purpose of the semi-structured interview, 4) the topics to be discussed, and 5) the expected contribution from participants. We sent two e-mail reminders within one 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 manual, and collected the Conflicts of interest (CoI) form of each participant. We continued to recruit participants and collect data until we reached saturation.

2.2. Data collection

We designed an interview guide based on checklists previously developed by our group, and the experience obtained with the development of the RIGHT-Ad@pt checklist (23, 27, 28). The interview guide included four sections: 1) characteristics of participants (country, experience in the field of the health-related CGs and CGs 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 when it is applicable. Interviews were conducted face to face or via teleconference and lasted approximately 40 minutes. We audio-recorded each interview with the participant's permission. One researcher (YS, PhD(c), female, who has guideline development and adaptation experience) conducted the semi-structured interviews and transcribed them verbatim.

2.3. 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 (29). 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 semi-structured interviews findings against the resulting thematic framework, revised and merged codes into themes as new aspects emerged. Finally, we proposed subthemes under the draft 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 (30, 31). 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 corresponded quotations. A second senior author (PAC) reviewed the framework and themes. A final structure was confirmed by discussion and approved by all the co-authors. We used NVivo (version 12 for Mac, QSR International) for qualitative analysis (32).

2.4. Ethics approval

The protocol obtained a waiver 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). We anonymised all collected data.

2.5 Patient and public involvement

The patient and public were not involved in the study.

3. 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 semi-structured interviews between November 2019 and January 2020 until data saturation was reached.

3.1. 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 (HIC) (60%; 6/10). Most participants had more than five years' experience in CGs adaptation (70%; 7/10). Most of the included organisations were research/knowledge-producing centres (67%; 6/9), had more than five years' experience in CGs adaptation (78%; 7/9), had a working group size that ranged from 6 to 20 members (78%; 7/9) and spent less than two 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 co-author of published adaptation methodology. Other participants have nothing to declare.

3.2. Reasons for adapting Clinical Guidelines

We identified four main reasons for CGs adaptation (Table 2, Appendix 02): 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. 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 are discrepancies among different recommendations for the same topic.

3.3. Current practice

Six participants reported they used their own adaptation methodology (8, 33-38). Three of these methodologies 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 (39). Two used a guideline quality assessment tool named DELBI to inform the CG adaptation process in their setting (40). Lastly, one participant reported not using a formal methodology. See Appendix 03 for detailed new methodologies.

Participants reported using the following nine CGs adaptation methodologies (Table 3):

1) ADAPTE instrument (9)
2) Adopt–Contextualise–Adapt (ACA) framework (37, 38)
3) American College of Physicians (ACP) guidance statement (35)
4) American Society of Clinical Oncology (ASCO) CG endorsement/adaptation methodology (33)

5) Cancer Care Ontario's (CCO) endorsement protocol (36)
6) DynaMed editorial methodology (34)
7) German Instrument for Methodological Guideline Appraisal (DELBI) (40)
8) GRADE-ADOLOPMENT framework (4), and
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):

I. Selection of CGs scope and source CGs

CGs adaptation groups defined or identified CGs 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, 33, 34, 36). Some also identified key questions from newly released, well-known, and trustworthy CGs (4, 36). The screening criteria of source CGs for a further appraisal at this preliminary stage were: 1) stakeholders' preferences of CG topic (4, 33, 36); 2) a good reputation of the CGs developers (33, 35, 36); 3) methodological quality of the source CGs (8, 9); 4) clinical relevance to the target context (34), and 5) CoIs management and funding independence of the source CGs (33).

II. Assessment of source materials

CGs 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 to clinical practice and relevance, resource availability, and reflecting latest evidence (up to date) were assessed (9, 33-36, 38). To evaluate CG quality, most participants applied the AGREE II instrument. To ensure source CGs were up to date, some participants did 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 (e.g., how the net benefit, resources, patients' values, and other criteria were considered), as well as the strength of recommendation were reviewed (8, 9, 33-36). Some participants used a CG summary format to display recommendations and facilitate panel discussion (8, 33, 40). Recommendations were modified as needed based on the discussion of evidence (4, 34, 35).

- **Evidence level:** The certainty of the supportive evidence from the source recommendations was reviewed (4, 6, 9, 34-36). Some participants assessed the risk of bias of included primary studies and systematic reviews, and the certainty of the source evidence (33, 34). Besides, updating the original search or supplementing with new evidence was also conducted at this level, if necessary (4, 6, 8, 33, 34, 40). The reasons to update source evidence were: 1) not answering clearly all the key questions; 2) not adequately searched or appraised; 3) considered out of date (e.g., more than three years since the last search), or 4) when panel experts recommended it (Table 2, Appendix 02).

III. Decision-making process

CGs 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 recommendations and supporting evidence. In cases where CGs developers of source CGs used GRADE - ADOLOPMENT, the GRADE EtD frameworks of source CGs were reviewed or completed by the CGs adaptation groups (4). Decisions were made mostly through panel discussion or voting.

IV. 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 of source recommendations made (9, 33).

3.4. Challenges for adapting CGs

Most participants reported challenges to the adaptation and development of CGs in general (Table 2, Appendix 02). Challenges of the adaptation process were: 1) limitations from source CGs, including its poor reporting and poor quality; 2) limited advanced CG development and adaptation skills of the CGs adaptation group; 3) resource and time intensity required for 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 CGs adaptation.

We identified participants' strategies for dealing with the specific challenges within the adaptation process and implementation issues (Table 2, Appendix 02):

I. Addressing context differences between source CGs 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 a panel discussion and experts' opinions. CGs adaptation groups could address these differences at different 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, or other factors (e.g., acceptability or feasibility), or formulating new recommendations (e.g., new recommendations for subgroup population), and 3) at evidence level, by supplementing new evidence (e.g., local data). Finally, participants stated the differences and modifications were reported or documented along with the adapted CG.

II. Addressing inconsistencies between recommendations from different source CGs

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 supportive evidence was sufficient or up to date, and 3) the evidence was interpreted appropriately. At the evidence level, whether the source evidence was appropriately assessed.

III. Updating source evidence

CGs 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 (e.g., PubMed, local databases, or Cochrane database), updating the source search, or experts' suggestions. However, half of the participants expressed their unwillingness to supplement 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.

IV. Considering implementation barriers

CGs 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 (e.g., policymakers, primary carers, or adaptation CG panel) or literature search (e.g., local data). Most of the CGs adaptation groups conducted a discussion to address implementation barriers by considering the applicability of their settings. As a result, either the recommendations or the implementation plan was modified to facilitate the CGs adaptation. Finally, the differences in implementation considerations compared to the source CGs and the modifications were documented in the adapted CGs.

4. Discussion

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

4.1. 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). Fevers et al. in 2006 defined CGs adaptation as an alternative methodology to develop *de novo* CGs or as a systematic method to improve implementation (41). Our finding reflects this definition and indicates 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 CGs adaptation groups have been using, two of which have described by previous reviews, while seven not (1, 7). Unlike previous reviews, our study, in addition to summarising and comparing published frameworks, describes used adaptation processes in a novel structured way, including the stratification source materials assessment. This stratification fits the conceptual progression of CGs adaptation; Fevers et al. considered two levels in this process, the CGs level (quality of source CGs) and recommendation level (coherence between evidence and recommendations, and the applicability of specific recommendations) (41). More recently, Wang et al. described a shift towards an evidence level (supportive evidence of recommendations) (7).

Very few studies up to now 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 for informing 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, supplementing new evidence through a literature search or experts' suggestions; for implementation, conducting panel discussion, and considering modifying recommendations or implementation plan if necessary.

4.2. Limitation and strengths

Our study has some limitations. We only conducted ten interviews with English-speaking participants, and we could have missed additional adaptation methods from other countries. Another limitation is that we did not conduct data analysis based on country income due to the small sample size and fewer participants from LMICs where resources are more limited and technical/methodological experts are few (22). The challenges highlighted by our study are likely to be universal (e.g., intensity and complexity of adaptation process, limitations of source CGs, and implementation barriers). However, some specific challenges, such as specific contextualisation issues, would be more pronounced in LMICS and therefore under-reported in our study.

Our study also has some strengths. We invited CGs adaptation experts through 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 CGs 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.

4.3. Implication for practice

CGs 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 (42). 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 central steps of the adaptation process and assessment levels could help CGs adaptation groups streamline their future initiatives. CGs adaptation groups could predefine the level of source materials to evaluate, simplifying the adaptation process while remaining rigorous. The adaptation process overlaps with the CGs *de novo* process when assessing source materials at the recommendation level and the evidence level. At the recommendation level, CGs adaptation groups need to review the factors considered to formulate source recommendations. This process follows a similar approach conducted by the source panels and requires explicit and transparent reporting about making source recommendations to achieve feasibility. For example, if source CGs followed the GRADE EtD frameworks, the adaptation groups need to review the interpretation of evidence regarding each factor considered under the EtD frameworks. Not all robust source CGs use the GRADE EtD frameworks, but nevertheless, 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 *de novo* process conducts a full *de novo* search while the adaptation process updates source search or supplements with local evidence. Although the structured adaptation process could be used as a framework, its usability should be further evaluated and validated formally.

4.4. 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 CGs adaptation. Besides, there is no framework to guide CGs 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 EtDs from source CGs. A standardised and pragmatic adaptation methodology, including guidance on how to make judgements, should be developed. Furthermore, there are still missing a validated quality assessment tool and comprehensive reporting guidance to improve the rigorous CGs adaptation. The structured adaptation process could be considered as critical aspects of the quality assessment.

Acknowledgements
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Author's contributions:
YS, PAC, LMG, MB, EAA, FC, and RWMV participated in protocol drafting. YS collected and analysed data. MB and JL reviewed the data for accuracy. ENDG provided methodological contributions for the data analysis. YS and PAC interpreted the results and wrote the first draft of the manuscript. All authors critically reviewed the manuscript and approved its final version.

Funding:
YS is funded by China Scholarship Council (No 201707040103).

Competing interests: EAA has intellectual CoIs related to his contribution to the development of methods of guideline adaptation, the RIGHT statement and methodological studies in the field. All other authors have nothing to declare.

Data Availability Statement: All relevant data were included.

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Tables

Table 1. Characteristics of study sample

Characteristic of interviewees (n=10)	n (%)
Continents (n=10)	
Africa	1 (10)
Asia	3 (30)
Europe	2 (20)
North America	4 (40)
Experience in the CGs field (n=10)	
Experience in developing CGs[#]	8 (80)
Experience in adapting CGs[#]	8 (80)
Methodological experience in developing CGs[ʃ]	7 (70)
Methodological experience in adaptation CGs[ʃ]	9 (90)
CGs user	4 (40)
Years of CGs adaptation experience (n=10)	
0-5 years	3 (30)
6-10 years	3 (30)
11-20 years	4 (40)
Characteristic 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 CGs 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 CGs adaptation working group (n=9)	
0-5	1 (11)
6-10	2 (22)
11-20	5 (56)
>20	1 (11)
Average time for CGs 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)

Abbreviation: CGs – Clinical Guidelines. *One expert is from Australia but develops CGs adaptation in Philippines, we classify the country as Philippines. [#]Participation in a CG development/adaptation group at least once in the past year. [ʃ]Participation in a CG technical team at least once in the past year or participation in methodological research.

Table 2. Views and experiences of CGs adaptation

Themes	Number 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
- Implement/ Endorse for target settings	5
- Updating existing CGs	3
- Solve recommendations' controversial	1
CGs adaptation challenges	
- Poor reporting or the limitations of source CG(s)	2
- Limited skills in advanced CGs development and adaptation	3
- The intensity in terms of resources and time for adaptation	2
- Specific steps of adaptation process:	
• Address context differences between source CG(s) and adapted CG	4
• Address inconsistency and integrate recommendations from different source CG(s)	3
• Update or supplement with research evidence	1
- Implementation barriers	5
Address context differences between source CG(s) and the adapted CG	
- Through panel discussion	7
- Adapt for the target context (at CGs level)	
• Prioritise the source CG(s) according to different factors	2
• Discard the source CG(s)	1
- Adapt for the target context (at recommendations level)	
• Evaluate the reason behind and reconsider the strength of the recommendations	1
• Contextualise by considering different factors	3
• Formulate new recommendations for a specific population (e.g., subgroups)	1
- Adapt for the target context (at evidence level)	
• Supplement new evidence/other considerations	2
- Report the differences when drafting the recommendation	3
Address inconsistency between recommendations from different source CG(s)	
- Through panel discussion	2
- Select source CG(s) with different criteria (at CG level)	
• Good quality / rigorous of development of source CG(s)	5
• Content relevance/suitability to the target context	2
• Most up to date	2
• Trustworthy source CG(s)	1
- Assess 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 interested	3
• Source CG(s) are out of date	1
• Source CG(s) are consensus-based	2
• Experts' suggestions	2
- Way of including new evidence	
• Literature search (e.g., 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 considering	
• Modify the practice instead of change recommendations	1
• Modify the recommendations	1
- Report the differences	4

Abbreviation: CGs – Clinical Guidelines.

Table 3. Main steps of the adaptation process

Adaptation methodology/Year	Selection of CGs scope and source CG(s)	Assessment of source materials	Decision-making Process	External review and follow up
ADAPTE 2010 (9)	○ Determine the health question ○ Search for existing CGs/other relevant documents ○ Screen and select source CG(s)	○ Assess source CG quality ○ Assess source CG currency ○ Assess source CG content ○ Assess source CG consistency ○ Assess acceptability & applicability of recommendations	○ Review assessment ○ Select between source CGs and recommendations	○ External review and acknowledgement of source CG(s) ○ Consult source CG(s)
Adopt–Contextualise–Adapt Framework 2016 (37, 38)	○ Predefine CG topics [1] ○ Search for international existing CGs ○ Select source CG(s) by evaluating the implementable of question to the target setting	○ Evaluate the methodological quality of the source CG(s) [a] ○ Content review and recommendations and evidence summary ○ Identify recommendations relevant to steps along the patient journey ○ Deal with two or more relevant recommendations ○ Supplement with local evidence [a]	○ Develop composite recommendations [α] ○ Decision made as adoption, contextualisation/adaptation according to the local context	○ Plan Implementation ○ Undertake focused public consultation ○ Plan and evaluate the CG adaptation roll out ○ Establish partnerships
ACP guidance statement 2019 (35)	○ Choose topics with recommendation conflictions ○ Search and select national-level source CG(s) within five years [2]	○ Evaluate the quality and process transparency of source CG(s) ○ Evaluate the interpretation of the evidence (benefits, harms, costs, and patient values and preferences) ○ Review the source evidence [b]	○ Present evidence summary and propose recommendations ○ Reach consensus by discussion or voting	○ Public panel review ○ Peer review process ○ Publication ○ Financial support ○ Reporting ○ Updating
ASCO CG endorsement/adaptation methodology 2019 (33)	○ Base on the ASCO's priority topics ○ Select source CGs matched by criteria [3]	○ Appraise the quality of source CGs using AGREE II [c] ○ Content review with expert's agreement on recommendations ○ Appraise SRs using AMSTAR and search for new evidence (e.g., when the evidence-based is out of date.)	○ Synthesise the evidence with a matrix contains recommendations and supporting evidence ○ Independent evidence review by the expert panel ○ The decision of modification (e.g., 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
CCO endorsement protocol 2019 (36)	○ Define key topics based on the release of well-known CGs that meet the interest of CCO or ○ Define key topics based on CGs related project and identify existing	○ Initially assess and select source CG(s) [d] ○ Assess source recommendations [e] ○ Evaluate the likelihood of new evidence (if so, a *de novo* development will start)	○ Review the draft endorsement document by an expert panel ○ Reach consensus and get approval	○ Professional Consultation ○ Final Publication ○ Maintenance/Updating

	CG address CCO's topic			
DynaMed editorial methodology 2019 (34)	○ Base on the current existing topics of Dynamed ○ Screen and select the best available evidence based on relevance and potential impact on clinical decision-making and patient care	○ Critically appraise source CGs about trustworthiness, relevance, and clinical value ○ Rate the strength of the recommendations (e.g., net benefit, cost and burdens, and patients' value) [f] ○ Rate the potential source of bias and the certainty of the evidence	○ Report the evidence and review by clinicians ○ Synthesise multiple evidence reports [β] ○ Base 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 (40)	○ Define key questions before selection of source CGs [4] ○ Systematically search for existing CGs ○ Describe the criteria for source CG(s) selection	○ Review the quality of source CG(s) [g] ○ Review source recommendations [g] ○ Systematically updat searches of primary evidence	○ Describe the modifications of recommendations	○ External review CG adaptation process [*]
GRADE-ADOLOPMENT 2017 (4)	○ Select CG topics and source CG(s) [5] ○ Prioritise questions from selected source CGs by the panel	○ Check the EtD availability of source CGs ○ Complet the GRADE EtD frameworks ○ Update systematic reviews of health effects and identify local data [h]	○ Prepare GRADE EtDs frameworks and review by an expert panel ○ Formulate recommendations through consensus or voting	○ NA
Piloted adaptation framework 2017 (8)	○ Prioritise CG topics and approve by the Ministry of Health ○ Search CGs from National guideline Clearinghouse	○ Assess source CG quality [i] ○ Identify relevant recommendations from source CG(s) based on panel expertise and clinical practice settings	○ Compile adopted/adapted/new recommendations ○ Experts review	○ External review ○ Online available for public consultation ○ Updating
Adaptation experience 2019	○ Predefine health questions [6] ○ Search for existing CG(s) [6]	○ Assess source CG quality using AGREE II [j] ○ Identify evidence from the most up to date Gs [j] ○ Review the underlying evidence [j]	○ Review evidence from source CG(s) ○ Decision was made by a national level of experts without further detail provided [μ]	○ External review nationally [ł]

The criteria or clarification for selecting topic/scope/questions and screening source CG(s):

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 of 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 EtD 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)

d: 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 timeliness, 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)

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)

ŧ 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)

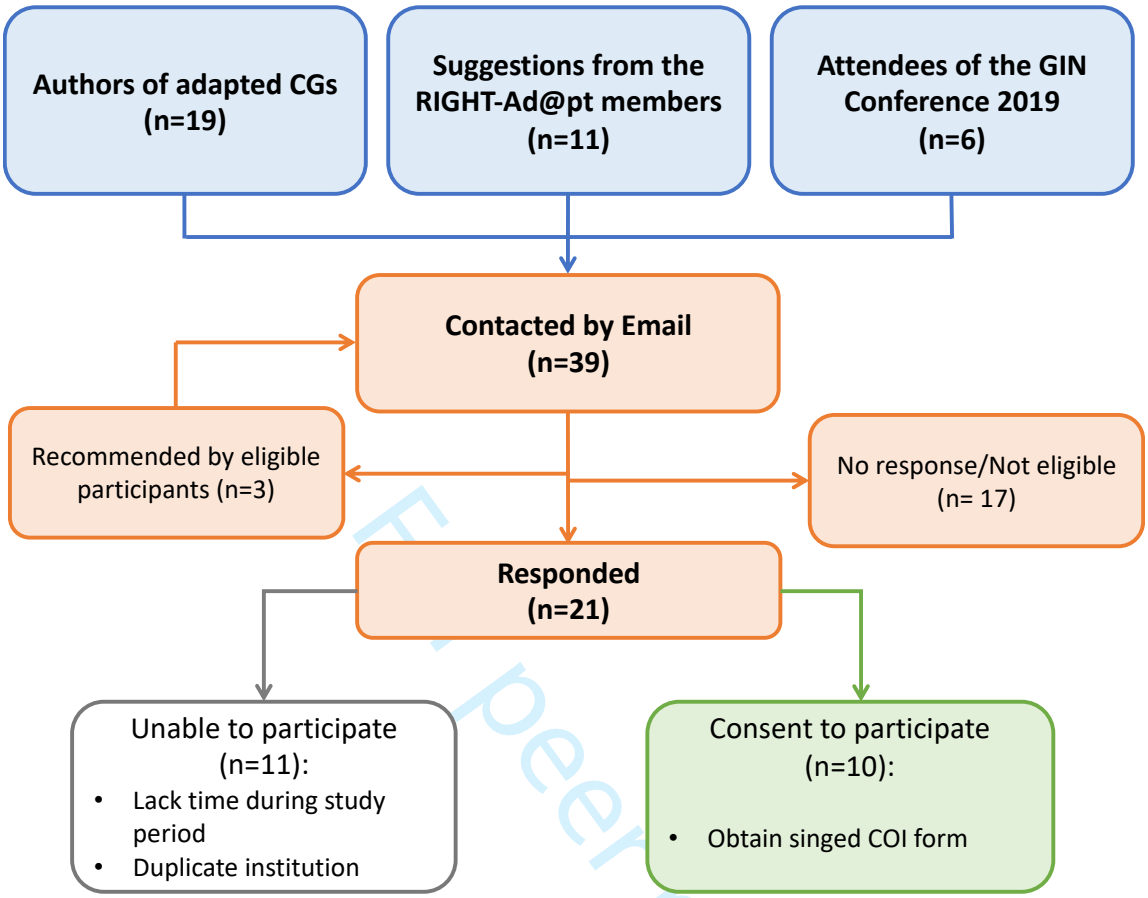
Abbreviations: AGREE II – Appraisal of Guidelines for Research & Evaluation II; CCO: Cancer Care Ontario; CGs – Clinical CGs; CoI – Conflict of interest; EtD: Evidence to Decision; DELBI is a CG assessment tool used by adaptation group to inform CG adaptation; EtDs – Evidence to decisions; GRADE – Grading of Recommendations, Assessment, Development and Evaluations; NA – Not applicable; NICE – National Institute for Health and Care Excellence; SR – Systematic review.

Figures

Figure 1. Participant's recruitment flow diagram

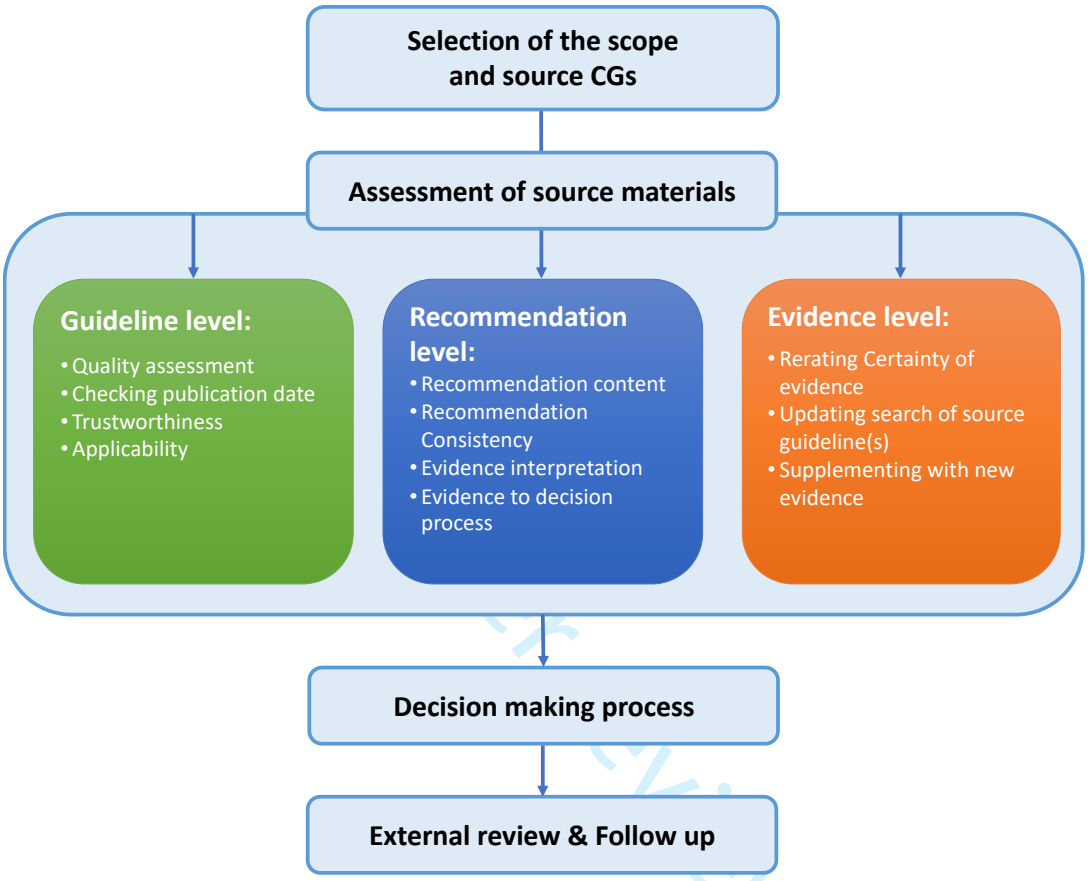
Figure 2. Main steps of the adaptation process

Figure 1. Participant's recruitment flow diagram



* Relevant conference attendees were identified through a review of the list of conference attendees and oral presentation regarding CGs adaptation.
Abbreviations: CoI: conflict of interest, CGs: clinical CGs, GIN: CGs International Network.

Figure 2. Main steps of the adaptation process



Abbreviations: CGs: clinical CGs.

Appendices

Appendix 01. Identification of the published adapted CGs

One author (YS) screened and selected the adapted CGs based on established eligibility criteria: "adapted guidelines", "reported at least one recommendation", "described the adaptation process", and "published in English". Another author (RV) double-checked the findings. We contacted the first author of adapted CGs for participation. If the first author did not respond, we contacted the corresponding author. If they could not participate, we asked for a recommendation of another potential participant. We finally identified 472 records from the pragmatic search, after removing the duplicate and screening title and abstract, we reviewed 41 full texts and 16 adapted CGs to extract contact information.

The pragmatic search strategy of published adapted clinical guidelines and included studies

Search strategy (PubMed from 1992 December to 2019 September)	
#1	"Practice Guidelines as Topic"[Major]
#2	Practice guideline*[tiab]
#3	Clinical guideline*[tiab]
#4	Evidence based guideline*[tiab]
#5	Guideline*[ti]
#6	Recommendation*[ti]
#7	Adopt*[ti]
#8	Adapt*[ti]
#9	Adaptation[tiab]
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6
#11	#7 OR #8 OR #9
#12	#10 AND #11
Included studies	
1	Nishiyama H. Asia Consensus Statement on NCCN Clinical Practice Guideline for bladder cancer. Jpn J Clin Oncol. 2018;48(1):3-6.
2	Guideline Adaptation Committee. Clinical Practice Guidelines and Principles of Care for People with Dementia. Sydney. Guideline Adaptation Committee; 2016.
3	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.
4	Hu J, Yu L, Jiang L, Yuan W, Bian W, Yang Y, et al. Developing a Guideline for Endotracheal Suctioning of Adults With Artificial Airways in the Perianesthesia Setting in China. J Perianesth Nurs. 2018.
5	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.

6	CAN-ADAPTT. (2011). 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.
7	Remington G, Addington D, Honer W, Ismail Z, Raedler T, Teehan M. Guidelines for the Pharmacotherapy of Schizophrenia in Adults. Can J Psychiatry. 2017;62(9):604-16.
8	Pringsheim T, Addington D. Canadian Schizophrenia Guidelines: Introduction and Guideline Development Process. Can J Psychiatry. 2017;62(9):586-93.
9	Laver K, Cumming R, Dyer S, Agar M, Anstey KJ, Beattie E, et al. Evidence-based occupational therapy for people with dementia and their families: What clinical practice guidelines tell us and implications for practice. Aust Occup Ther J. 2017;64(1):3-10.
10	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.
11	Kim KI, Jung HK, Kim CO, Kim SK, Cho HH, Kim DY, et al. Evidence-based guidelines for fall prevention in Korea. Korean J Intern Med. 2017;32(1):199-210.
12	Novo A, Subotic-Popovic A, Strbac S, Kandic A, Horga M. Application of Agree II Instrument for Appraisal of Postpartum Hemorrhage Clinical Practice Guidelines in Bosnia and Herzegovina. Acta Inform Med. 2016;24(3):211-4.
13	McGowan J, Muratov S, Tsepke A, Issina A, Slawecki E, Lang ES. Clinical practice guidelines were adapted and implemented meeting country-specific requirements–the example of Kazakhstan. J Clin Epidemiol. 2016;69:8-15.
14	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.
15	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.
16	Abdollah Zadegan S, Ghodsi SM, Arabkheradmand J, Amirjamshidi A, Sheikhrezaei A, Khadivi M, et al. Adaptation of Traumatic Brain Injury Guidelines in Iran. Trauma Mon. 2016;21(2):e28012.

Appendix 02. Views and experiences on guideline adaptation

Themes	Quotations
Questions: What is the trigger for your institution to adapt source guideline(s)?	
Developing their guidelines (7 Participants)	✔ **As part of *de novo* guideline development process (3 participants):** *"The trigger will be for developing a de novo guideline. We adapt multiple guidelines at a time. The multiple guidelines are usually developed in countries like the UK, Canada, the US etc. Then we adapt those for those resources constrain setting." – (Participant 02)* *"For developing de novo guideline. Basically, we are based on the evidence from existing evidence and then may search for new evidence" – (Participant 04)* *"Generally, we develop our research question and search for evidence/source guidelines to answer our question. If we find a guideline that answered our question, that is the trigger for us to adapt the guideline potentially." – (Participant 05)*
	✔ **To avoid duplicates and save efforts (1 Participant)** *"Basically, the trigger is to avoid the duplication of the guideline development efforts. Especially the searching and appraising the primary evidence. We advise them to use aggregate evidence before they do their own research. This is one hand, and for another hand will pause to do systematic reviews" (Participant 03)*
	✔ **To save resources and time (3 Participants)** *"If the guideline group plan to develop a new guideline, they will search for the existing evidence first. However, in the process of adaptation, they always realise that they could not only implement a source guideline because there is some difference between the target settings. If there is already evidence-based up to date guidelines, groups want to use them for their own guideline to avoid or minimise efforts of systematic searches." (Participant 06)* *"First, to say primarily, the first we don't want to spend resources on developing de novo. Ideally, we would adapt the source guideline(s). The first trigger for adaptation is that we want to limit the cost and to save resources." (Participant 09)* *"We needed to develop in a short period, and we did not have enough money and people to be involved." (Participant 10)*
Implementing/Endorsing for target settings (5 Participants)	✔ **Implementing (3 Participants)** *"Given time and resource constraints, the task force discounted developing new guidelines and opted to adaptation. We use a pragmatic method by which evidence-based guidelines could be adapted to suit our context. New review questions were recommended only for areas not covered by existing guidelines." (Participant 08)*

	"Government support to adapt for implementation: To be realistic, sometimes the policies or others suggest there is a need to adapt." (Participant 09) *"We were consulted to assist in developing guidelines that were relevant and implementable in a resource-limited setting." (Participant 10)*
	✔ **Endorsing (2 Participants)** *"We also do guideline endorsement; sometimes, other organisations come to ASCO to ask us to endorse their guidelines. This could be the single source guidelines. We ask our panel to not change anything of the source guideline(s). In minority times, they made some modifications based on other processes of our own. It's a similar process with what we called adaptation." (Participant 02)* *"We will not search for new evidence when endorsement or adaptation if the source guideline did not answer all of our questions, we will conduct the new systematic review for the rest questions". (Participant 05)*
Updating existing guidelines (3 Participants)	*"We will update our guideline when a new guideline comes out by considering whether the new guideline will change our guideline or not, if so, we will adapt/adopt to our topic" (Participant 01)* *"When updating an existed guideline, the group will want to adapt a good guideline when updating. We will first look at the existing guideline if you could make a single recommendation, so in some updated guidelines they choose to adapt two of the recommendations, they made also search for systematic reviews, so another five recommendations are based on systematic reviews, and other recommendations are based on primary studies. Other recommendations are based on experts' consensus." (Participant 06)* *"The other trigger for adaptation could also be when new evidence showing up, and if new primary evidence changes the recommendations/practice, we will choose adapted the recommendation, to be realistic." (Participant 09)*
When existing guidelines are controversial (1 Participant)	*"We do adaptation only when guidelines are controversial, and we intend to harmonise the guidelines." (Participant 07)*
Questions: According to your experience, which part is the most challenging for your institution when adapting guidelines?	
Poor reporting or the limitations of source guideline(s) (2 Participants)	*"The most challenging is the guidelines often do a **very poor reporting** of how they make their decision exactly what was based on, what value they were considering, what methodology is, what is the evidence. So sometimes you get the recommendations, but you don't get the why, and you don't get what evidence they considered, and how they rate it and understand it. So poor reporting would be the biggest challenging part for adaptation." (Participant 01)*

	"This is most challenging because as a methodologist I have not read all the evidence, I haven't searched for it all, so I don't know it well. If there are all guidelines and they all consistency, and they all have the same kind of evidence, and then I feel more confident. Sometimes I do a quick search to see if something is outside the source guideline, but really I rely on my experts' panel in this field if they can endorse these recommendations pretty much as it is and if they think the new evidence is going to change the recommendations." (Participant 05)
Limited skills in advanced guideline development and adaptation (3 Participants)	*"I would say* evaluating the evidence (source guideline or systematic reviews) is the most challenging part. *We don't look at the methods the source guideline(s) used for the evidence appraisal. We reevaluated the quality and certainty of the evidence from source guidelines by ourselves." (participant 07)* *"I want to say all of these are challenging. Because I think health questions are difficult for people to phrase, people don't have technical skill for searching evidence, we have limited skill to appraisal and identify guidelines that we are using, and there have very few groups that have specific methods to move evidence to a decision." (Participant 09)* *"Framing the health question: sometimes the experts even could not draft the health question correct； Choosing the health question; Searching for evidence (source guideline or systematic reviews) and making recommendations from evidence" (Participant 10)*
The intensity in terms of resources and time for adaptation (2 Participants)	*"They have to go down to two-level to see the basis of adaptation. But we don't want them to spend a lot of time to see the weeds of primary evidence. We want them to kind of be able to go from the recommendation level directly." (Participant 02)* *"For the guideline development groups, the greatest challenging **is very time-consuming**. Also, **the resource intense**. Or do I need to do an extra evaluation of the source guideline is not good enough?" - (Participant 03)*
Challenges arising from specific steps of adaptation process	✔ Addressing context differences between source CGs and adapted CG **(including reporting the differences) (4 Participants)** *"Sometimes, they also are struggling with translating the evidence to recommendations, because the evidence just not fit to the target population. It is a typical problem of indirectness or imprecision of these things." (Participant 03)* *"I think choosing the health questions and also making the recommendations from the evidence-based on our characteristic. Not all the clinical questions are the same for our region because the character is different" (Participant 04)"* *"We suggested guideline adaptation group to justify the deviations from source guidelines, but regularly they do not include the reason (reporting). When we ask to clarify the deviations, they said it is too difficult for them to report the reason for deviations. I think*

	it is really too difficult for them to explain. I think this is the real challenging for them because this issue was really discussed in a consensus conference, but nobody really reports the augments (reporting)." (Participant 06) *"The real challenge when you put guidelines together is that you would probably know different guideline groups do their methods differently." (participants 10)* ✔ **Addressing inconsistency and integrating recommendations from** different source CGs **(3 participants)** *"I would say it related to the "**making evidence to recommendations**". From our adaptation experience, you know you have the extra layer, the source guideline, the SR that described and to inform the recommendations, and the basic primary studies; then we come into the adaptation, they have to go down to two-level to see the basis of adaptation. But we don't want them to spend a lot of time to see the weeds of primary evidence. We want them to kind of be able to go from the recommendation level directly.* ***For solving the inconsistency of recommendations is also a challenging part"** (Participant 02)* *"I would say **making recommendations from Evidence.** If there are evidence that may change the recommendation; is the guideline suitable for our setting? Because it is the link between evidence and recommendations. For adaptation for us is the same with endorsement. If we need to make major change of the recommendation, we will need to develop our own recommendations." (Participant 05)* *"There wasn't enough guidance for how to adapt a guideline and even now. **There was very limited to no evidence in how recommendations from multiple sources can be put together.** Because most of the adapted guideline in practice they only chose one guideline." (Participant 10)* ✔ **Updating or supplementing additional research evidence (1 Participant)** *"The evidence base of the source guidelines was complemented by systematic update searches of primary evidence." is a challenge for guideline adaptation group. (Participant 06)*
Implementation barriers (5 Participants)	*"The very most challenging is stratifying the recommendations, decided them into different practice settings" (Participant 02)* *"Also, I do believe that like many organisations, implementation is also a great challenge. We do our best to develop our guidelines, but implementation still is a hot topic." (Participant 03)* *"And implementation is a whole separate thing and also challenging". (Participant 09)*

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	"Required the resources which might not apply in the target setting. For example, diabetic foot, the evidence and recommendations suggested to conduct yearly foot assessment, however, in practice, none of the clinicians knows how to do a foot examination; Also adherence to the guideline recommendation in the culture of Indian would also be challenging." (Participant 08) *"For example: for our setting, who is the best health professional you should contact or deliver the care, and that is a very local context field. Because in some setting maybe they only have a nurse." (Participant 10)*
Questions: According to your experience, how does your institution consider the difference between source guideline(s) and targeted context? Like the population, the setting/health systems, or practice variation/target users?	
Experts' opinions and Panel discussion (7 Participants)	*"In general, we address the differences according to the feedback from international panel experts/clinicians." (Participant 02)* *"Mostly addressed in group discussions, when it comes to reviewing the source guidelines. Then decide if they adopt them or they check if they are adoptable for the national systems. So mostly it's experts' opinions that come in." (Participant 03)* *"We made a group discussion; all the participants of my study attend to a seminar and discuss their opinion about the differences." (Participant 04)* *"We are looking for the similar guidelines. If there are differences, we discuss through our panel and decide to use it or not." (Participant 05)* *"Some group solve differences by discussion or consensus." (Participant 06)* *"By discussion within the development group and acknowledge the difference in a document." (Participant 08)* *"They solve the differences by discussion in the panel, and they may come to a consensus." (Participant 09)*
Modifying for the target context	***On the guideline level:*** ✔ ***Prioritise* the source guideline according to different factors (3 Participants)** *"We do prioritise according to language because we are working in English. First, by prioritisation according to the quality of guideline development institution, published in English, and sometimes for the global population, which means, common users of our guidelines." (Participant 01)* *"You have to look at each guideline methodologically and to see which one is regularly doing and try to lean towards that but also really on AGREE ii instrument evaluation as well and use that to filter which is a good guideline and which is not. The methodological*

rigorous is important, but on top of that is the interpretation of the evidence and do recommendations. And often look at the evidence directly as well." (Participant 07)

✔ ***Discard source guideline (1 Participant)***
"We develop our own research question. If the source guideline did not answer our question, we will not consider using them. For example, we are looking for the similar guidelines. If there are differences, we discuss through our panel and decide to use it or not." (Participant 05)

On the recommendation level:

✔ ***Modify strength of the recommendations (1 Participant)***

"If there is not certain difference between population, but different considerations or opinions, we will rate down certainty due to inconsistency; If the guidelines are from different regions, we may give weak recommendation with documented justifications." (Participant 01)

✔ ***Contextualize by considering different factors (3 Participants)***

"The working group judge whether to adapt according to the context/new balanced benefits and harms and decide through discussion." (Participant 06)

"The recommendation could be changed due to the difference of health settings/target users/population; we request the guideline development group to provide those modifications as well as the justifications." (Participant 08)

"I think this was most helpful about the Evidence to decision framework. Because even if the recommendations were come from other setting, you will go through the acceptability, feasibility. In feasibility, if a drug is not available in your country or you need a different formulation, or the price is inaccessible, then it will influence the recommendations. After the decision was made by the guideline panel, the recommendations will go to another level of group for considering whether it is justified and feasible. So, this is a kind of internal quality insurance." (Participant 09)

✔ ***Do a recommendation for subgroup population (1 Participant)***
"If there is a certain difference between population, we do a subgroup population and mark clearly which population suits which context." (Participant 01)

On the level of evidence:
✔ ***Supplement new evidence/other considerations (2 Participants)***

	"Also, we do check the existing policies that need to be addressed. It is not systematically searchable, but it is addressed by group discussion." (Participant 03) *Even at the start, the questions can be contextualised. Which question and which guideline should we practice? Sometimes we did not find any answers. Hence, for some recommendations, we consider some source of information from the local context." (Participant 10)*
Reporting the differences when drafting the recommendation (3 Participants)	*"If there is a certain difference between population, we do a subgroup population and mark clearly which population suits which context; If the guidelines are from different regions, we may give weak recommendation with documented justifications." (Participant 01)* *"By discussion within the development group and acknowledge the difference in a document. We request the guideline development group to provide those modifications as well as the justifications." (Participant 08)* *"We did not put them together but will report in the appendix." (Participant 10)*
Questions: According to your experience, how does your organization solve inconsistency of recommendations from different source CGs?	
Panel discussion (2 Participants)	*"We deal it more by discussion. There is not a table or formula to tell you how to deal with inconsistency; you have to figure out the reasons for the inconsistency." (Participant 01)* *"I would say that is a challenging part. We do a discussion about the inconsistency and then we do grate the strength of the recommendation based on published criteria." (Participant 02)*
Selection criteria (On the guideline level)	✔ ***Good quality and rigorous developed (1 Participant):*** *"We use matrixes/tables to map the differences. Sometime if they have a good guideline, they will stop to search another guideline. We Used AGREE II to identify the methodological quality of the guidelines and prioritised by methodology sound recommendations." (Participant 03)* ✔ ***Good quality (3 Participants):*** *"We don't have a critical cut off to choose which guideline to use, we do prioritise by quality of the guideline. Some group solve differences by discussion or consensus." (Participant 06)* *"We do not have a cut-off of the AGREE score, because sometimes there are few source guidelines for the consideration of adaptation. By considering guideline quality:1) from the NGC; or 2) consider the results with AGREE II assessment." (Participant 08)* *"So, if it is coming from a higher-level study, and if it's of good quality, and if it's pointing the same direction." (Participant 10)*

	✔ ***Trustworthiness, good quality, and most up to date (1 Participant):*** *"We do not have a numeric cut-off for AGREE ii. We don't use a qualitative cut-off with the results of AGREE ii, but we do consider the highest quality are guidelines from well-known guideline development institution that has used systematic reviewed based guideline development methods and has fully describe their methods.* *And we also can only adapt guidelines that were not funded by industry.* *The decision to adapt a specific guideline or guidelines, is based on:* *o the results of the content review and the level of agreement with the recommendations* *o A quality appraisal of available guideline(s)* *o the time since completion of the best available guideline(s)" (ASCO guideline development manual)" (Participant 02)* ✔ ***Up to date (1 Participant):*** *"We don't go simply from recommendation to recommendation, we identify the evidence from the most up to date high quality guidelines, also panel will want to look at the primary studies." (Participant 09)* ✔ ***Relevant to the target context (2 Participant):*** *"We did our plan to evaluate the inconsistency and solve it by considering whether it suits our context." (Participant 04)* *"Through panel discussion to make the decision whether this guideline is suitable for Ontario context or not." (Participant 05)*
Assessing the reason for inconsistency: **(On the recommendations level and evidence level)**	✔ ***Assessing on recommendation level (4 Participants)*** *"We gonna look into what is the recommendation. If the recommendation is different in different guidelines, then we have to figure out do we think one is right and one is wrong and explain it. Or we just say there is a reason for differences of opinion, and we give a weak recommendation overall, because they disagree. Maybe if you look carefully, the guidelines were actually focusing on different population, and there are not truly inconsistent or giving newer on the strong recommendations, in which case you may agree with both guidelines, and then present it more clearly." (Participant 01)* *"We ask them to really compare the guideline and see where the inconsistency comes from on the level of individual recommendations." (Participant 03)* *"In another case, more than one guideline was used, some groups consider the consistency by using synopsis of each recommendation and checking the inconsistency but some not." (Participant 06)* *"We have to look at the inconsistency, uninformative thoughts, the strength of recommendations that will be based on the quality of your evidence and the level of evidence." (Participant 10)*

	✔ ***Assessing on evidence level (3 Participants)*** *Or maybe one guideline has more evidence or more currency than the other, you may ignore the guideline that wasn't aware all the evidence when they made the recommendations. But until you understand why there is inconsistency, you can determine what to do. We don't have a comment table to work through how to do it, the team uses their judgment to explore this and use their experience." (Participant 01)* *"If there is consistency, we will only consider the SRs they are using, using other persons SR, or conduct the SR by our-selves." (Participant 05)* *"By looking at the evidence interpretation (the appraisal of the evidence, if they are not good, would go into the individual studies and reassess the quality of the evidence) the quality and rigorous of development (assessed by AGREE ii score)." (Participant 07)*
Single guideline was included (4 Participants)	*"I have in the past looked at whether guidelines have recommended the same treatment. However, recently we have been selecting only one guideline to endorse/adapt." (Participant 05)* *"In one case, the group only pick up one good guideline and use it." (Participant 06)* *"We did not meet one situation of more than one guideline were included and I do not know how to solve." (Participant 09)* *"What people have done is that they chose one guideline one and adapt this guideline for their setting." (Participant 10)*
Questions: According to your experience, how does your organization consider other systematic reviews or new evidence?	
Trigger for complement / update search of source guideline(s)	✔ ***Source guideline did not answer all the questions of the adapted guideline (3 Participants):*** *"If the source guideline did not answer all of our questions, we will conduct the new systematic review for the rest questions." (Participant 05)* *"If they find there is no clear answers for their question in the source guidelines, they looked at existing Cochrane SRs but do not conduct a new one." (Participant 08)*

	"No guideline answers your question, we do consensus process. If the source guideline has limited evidence for specific questions, we will make a consensus process." (Participant 10) ✔ ***Source guideline(s) are out of date (1 Participant):*** *"If it is a great guideline but it's 3 years old, and since then there are new primary studies come out, they will want to look at that." (Participant 09)* ✔ ***Source guideline(s) are consensus based (2 Participants):*** *"Resource stratified guidelines means based on the source guidelines and considering resource use. For the source guidelines we did not do the updated;" (Participant 02)* *"For experts' consensus from source guidelines, expert panel decide sometimes in addition to do a systematic search for other aggregate sources of evidence, like Cochrane reviews, and sometimes they decide to have a full de novo search for primary evidence to answer the question." (Participant 03)* ✔ ***Expert panel recommended (2 Participants):*** *"For the other guidelines if we adapt them, yes. In general, we may need to update the literature search if the expert panel think there are new evidence published outside the systematic reviews that particular relevant." (Participant 02)* *"We made national wide guidelines launched by the ministry of health. There are more experts connected with us to make more comprehensive guideline, and they do have other source of evidence. Our group starting by searching the databases like PubMed, etc." (Participant 04)*
If the source guideline(s) were not evidence based	✔ ***Discard the recommendation, (1 Participant):*** *"For consensus recommendations from source guidelines, sometimes the group decides to maybe discard specific recommendations from source guidelines but rather than have a consensus-based recommendation in Germany." (Participant 03)* ✔ ***Conduct consensus process, (1 Participant):*** *"No guideline answers your question, we do consensus process. If the source guideline has limited evidence for specific questions, we will make a consensus process." (Participant 10)* ✔ ***Start guideline de novo process (3 Participants):*** *Start guideline de novo process: "We will not search for new evidence when endorsement or adaptation, if the source guideline did not answer all of our questions, we will conduct the new systematic review for the rest questions. We conduct our own SRs if the source guideline did not answer our research questions. We do that only when the source guideline did not address the specific research*

	questions in the case that we are doing multiple questions. Like if we have 5 research questions and the source guideline(s) only addressed 3 of them, then we need to conduct our own SRs to address the other 2. If we have to look for new evidence, we do the literature search. But for us the adaptation doesn't means we have to search new evidence, if we have to do it, then it is a de novo process." (Participant 05) *"We only limited the evidence of the source guideline; we do not do the supplement evidence otherwise the process will be very complicate. The critical difference of the guideline adaptation and guideline de novo process is you limited the evidence within the source guidelines. You are not looking at the additional information. We don't call them recommendations; recommendations only come out of guidelines that you do yourself." (Participant 07)* *"We do not conduct new systematic reviews due to the time limitation. In the case of good guideline absence, we would consider a guideline de novo process rather than an adaptation." (Participant 08)*
Way of including new evidence	✔ ***Conduct literature search for complement evidence (6 Participants):*** ***Pragmatic search (5 participants)*** *"Our group starting by searching the databases **like PubMed**, etc." (Participant 04)* *"Our guideline group will make a search for SRs." (Participant 06)* *"They did refer to the **Cochrane database**. If they find there is no clear answer for their question in the source guidelines, 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)* *"The guideline group link with organisations like the **Cochrane centre**, and all discuss very nicely to provide evidence." (Participant 09)* *"We do everything to ensure the search is comprehensive. We search for guideline has been published everywhere. For some questions we adapted, we take the new evidence around, for instance in the local context setting there might be a **new paper** that has been **published locally**, if the evidence answered the question of the local context." (Participant 10)* ***Full de novo search (1 Participants):*** *"For experts' consensus from source guidelines, expert panel decide sometimes in addition to do a systematic search for other aggregate sources of evidence, like Cochrane reviews, and sometimes they decide to have a full de novo search for primary evidence to answer the question." (Participant 03)*

	✔ ***Update the search from source guideline(s) (3 Participants):*** *"Like I said before, we conducted continuously monitoring of new evidence that relevant." (Participant 01)"* *"In general, we may need to update the literature search if the expert panel think there are new evidence published outside the systematic reviews that particular relevant." (Participant 02)* *"If it is a great guideline but its 3 years old, and since then there are new primary studies come out, they will want to look at that. If there is more up to date SR that includes additional studies, they will want to look at that." (Participant 09)* ✔ ***Experts'* suggestions (3 Participants)** *"There are more experts connected with us to make more comprehensive guideline, and they do have other source of evidence. Our group starting by searching the databases like PubMed, etc. And also, experts will recommend new studies if they have one." (Participant 04)* *"Experts from our group could recommend recently RCTs apart from SRs identified from the search. But we make the process transparently reported." (Participant 06)* *"There is a committee from the national government to find some of the prestigious policy questions. We haven't been involved in any guideline for professional society or private group, we haven't been charged much for conduction reviews. The primary research we don't do. Experts will ask for relevant evidence and we will conduct the synthesis and provide to them if needed to explain or facilitate the decision making." (Participant 09)*
Questions: According to your experience, how does your organization consider implementation barriers?	
Ways to obtain the information and Address it by group discussion (7 Participants)	✔ ***Experts opinion, literature search, group discussion (1 Participant)*** *"For the resource stratified guidelines, yes; I would say most by discussion. For example, we would include panel members who are in primary practice outside the academic medical settings, their experiences can inform what are the constrains and barriers that may impact on the implementation of recommendations. For the resource stratified guideline, we do also discussion and non-systematic environmental scan of the cost-effectiveness analysis literature. To see if the literature can influence the applicability of the implementation." (Participant 02)* ✔ ***Experts opinion, literature search, group discussion (1 Participant)***

	"Yes; For example, if one intervention was labelled in the US but off labelled in Germany, we asked the experts panel to assess if the evidence is really sound enough to do a such recommendation. Also, we do check the existing policies that need to be addressed. It is not systematically searchable, but it is addressed by group discussion." (Participant 03) ✔ ***Experts opinion, literature search (1 Participant):*** *"Usually from the government people, they have other field angle to see how we treat disease, this is different with the way of think a clinician. But I think they based on a good tele data to make the problem understandable and solve the problem." (Participant 04)* ✔ ***Experts opinion, group discussion (1 Participant):*** *"We ask our panel about the feasibility of implementing a treatment and discussed within our working group by considering the context of our settings." (Participant 05)* ✔ ***Search, (1 Participant):*** *"We only look at the cost of the intervention and look at the information available by PubMed." (Participant 07)* ✔ ***Group discussion, (1 Participant):*** *"They do discuss the recommendations and to see if the recommendation is appropriate in their setting, what kind of challenging they will have when implementing the recommendations that adapted. By discussion within the guideline development group. And provide the documented acknowledge." (Participant 08)* ✔ ***Literature search, Group discussion, (1 Participant):*** *"We only look at the cost of the intervention and look at the information available by PubMed.* *Our group will consider at least the feasibility, and within that there will be issue of regulatory issues, ethical issues, and access issues. So, feasibility, equity and cost will be considered." (Participant 09)*
Decision made after considering (2 Participants)	✔ ***Modified the practice instead of change recommendations:*** *"The source recommendations will not be change, however the practice way maybe tailored for the local context to make it applicable." (Participant 10)* ✔ ***Modified the recommendations:*** *"At least for medications, we see evidence on the use of medications, check if it's authorised to use. If it's not approved to use for any country, we won't make a recommendation to use even if there are some evidence." (Participant 01)*
Report the difference (4 Participants)	*"We will make the notation in the summary of medication to highlight the difference." – (Participant 01)*

	"If yes, advice the guideline users this is off-label in Germany and should take this into account when they inform the use for patients." – (Participant 03) *"We described difference constrains when published the guideline, like if the medical insurance did not cover the new intervention, we will mention it." - (Participant 06)* *"And provide the documented acknowledge." – (Participant 08)*

Appendix 03. Adaptation methodologies identified

Questions: Could you please describe the adaptation process your institution used or describe which framework or methods used for guideline adaptation?	
Adaptation Frameworks	**Quotes**
ADAPTE 2010	*"We used ADAPTE 2010 and supplement with GRADE system for assessing the level of evidence." (Participant 04)*
ASCO endorsement/adaptation methodology	*"We used a mixed method, some of them from ADAPTE methodology. We have published a paper on our methods and I´ll be happy to provide that, I think it may explain better than I do." (Participant 02)*
DynaMed methodology	*"We are using Dynamed methodology which is GRADE-based, you could find it in Dynamed website." (Participant 01)*
CCO endorsement protocol	*"We used to use more ADAPTE before, and now we are slowly covering to GRADE. For our group we do have an overarching CCO endorsement protocol, but I also use GRADE-ADOLOPMENT as it has more details" (Participant 05)*
GRADE-ADOLOPMENT	
ACP guideline development methods	*"We use others methodology of adaptation, which is call ACP guideline development methodology, you could find the information published." (Participant 07)*
Pilot adaptation Framework	*"The BMJ paper described the framework developed at that time by NICE and piloted it in our setting". (Participant 08)*
ACA framework	*"We have highlighted the methods in South Africa, and published this resource, and I could give you the references to this methodology. In some cases, questions could either be adopting" (Participant 10)*
DELBI	*"We do have a national version of the AGREE II instrument, which called DELBI, that is complemented with four specific questions to consider when it comes to guideline adaptation. Most group of our country did not use the whole ADAPTE instrument, but rather consequently used the four questions in DELBI." (Participate 03)* *"We use the DELBI to assess the guideline methodology quality. But when group adapting, they use question 30-34 to inform their process." (Participate 06)*
Adaptation Experience	*"I am trying to think the process. They don't have a standardised guideline development or adaptation protocol in the country. A lot of kinds of process will be in a national process and there will be a specific health questions and PICO. Then we will be asked to conduct SR, and then what we do have in that particular process is that the SR would including first to look at what guidelines are out there, and then we will look at what SRs are out there before we conduct our systematic review. If there is a guideline of good quality, those are the recommendations" (Participant 09)*

Details of newly identified methodology and organizations:

1. DynaMed editorial methodology [3]: DynaMed is a clinician-focused tool designed to facilitate efficient and evidence-based patient care. They review the medical literature daily and updates their CGs. However, Dynamed also adapts CGs when those retrieved reflect relevant differences with the original one.

2. American Society of Clinical Oncology (ASCO) CG endorsement/adaptation methodology [4]: ASCO is a scientific society that provides CG endorsement and adaptation for those resource constrained settings.
3. American College of Physicians (ACP) guidance statement [5]: ACP is a medical-specialty society that develops CG statements when CGs are controversial and finally achieve the adoption or adaptation.
4. Cancer Care Ontario's (CCO) endorsement protocol [6]: The CG development program of the CCO provides CG endorsement/adaptation of high-quality CGs from other authorized institutions.
5. German Instrument for Methodological Guideline Appraisal (DELBI) [7]: The Association of the Scientific Medical Societies in Germany (AWMF) developed DELBI to provide CGs as well as adaptation approval and registration in Germany. Guideline adaptation groups (GAGs) in Germany also use DELBI to inform their adaptation process.
6. Piloted adaptation Framework [8]: The Indian Ministry of Health and Family Welfare raised a call for adaptation process and piloted the adaptation framework developed by NICE in India context.
7. Adopt–Contextualise–Adapt (ACA) framework [9,10]: Based on a long-term partnership with the International Centre for Allied Health Evidence (iCAHE), one health centre in Philippines developed the ACA framework for practising CGs adaptation with adopt (no modifications from source CGs), contextualized (tailored for target context), and adapt (modified the evidence and recommendations) components.

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Table 1. Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No Item	Guide questions/description	Page (No.)
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	Page 5
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	Page 5
3. Occupation	What was their occupation at the time of the study?	Page 5
4. Gender	Was the researcher male or female?	Page 5
5. Experience and training	What experience or training did the researcher have?	Page 5
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	Page 5
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Page 5
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	Page 5 and 10
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Page 5
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	Page 5
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	Page 5
12. Sample size	How many participants were in the study?	Page 6
13. Non-participation	How many people refused to participate or dropped out? Reasons?	Page 6 and 21 (Figure 1)
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	Page 5
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	Page 5
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	Page 6
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Page 5
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	Page 5
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	Page 5
20. Field notes	Were field notes made during and/or after the interview or focus group?	Page 5
21. Duration	What was the duration of the interviews or focus group?	Page 5
22. Data saturation	Was data saturation discussed?	Page 6
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	Page 5
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	Page 5

25. Description of the coding tree	Did authors provide a description of the coding tree?	Page 5 and 16-20
26. Derivation of themes	Were themes identified in advance or derived from the data?	Page 5
27. Software	What software, if applicable, was used to manage the data?	Page 5
28. Participant checking	Did participants provide feedback on the findings?	Page 5
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number	Page 15 and appendix 2
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Page 6-8 and 15-20
31. Clarity of major themes	Were major themes clearly presented in the findings?	Page 6-8
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Page 6-8

Resources from: Allison Tong, Peter Sainsbury, Jonathan Craig, Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups, International Journal for Quality in Health Care, Volume 19, Issue 6, December 2007, Pages 349–357.
Also see from: https://www.equator-network.org/reporting-guidelines/coreq/

BMJ Open

Current practices and Challenges in adaptation of Clinical Guidelines: A qualitative study based on semi-structured interviews

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-053587.R1
Article Type:	Original research
Date Submitted by the Author:	07-Sep-2021
Complete List of Authors:	Song, Yang; Institut d'Investigació Biomèdica Sant Pau IIB Sant Pau, Iberoamerican Cochrane Centre Ballesteros, Monica; Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública Li, Jing; Vall d'Hebron Hospital Universitari, Research Institute (VHIR), Universitat Autònoma de Barcelona Martínez García, Laura; Institut d'Investigació Biomèdica Sant Pau IIB Sant Pau, Iberoamerican Cochrane Centre; Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública Niño de Guzman, Ena; Institut d'Investigació Biomèdica Sant Pau IIB Sant Pau, Iberoamerican Cochrane Centre Vernooij, Robin W.M. ; University Medical Centre Utrecht Department of Neurology, and Hypertension; Julius Center for Health Sciences and Primary Care Akl, Elie; McMaster University HEI; American University of Beirut, Department of Internal Medicine Cluzeau, Francoise; Consultant Alonso-Coello, Pablo; Institut d'Investigació Biomèdica Sant Pau IIB Sant Pau, Iberoamerican Cochrane Centre; Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública
Primary Subject Heading:	Evidence based practice
Secondary Subject Heading:	Health services research, Global health, Public health, Qualitative research
Keywords:	Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, QUALITATIVE RESEARCH, STATISTICS & RESEARCH METHODS

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Current practices and Challenges in adaptation of Clinical Guidelines: A qualitative study based on semi-structured 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 semi-structured 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 three 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, 2) assessment of source materials (guidelines, recommendations, and evidence level), 3) decision-making process, 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.

Keywords

Practice Guideline, adaptation, qualitative research, evidence-based practice.

Words count

Abstract	274/300
Manuscript	4045/5000

Abbreviations

AGREE II	Appraisal of Guidelines for Research & Evaluation II
CG	Clinical Guideline
CoI	Conflicts of interest
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
HIC	High-Income Country
LMIC	Low/Middle-Income Country
SR	Systematic Review

Strengths and limitations of this study

- To ensure participants' representativeness, we invited CG adaptation experts through different ways, including adapted CGs, attendees from the G-I-N 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 underreported in our study due to small the sample size and fewer participants from Low/Middle-Income Countries (LMICs).

1. 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 to 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 (9), Adapted ADAPTE (10), Alberta Ambassador program adaptation phase (11), GRADE Evidence to Decision frameworks for adoption, adaptation, and *de novo* development of trustworthy recommendations (GRADE-ADOLOPMENT) (4), Making GRADE the irresistible choice (MAGIC) (12), RAPADAPTE for rapid guideline development (13), Royal College of Nursing (RCN) (14), and Systematic Guideline Review (SGR) (15). Most of these frameworks are based on the ADAPTE tool (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 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 three years (7). Besides, most adaptation frameworks require methodology expertise; this might be a barrier for many CG adaptation groups, especially those from low/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.

2. 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 COREQ (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".

2.1. Participants

We sampled a group of CG developers, who had been involved in CG adaptation over the past three 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) (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 e-mail with an invitation letter including 1) an introduction to the RIGHT-Ad@pt project, 2) the eligibility criteria, 3) the purpose of the semi-structured interview, 4) the topics to be discussed, and 5) the expected contribution from participants. We sent two e-mail reminders within one 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.

2.2. 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 (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 minutes. We audio-recorded each interview with the participant's permission. One researcher (YS, PhD(c), female, with guideline development and adaptation experience) conducted the semi-structured interviews and transcribed them verbatim.

2.3. 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 semi-structured 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 (PAC) reviewed the framework and themes. A final structure was confirmed by discussion and approved by consensus. We used NVivo (version 12 for Mac, QSR International) for qualitative analysis (31).

2.4. Ethics approval

The protocol obtained a waiver 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). We anonymised all collected data.

2.5 Patient and public involvement

The patient and public were not involved in the study.

3. 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 semi-structured 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.

3.1. 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 (HIC) (60%; 6/10). Most participants had over five years of experience in CG adaptation (70%; 7/10). Most of the included organisations were research/knowledge-producing centres (67%; 6/9), had over five 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 two 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 co-author of published adaptation methodology. Other participants have nothing to declare.

3.2. Reasons for adapting Clinical Guidelines

We identified four main reasons for CG adaptation (Table 2, 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. 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.

3.3. 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 DELBI to inform the CG adaptation process in their setting (38). Lastly, one participant reported not using a formal methodology. See 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 (ACA) framework (36)

3) American College of Physicians (ACP) guidance statement (34)
4) American Society of Clinical Oncology (ASCO) CG endorsement/adaptation methodology (32)
5) Cancer Care Ontario's (CCO) endorsement protocol (35)
6) DynaMed editorial methodology (33)
7) German Instrument for Methodological Guideline Appraisal (DELBI) (38)
8) GRADE-ADOLOPMENT framework (4), and
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):

I. Selection of CG 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, 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).

II. 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-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 (e.g., 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 didn't clearly answer all the key questions; 2) it wasn't adequately searched or appraised; 3) it was considered outdated (e.g., more than three years since the last search), or 4) when panel experts recommended it (Table 2, Appendix 03).

III. 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.

IV. 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).

3.4. Challenges for adapting CGs

Most participants reported challenges to the adaptation and development of CGs in general (Table 2, 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 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, Appendix 03):

I. 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 (e.g., acceptability or feasibility), or formulating new recommendations (e.g., new recommendations for subgroup population); and 3) at evidence level, by supplementing with new evidence (e.g., local data). Finally, participants stated that differences and modifications were reported or documented along with the adapted CG.

II. 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.

III. 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 (e.g., 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.

IV. 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 (e.g., policymakers, primary carers, or CG adaptation panel) or literature search (e.g., 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.

4. 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.

4.1. 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). Fevers et al. in 2006 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; Fevers 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.

4.2. 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 (e.g., intensity and complexity of adaptation process, limitations of source CGs, and implementation barriers). However, some specific challenges, such as specific contextualisation issues, would be under-reported 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.

4.3. 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.

4.4. 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.

Acknowledgements
Yang Song is a doctoral candidate at the Paediatrics, Obstetrics and Gynaecology and Preventive Medicine Department, Universitat Autónoma de Barcelona, Barcelona, Spain.

Author's contributions:
YS, PAC, LMG, MB, EAA, FC, and RWMV participated in protocol drafting. YS collected and analysed data. MB and JL reviewed the data for accuracy. ENDG provided methodological contributions for the data analysis. YS and PAC interpreted the results and wrote the first draft of the manuscript. All authors critically reviewed the manuscript and approved its final version.

Funding:
YS is funded by China Scholarship Council (No 201707040103).

Competing interests: EAA has intellectual CoIs related to his contribution to the development of methods of guideline adaptation, the RIGHT statement and methodological studies in the field. All other authors have nothing to declare.

Data Availability Statement: All relevant data were included.

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Tables

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[ʃ]	7 (70)
Methodological experience in adapting CGs[ʃ]	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)

Abbreviation: CGs – Clinical Guidelines. *One expert is from Australia but develops CG adaptation in Philippines, we classified the country as Philippines. [#]Participation in a CG development/adaptation group at least once in the past year. [ʃ]Participation in a CG technical team at least once in the past year or participation in methodological research.

Table 2. Views and experiences of CG adaptation

Themes	Number 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
CG adaptation challenges	
- 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 (e.g., 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 (e.g., 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	
• Modifying the practice instead of change recommendations	1
• Modifying the recommendations	1
- Reporting the differences	4

Abbreviation: CGs – Clinical Guidelines.

Table 3. Main steps of the adaptation process

Adaptation methodology /Year	Selection of CG 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 & 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 [a] ○ 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 five 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 (e.g., 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 (e.g., 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
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 (e.g., 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]	○	Checking Evidence to Decision frameworks availability of source CGs	○	Preparing GRADE Evidence to Decisions frameworks and review by an expert panel	○	NA			
	○	Questions prioritisation by the panel from selected source CGs	○	Completing the GRADE Evidence to Decision frameworks	○	Formulating recommendations through consensus or voting					
			○	Updating systematic reviews of health effects and identifying local data [h]							
Piloted adaptation framework 2017 (8)	○	CG topic prioritisation and Ministry of Health approval	○	Source CG quality assessment [i]	○	Adopted/adapted/new recommendation compilation	○	External review			
	○	CG search from National guideline Clearinghouse	○	Identifying relevant recommendations from source CG(s) based on panel expertise and clinical practice settings	○	Expert review	○	Online access for public consultation			
							○	Updating			
Adaptation experience 2019	○	Predefining health questions [6]	○	Source CG quality assessment using AGREE II [j]	○	Evidence review from source CG(s)	○	National external review [ł]			
	○	Searching for existing CG [6]	○	Identifying evidence from the most up-to-date CGs [j]	○	Decision-making by national-level experts with no further details provided [μ]					
			○	Underlying evidence review [j]							

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:

α: 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)

d: 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)

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)

ł 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)

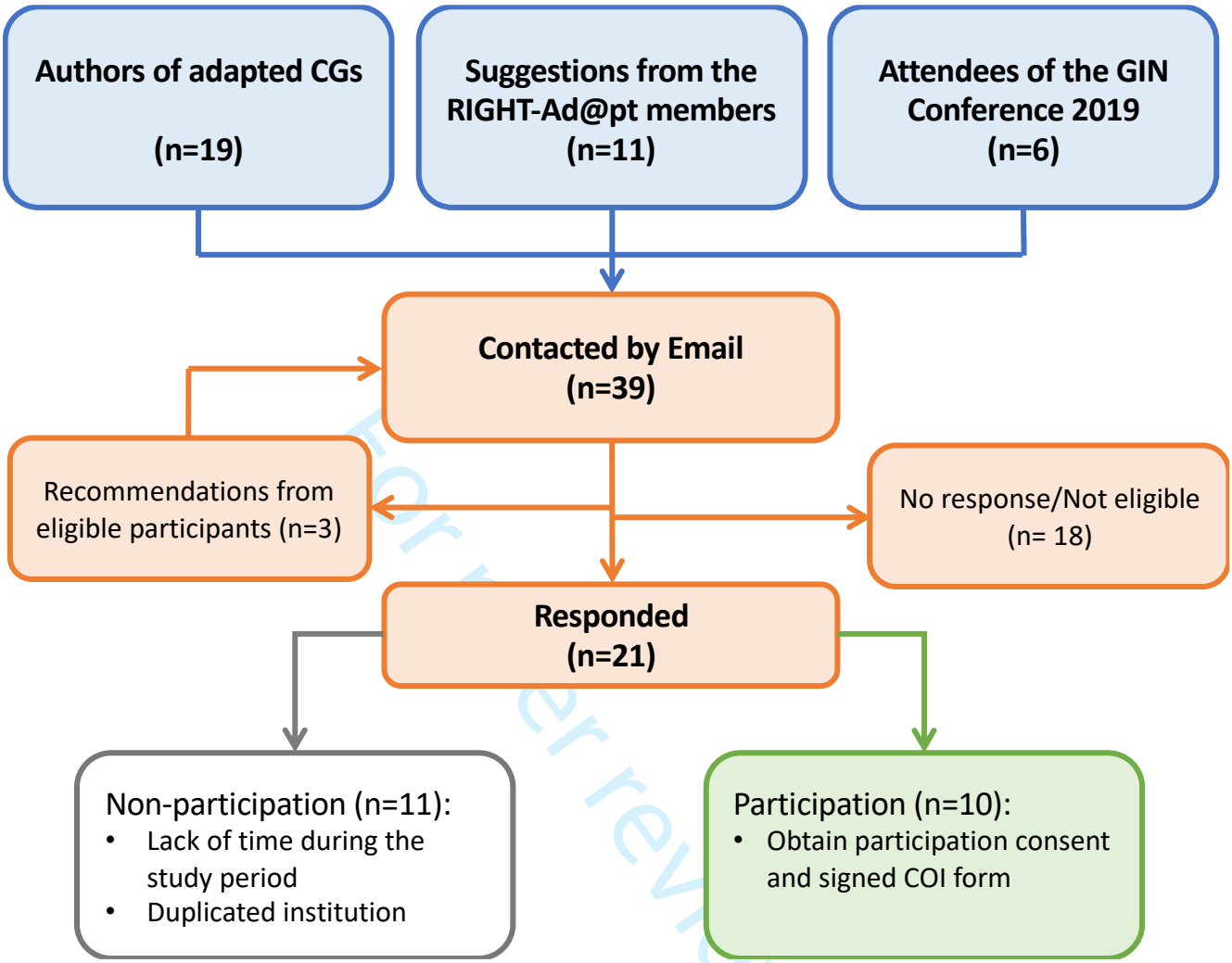
Abbreviations: AGREE II – Appraisal of Guidelines for Research & Evaluation II; CCO: Cancer Care Ontario; CGs – Clinical guidelines; CoI – Conflict of interest; DELBI is a CG assessment tool used by adaptation group to inform CG adaptation; GRADE – Grading of Recommendations, Assessment, Development and Evaluations; NA – Not applicable; NICE – National Institute for Health and Care Excellence; SR – Systematic review.

Figures

Figure 1. Participant recruitment flow diagram

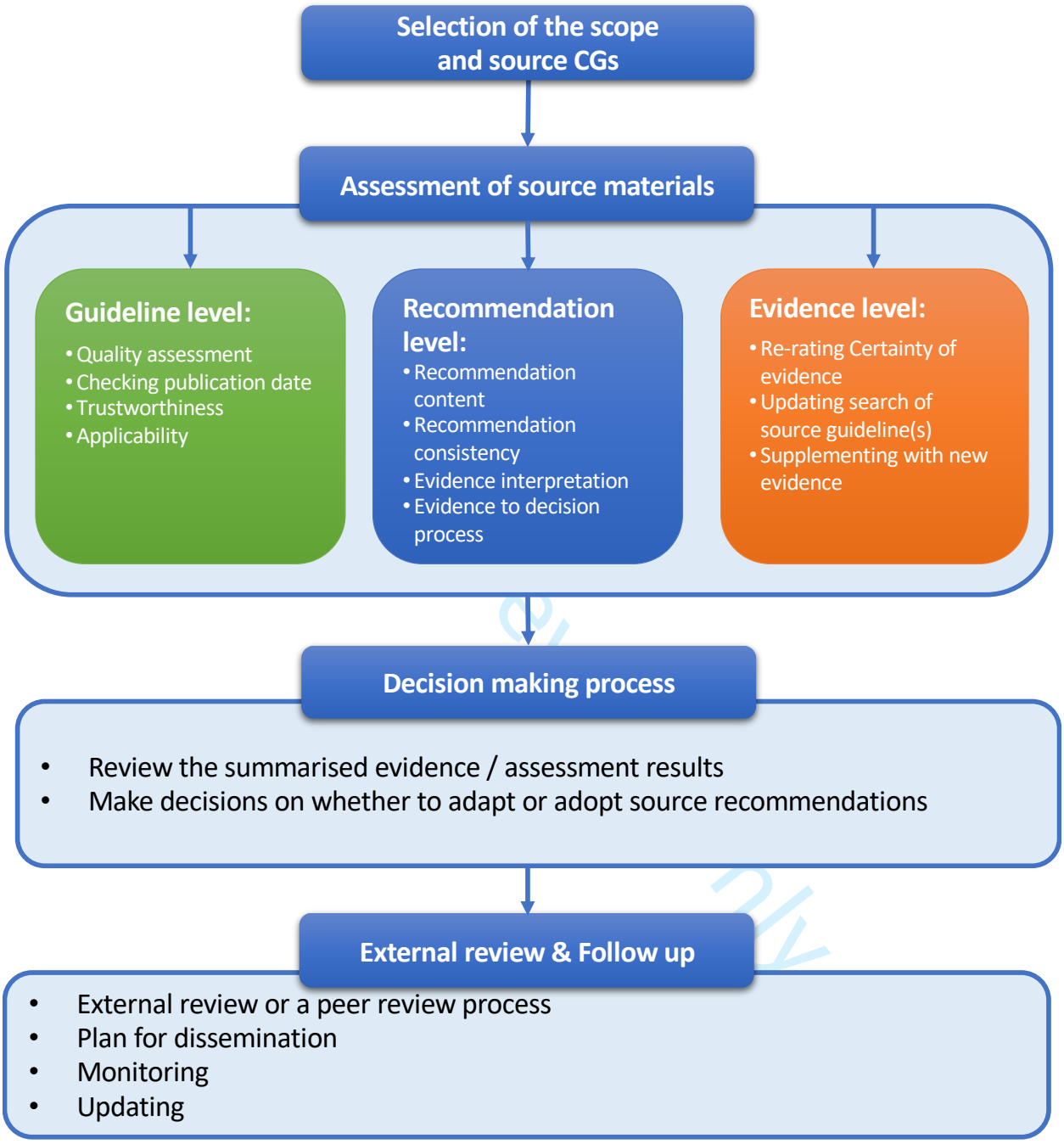
Figure 2. Main steps of the adaptation process

Figure 1. Participant recruitment flow diagram



* Relevant conference attendees were identified by screening the list of conference attendees and oral presentation regarding CG adaptation.
Abbreviations: CoI: conflict of interest, CGs: clinical guidelines, GIN: CGs International Network.

Figure 2. Main steps of the adaptation process



Abbreviations: CGs: clinical guidelines.

Appendices

Appendix 01. Identification of published adapted CGs

One author (YS) screened and selected adapted CGs based on pre-established eligibility criteria: "adapted guidelines", "reported at least one recommendation", "described the adaptation process", and "published in English". Another author (RV) double-checked the findings. We contacted the first author of adapted CGs for participation. If the first author did not respond, we contacted the corresponding author. If they could not participate, we requested they recommended another potential participant. We finally identified 472 records from the pragmatic search, after removing the duplicates and screening title and abstract, we reviewed 41 full texts and 16 adapted CGs to extract contact information.

The pragmatic search strategy of published adapted clinical guidelines and included studies

Search strategy (PubMed from 1992 December to 2019 September)	
#1	"Practice Guidelines as Topic"[Major]
#2	Practice guideline*[tiab]
#3	Clinical guideline*[tiab]
#4	Evidence based guideline*[tiab]
#5	Guideline*[ti]
#6	Recommendation*[ti]
#7	Adopt*[ti]
#8	Adapt*[ti]
#9	Adaptation[tiab]
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6
#11	#7 OR #8 OR #9
#12	#10 AND #11
Included studies	
1	Nishiyama H. Asia Consensus Statement on NCCN Clinical Practice Guideline for bladder cancer. Jpn J Clin Oncol. 2018;48(1):3-6.
2	Guideline Adaptation Committee. Clinical Practice Guidelines and Principles of Care for People with Dementia. Sydney. Guideline Adaptation Committee; 2016.
3	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.

4	Hu J, Yu L, Jiang L, Yuan W, Bian W, Yang Y, et al. Developing a Guideline for Endotracheal Suctioning of Adults With Artificial Airways in the Perianesthesia Setting in China. J Perianesth Nurs. 2018.
5	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.
6	CAN-ADAPTT. (2011). 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.
7	Remington G, Addington D, Honer W, Ismail Z, Raedler T, Teehan M. Guidelines for the Pharmacotherapy of Schizophrenia in Adults. Can J Psychiatry. 2017;62(9):604-16.
8	Pringsheim T, Addington D. Canadian Schizophrenia Guidelines: Introduction and Guideline Development Process. Can J Psychiatry. 2017;62(9):586-93.
9	Laver K, Cumming R, Dyer S, Agar M, Anstey KJ, Beattie E, et al. Evidence-based occupational therapy for people with dementia and their families: What clinical practice guidelines tell us and implications for practice. Aust Occup Ther J. 2017;64(1):3-10.
10	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.
11	Kim KI, Jung HK, Kim CO, Kim SK, Cho HH, Kim DY, et al. Evidence-based guidelines for fall prevention in Korea. Korean J Intern Med. 2017;32(1):199-210.
12	Novo A, Subotic-Popovic A, Strbac S, Kandic A, Horga M. Application of Agree II Instrument for Appraisal of Postpartum Hemorrhage Clinical Practice Guidelines in Bosnia and Herzegovina. Acta Inform Med. 2016;24(3):211-4.
13	McGowan J, Muratov S, Tsepke A, Issina A, Slawecki E, Lang ES. Clinical practice guidelines were adapted and implemented meeting country-specific requirements–the example of Kazakhstan. J Clin Epidemiol. 2016;69:8-15.
14	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.
15	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.
16	Abdollah Zadegan S, Ghodsi SM, Arabkheradmand J, Amirjamshidi A, Sheikhrezaei A, Khadivi M, et al. Adaptation of Traumatic Brain Injury Guidelines in Iran. Trauma Mon. 2016;21(2):e28012.

Appendix 02. Interview Open-ended questions

Section 1: Characteristics of participants	
Questions	**Probes/Answers**
Country	
Organisation	
Please choose the option that best describes **your organisation**	☐ Hospital ☐ Primary care / General practice ☐ Research / Knowledge production organisation ☐ Service provider organisation (community) ☐ University ☐ Other
If OTHER, please specify	
How many years of experience in guideline adaptation do you have?	
Please choose the option that best describes your current experience in the **health-related guidelines field** (please select all that apply)	☐ **Experience in developing** clinical guidelines (participation in a guideline development group at least once in the past year). ☐ **Experience in adaptation** clinical guidelines (participation in a guideline adaptation group at least once in the past year). ☐ **Methodological experience in developing** clinical guidelines (participation in a guideline technical team at least once in the past year and/or participation in methodological research). ☐ **Methodological experience in adaptation** clinical guidelines (participation in a guideline technical team at least once in the past year and/or participation in methodological research). ☐ Clinical guidelines **user** (use of clinical guidelines on a daily basis). ☐ Other: ( )
Section 2. Characteristics of health-related guideline developing organisation	
Questions	**Probes/Answers**
Does your organisation **develop** health-related guidelines (HRGs)?	☐ Yes ☐ No ☐ Do not know
How many HRGs has your organisation published?	
How many years has your organisation been developing HRGs?	
What is the **average size** of your HRG development group?	
Does your organisation **adapt** HRGs?	☐ Yes ☐ No ☐ Do not know
How many adapted HRGs has your organisation published in the last 3 years?	
How many years has your organisation been adapting HRGs?	
What is the average size of your adaptation group?	
What is the average time for your organisation to develop an adapted guideline?	☐ 0 – 1 year ☐ 1 – 2 years

	☐ 2 – 3 years ☐ ≥ 3 years
Which role does your guideline adaptation group include?	1. Clinicians 2. Patients 3. Methodologists 4. Policy makers 5. Other roles If other, please specify _____
Section 3. Current practices regarding guideline adaptation in your organisation	
Questions	**Probes/Answers**
1. What is the trigger for your organisation to adapt source guideline(s)?	☐ Implementing the source guideline in your setting ☐ Developing a *de novo* guideline ☐ Others ☐ Do not know
If others, please specify:	
2. Could you please describe the **adaptation process** or which **framework or methods** your organisation used for guideline adaptation?	☐ ADAPTE 2010 based ☐ GRADE based (MAGIC, GRADE-ADOLOPMENT) ☐ Others
If others, please describe and provide citations (if applicable):	
3. Does your organisation **assess the quality, currency, or content** of the included source guideline(s)?	☐ Yes ☐ No
If yes, how does your organisation assess those aspects? Please specify	
4. Does your organisation consider the **difference** between source guideline(s) and target context? Like the population, the setting/health systems, or practice variation/target users?	☐ Yes ☐ No
According to your experience, how does your organisation solve the differences? Please specify	
5. Does your organisation assess the **consistency** of the included source guideline(s)? (Only when ≥ 1 source guideline included)	☐ Yes ☐ No ☐ Only one source guideline included, not applicable
According to your experience, how does your organisation solve the inconsistency? Please specify	
6. Does your organisation consider **other systematic reviews/new evidence** that might not be included in the source guideline(s)?	☐ Yes ☐ No
According to your experience, how does your organisation consider other systematic reviews or new evidence?	☐ Incentive of starting ☐ Literature search ☐ Experts' groups ☐ Others
If using other methods, please describe:	
7. Does your organisation typically consider **constrains/barriers** like legislation, policies, or healthcare-setting resources that might impact the implementation when adapting?	☐ Yes ☐ No

According to your experience, how does your organization consider implementation barriers?	
8. Does your organisation externally review the guidelines you adapt prior to publication?	☐ Yes ☐ No ☐ Do not know
9. What is the funding source for guideline adaptation in your organisation?	
Section 4. Challenges during guideline adaptation process	
Questions	**Probes/Answers**
1. According to your experience, which part **is the most challenging** for your organisation when adapting guidelines?	☐ Choosing the health question ☐ Searching for evidence (source guidelines or systematic reviews) ☐ Evaluating the evidence (source guidelines or systematic reviews) ☐ Making recommendations from evidence ☐ Implementation
If others, please describe the identification process:	

Appendix 03. Views and experiences on guideline adaptation

Themes	Quotations
Question: What is the trigger for your organisation to adapt source guideline(s)?	
Developing their guidelines (7 Participants)	✔ **As part of *de novo* guideline development process (3 participants):** *"The trigger will be for developing a de novo guideline. We adapt multiple guidelines at a time. The multiple guidelines are usually developed in countries like the UK, Canada, the US etc. Then we adapt those for those resources constrain setting." – (Participant 02)* *"For developing de novo guideline. Basically, we are based on the evidence from existing evidence and then may search for new evidence" – (Participant 04)* *"Generally, we develop our research question and search for evidence/source guidelines to answer our question. If we find a guideline that answered our question, that is the trigger for us to adapt the guideline potentially." – (Participant 05)*
	✔ **Avoiding duplicates and saving efforts (1 participant)** *"Basically, the trigger is to avoid the duplication of the guideline development efforts. Especially the searching and appraising the primary evidence. We advise them to use aggregate evidence before they do their own research. This is one hand, and for another hand will pause to do systematic reviews" (Participant 03)*
	✔ **Saving resources and time (3 participants)** *"If the guideline group plan to develop a new guideline, they will search for the existing evidence first. However, in the process of adaptation, they always realise that they could not only implement a source guideline because there is some difference between the target settings. If there is already evidence-based up to date guidelines, groups want to use them for their own guideline to avoid or minimise efforts of systematic searches." (Participant 06)* *"First, to say primarily, the first we don't want to spend resources on developing de novo. Ideally, we would adapt the source guideline(s). The first trigger for adaptation is that we want to limit the cost and to save resources." (Participant 09)* *"We needed to develop in a short period, and we did not have enough money and people to be involved." (Participant 10)*
Implementing/Endorsing for target settings (5 participants)	✔ **Implementing (3 participants)** *"Given time and resource constraints, the task force discounted developing new guidelines and opted to adaptation. We use a pragmatic method by which evidence-based guidelines could be adapted to suit our context. New review questions were recommended only for areas not covered by existing guidelines." (Participant 08)* *"Government support to adapt for implementation: To be realistic, sometimes the policies or others suggest there is a need to adapt." (Participant 09)*

	"We were consulted to assist in developing guidelines that were relevant and implementable in a resource-limited setting." (Participant 10)
	✔ **Endorsing (2 participants)** *"We also do guideline endorsement; sometimes, other organisations come to ASCO to ask us to endorse their guidelines. This could be the single source guidelines. We ask our panel to not change anything of the source guideline(s). In minority times, they made some modifications based on other processes of our own. It's a similar process with what we called adaptation." (Participant 02)* *"We will not search for new evidence when endorsement or adaptation if the source guideline did not answer all of our questions, we will conduct the new systematic review for the rest questions". (Participant 05)*
Updating existing guidelines (3 participants)	*"We will update our guideline when a new guideline comes out by considering whether the new guideline will change our guideline or not, if so, we will adapt/adopt to our topic" (Participant 01)* *"When updating an existed guideline, the group will want to adapt a good guideline when updating. We will first look at the existing guideline if you could make a single recommendation, so in some updated guidelines they choose to adapt two of the recommendations, they made also search for systematic reviews, so another five recommendations are based on systematic reviews, and other recommendations are based on primary studies. Other recommendations are based on experts' consensus." (Participant 06)* *"The other trigger for adaptation could also be when new evidence showing up, and if new primary evidence changes the recommendations/practice, we will choose adapted the recommendation, to be realistic." (Participant 09)*
Controversial existing guidelines(1 participant)	*"We do adaptation only when guidelines are controversial, and we intend to harmonise the guidelines." (Participant 07)*
Question: According to your experience, which part is the most challenging for your organisation when adapting guidelines?	
Poor reporting or limitations of source guideline(s) (2 participants)	*"The most challenging is the guidelines often do a **very poor reporting** of how they make their decision exactly what was based on, what value they were considering, what methodology is, what is the evidence. So sometimes you get the recommendations, but you don't get the why, and you don't get what evidence they considered, and how they rate it and understand it. So poor reporting would be the biggest challenging part for adaptation." (Participant 01)* *"This is most challenging because as a methodologist I have not read all the evidence, I haven't searched for it all, so I don't know it well. If there are all guidelines and they all consistency, and they all have the same kind of evidence, and then I feel more confident. Sometimes I do a quick search to see if something is outside the source guideline, but really I rely on my experts' panel in this field if they can endorse these recommendations pretty much as it is and if they think the new evidence is going to change the recommendations." (Participant 05)*

Limited skills in advanced guideline development and adaptation (3 participants)	*"I would say* evaluating the evidence (source guideline or systematic reviews) is the most challenging part. *We don't look at the methods the source guideline(s) used for the evidence appraisal. We reevaluated the quality and certainty of the evidence from source guidelines by ourselves." (participant 07)* *"I want to say all of these are challenging. Because I think health questions are difficult for people to phrase, people don't have technical skill for searching evidence, we have limited skill to appraisal and identify guidelines that we are using, and there have very few groups that have specific methods to move evidence to a decision." (Participant 09)* *"Framing the health question: sometimes the experts even could not draft the health question correct； Choosing the health question; Searching for evidence (source guideline or systematic reviews) and making recommendations from evidence" (Participant 10)*
The intensity in terms of resources and time for adaptation (2 participants)	*"They have to go down to two-level to see the basis of adaptation. But we don't want them to spend a lot of time to see the weeds of primary evidence. We want them to kind of be able to go from the recommendation level directly." (Participant 02)* *"For the guideline development groups, the greatest challenging **is very time-consuming**. Also, **the resource intense**. Or do I need to do an extra evaluation of the source guideline is not good enough?" - (Participant 03)*
Challenges arising from specific steps of adaptation process	✔ Addressing context differences between source CGs and adapted CG **(including reporting the differences) (4 participants)** *"Sometimes, they also are struggling with translating the evidence to recommendations, because the evidence just not fit to the target population. It is a typical problem of indirectness or imprecision of these things." (Participant 03)* *"I think choosing the health questions and also making the recommendations from the evidence-based on our characteristic. Not all the clinical questions are the same for our region because the character is different" (Participant 04)"* *"We suggested guideline adaptation group to justify the deviations from source guidelines, but regularly they do not include the reason (reporting). When we ask to clarify the deviations, they said it is too difficult for them to report the reason for deviations. I think it is really too difficult for them to explain. I think this is the real challenging for them because this issue was really discussed in a consensus conference, but nobody really reports the augments (reporting)." (Participant 06)* *"The real challenge when you put guidelines together is that you would probably know different guideline groups do their methods differently." (participant 10)* ✔ **Addressing inconsistency and integrating recommendations from** different source CGs **(3 participants)** *"I would say it related to the "**making evidence to recommendations**". From our adaptation experience, you know you have the extra layer, the source guideline, the SR that described and to inform the recommendations, and the basic primary studies; then we come into the adaptation, they have to go down to two-level to see the basis of adaptation. But we don't want them to spend a lot of time to see the weeds of primary evidence. We want them to kind of be able to go from the recommendation level directly.*

	For solving the inconsistency of recommendations is also a challenging part" *(Participant 02)* *"I would say* ***making recommendations from Evidence.*** *If there are evidence that may change the recommendation; is the guideline suitable for our setting? Because it is the link between evidence and recommendations. For adaptation for us is the same with endorsement. If we need to make major change of the recommendation, we will need to develop our own recommendations." (Participant 05)* *"There wasn't enough guidance for how to adapt a guideline and even now.* ***There was very limited to no evidence in how recommendations from multiple sources can be put together.*** *Because most of the adapted guideline in practice they only chose one guideline." (Participant 10)* ✔ **Updating or supplementing additional research evidence (1 participant)** *"The evidence base of the source guidelines was complemented by systematic update searches of primary evidence." is a challenge for guideline adaptation group. (Participant 06)*
Implementation barriers (5 participants)	*"The very most challenging is stratifying the recommendations, decided them into different practice settings" (Participant 02)* *"Also, I do believe that like many organisations, implementation is also a great challenge. We do our best to develop our guidelines, but implementation still is a hot topic." (Participant 03)* *"And implementation is a whole separate thing and also challenging". (Participant 09)* *"Required the resources which might not apply in the target setting. For example, diabetic foot, the evidence and recommendations suggested to conduct yearly foot assessment, however, in practice, none of the clinicians knows how to do a foot examination; Also adherence to the guideline recommendation in the culture of Indian would also be challenging." (Participant 08)* *"For example: for our setting, who is the best health professional you should contact or deliver the care, and that is a very local context field. Because in some setting maybe they only have a nurse." (Participant 10)*
Question: According to your experience, how does your organisation consider the difference between source guideline(s) and target context? Like the population, the setting/health systems, or practice variation/target users?	
Experts' opinions and panel discussion (7 participants)	*"In general, we address the differences according to the feedback from international panel experts/clinicians." (Participant 02)* *"Mostly addressed in group discussions, when it comes to reviewing the source guidelines. Then decide if they adopt them or they check if they are adoptable for the national systems. So mostly it's experts' opinions that come in." (Participant 03)* *"We made a group discussion; all the participants of my study attend to a seminar and discuss their opinion about the differences." (Participant 04)*

	"We are looking for the similar guidelines. If there are differences, we discuss through our panel and decide to use it or not." (Participant 05) *"Some group solve differences by discussion or consensus." (Participant 06)* *"By discussion within the development group and acknowledge the difference in a document." (Participant 08)* *"They solve the differences by discussion in the panel, and they may come to a consensus." (Participant 09)*
Modifying for the target context	***At the guideline level:*** ✔ ***Prioritising* the source guideline according to different factors (3 participants)** *"We do prioritise according to language because we are working in English. First, by prioritisation according to the quality of guideline development organisation, published in English, and sometimes for the global population, which means, common users of our guidelines." (Participant 01)* *"You have to look at each guideline methodologically and to see which one is regularly doing and try to lean towards that but also really on AGREE ii instrument evaluation as well and use that to filter which is a good guideline and which is not. The methodological rigorous is important, but on top of that is the interpretation of the evidence and do recommendations. And often look at the evidence directly as well." (Participant 07)* ✔ ***Discarding source guideline (1 participant)*** ***"****We develop our own research question. If the source guideline did not answer our question, we will not consider using them. For example, we are looking for the similar guidelines. If there are differences, we discuss through our panel and decide to use it or not." (Participant 05)* ***At the recommendation level:*** ✔ ***Modifying strength of the recommendations (1 participant)*** *"If there is not certain difference between population, but different considerations or opinions, we will rate down certainty due to inconsistency; If the guidelines are from different regions, we may give weak recommendation with documented justifications." (Participant 01)* ✔ ***Contextualizing by considering different factors (3 participants)*** *"The working group judge whether to adapt according to the context/new balanced benefits and harms and decide through discussion." (Participant 06)*

	"The recommendation could be changed due to the difference of health settings/target users/population; we request the guideline development group to provide those modifications as well as the justifications." (Participant 08) *"I think this was most helpful about the Evidence to decision framework. Because even if the recommendations were come from other setting, you will go through the acceptability, feasibility. In feasibility, if a drug is not available in your country or you need a different formulation, or the price is inaccessible, then it will influence the recommendations. After the decision was made by the guideline panel, the recommendations will go to another level of group for considering whether it is justified and feasible. So, this is a kind of internal quality insurance." (Participant 09)* ✔ ***Making a recommendation for subgroup population (1 participant)*** *"If there is a certain difference between population, we do a subgroup population and mark clearly which population suits which context." (Participant 01)* ***At the evidence level:*** ✔ ***Supplementing new evidence/other considerations (2 participants)*** *"Also, we do check the existing policies that need to be addressed. It is not systematically searchable, but it is addressed by group discussion." (Participant 03)* *Even at the start, the questions can be contextualised. Which question and which guideline should we practice? Sometimes we did not find any answers. Hence, for some recommendations, we consider some source of information from the local context." (Participant 10)*
Reporting the differences when drafting the recommendation (3 participants)	*"If there is a certain difference between population, we do a subgroup population and mark clearly which population suits which context; If the guidelines are from different regions, we may give weak recommendation with documented justifications." (Participant 01)* *"By discussion within the development group and acknowledge the difference in a document. We request the guideline development group to provide those modifications as well as the justifications." (Participant 08)* *"We did not put them together but will report in the appendix." (Participant 10)*
Question: According to your experience, how does your organisation solve inconsistency of recommendations from different source CGs?	
Panel discussion (2 participants)	*"We deal it more by discussion. There is not a table or formula to tell you how to deal with inconsistency; you have to figure out the reasons for the inconsistency." (Participant 01)* *"I would say that is a challenging part. We do a discussion about the inconsistency and then we do generate the strength of the recommendation based on published criteria." (Participant 02)*
Selection criteria (At the guideline level)	✔ ***Good quality and rigorously developed (1 participant):***

	"We use matrixes/tables to map the differences. Sometime if they have a good guideline, they will stop to search another guideline. We Used AGREE II to identify the methodological quality of the guidelines and prioritised by methodology sound recommendations." (Participant 03) ✔ ***Good quality (3 participants):*** *"We don't have a critical cut off to choose which guideline to use, we do prioritise by quality of the guideline. Some group solve differences by discussion or consensus." (Participant 06)* *"We do not have a cut-off of the AGREE score, because sometimes there are few source guidelines for the consideration of adaptation. By considering guideline quality:1) from the NGC; or 2) consider the results with AGREE II assessment." (Participant 08)* *"So, if it is coming from a higher-level study, and if it's of good quality, and if it's pointing the same direction." (Participant 10)* ✔ ***Trustworthiness, good quality, and mostly up-to-date (1 participant):*** *"We do not have a numeric cut-off for AGREE ii. We don't use a qualitative cut-off with the results of AGREE ii, but we do consider the highest quality are guidelines from well-known guideline development organisation that has used systematic reviewed based guideline development methods and has fully describe their methods.* *And we also can only adapt guidelines that were not funded by industry.* *The decision to adapt a specific guideline or guidelines, is based on:* *o the results of the content review and the level of agreement with the recommendations* *o A quality appraisal of available guideline(s)* *o the time since completion of the best available guideline(s)" (ASCO guideline development manual)" (Participant 02)* ✔ ***Up-to-date (1 participant):*** *"We don't go simply from recommendation to recommendation, we identify the evidence from the most up to date high quality guidelines, also panel will want to look at the primary studies." (Participant 09)* ✔ ***Relevant to the target context (2 participant):*** *"We did our plan to evaluate the inconsistency and solve it by considering whether it suits our context." (Participant 04)* *"Through panel discussion to make the decision whether this guideline is suitable for Ontario context or not." (Participant 05)*
Assessing the reason for inconsistency: **(At the recommendations and evidence level)**	✔ ***Assessing at recommendation level (4 participants)*** *"We gonna look into what is the recommendation. If the recommendation is different in different guidelines, then we have to figure out do we think one is right and one is wrong and explain it. Or we just say there is a reason for differences of opinion, and we give a weak recommendation overall, because they disagree. Maybe if you look carefully, the guidelines were actually focusing on different population, and there are not truly inconsistent or giving newer on the strong recommendations, in which case you may agree with both guidelines, and then present it more clearly." (Participant 01)*

	"We ask them to really compare the guideline and see where the inconsistency comes from on the level of individual recommendations." (Participant 03) *"In another case, more than one guideline was used, some groups consider the consistency by using synopsis of each recommendation and checking the inconsistency but some not." (Participant 06)* *"We have to look at the inconsistency, uninformative thoughts, the strength of recommendations that will be based on the quality of your evidence and the level of evidence." (Participant 10)* ✔ ***Assessing at evidence level (3 participants)*** *Or maybe one guideline has more evidence or more currency than the other, you may ignore the guideline that wasn't aware all the evidence when they made the recommendations. But until you understand why there is inconsistency, you can determine what to do. We don't have a comment table to work through how to do it, the team uses their judgment to explore this and use their experience." (Participant 01)* *"If there is consistency, we will only consider the SRs they are using, using other persons SR, or conduct the SR by our-selves." (Participant 05)* *"By looking at the evidence interpretation (the appraisal of the evidence, if they are not good, would go into the individual studies and reassess the quality of the evidence) the quality and rigorous of development (assessed by AGREE ii score)." (Participant 07)*
One single guideline was included (4 participants)	*"I have in the past looked at whether guidelines have recommended the same treatment. However, recently we have been selecting only one guideline to endorse/adapt." (Participant 05)* *"In one case, the group only pick up one good guideline and use it." (Participant 06)* *"We did not meet one situation of more than one guideline were included and I do not know how to solve." (Participant 09)* *"What people have done is that they chose one guideline one and adapt this guideline for their setting." (Participant 10)*
Question: According to your experience, how does your organisation consider other systematic reviews or new evidence?	
Triggers for complementing / updating the search for source guideline(s)	✔ ***Source guideline did not answer all the questions of the adapted guideline (3 participants):*** *"If the source guideline did not answer all of our questions, we will conduct the new systematic review for the rest questions." (Participant 05)*

	"If they find there is no clear answers for their question in the source guidelines, they looked at existing Cochrane SRs but do not conduct a new one." (Participant 08) *"No guideline answers your question, we do consensus process. If the source guideline has limited evidence for specific questions, we will make a consensus process." (Participant 10)* ✔ ***Source guideline(s) were outdated(1 participant):*** *"If it is a great guideline but it's 3 years old, and since then there are new primary studies come out, they will want to look at that." (Participant 09)* ✔ ***Source guideline(s) were consensus based (2 participants):*** *"Resource stratified guidelines means based on the source guidelines and considering resource use. For the source guidelines we did not do the updated;" (Participant 02)* *"For experts' consensus from source guidelines, expert panel decide sometimes in addition to do a systematic search for other aggregate sources of evidence, like Cochrane reviews, and sometimes they decide to have a full de novo search for primary evidence to answer the question." (Participant 03)* ✔ ***Expert-panel recommended it (2 participants):*** *"For the other guidelines if we adapt them, yes. In general, we may need to update the literature search if the expert panel think there are new evidence published outside the systematic reviews that particular relevant." (Participant 02)* *"We made national wide guidelines launched by the ministry of health. There are more experts connected with us to make more comprehensive guideline, and they do have other source of evidence. Our group starting by searching the databases like PubMed, etc." (Participant 04)*
If the source guideline(s) were not evidence based	✔ ***Discarded the recommendation, (1 participant):*** *"For consensus recommendations from source guidelines, sometimes the group decides to maybe discard specific recommendations from source guidelines but rather than have a consensus-based recommendation in Germany." (Participant 03)* ✔ ***Conducted consensus process, (1 participant):*** *"No guideline answers your question, we do consensus process. If the source guideline has limited evidence for specific questions, we will make a consensus process." (Participant 10)* ✔ ***Started guideline* de novo *process (3 participants):*** *Start guideline de novo process: "We will not search for new evidence when endorsement or adaptation, if the source guideline did not answer all of our questions, we will conduct the new systematic review for the rest questions. We conduct our own SRs if the source guideline did not answer our research questions. We do that only when the source guideline did not address the specific research questions in the case that we are doing multiple questions. Like if we have 5 research questions and the source guideline(s) only*

	addressed 3 of them, then we need to conduct our own SRs to address the other 2. If we have to look for new evidence, we do the literature search. But for us the adaptation doesn't means we have to search new evidence, if we have to do it, then it is a de novo process." (Participant 05) *"We only limited the evidence of the source guideline; we do not do the supplement evidence otherwise the process will be very complicate. The critical difference of the guideline adaptation and guideline de novo process is you limited the evidence within the source guidelines. You are not looking at the additional information. We don't call them recommendations; recommendations only come out of guidelines that you do yourself." (Participant 07)* *"We do not conduct new systematic reviews due to the time limitation. In the case of good guideline absence, we would consider a guideline de novo process rather than an adaptation." (Participant 08)*
Way of including new evidence	✔ ***Conducting literature search for complement evidence (6 participants):*** ***Pragmatic search (5 participants)*** *"Our group starting by searching the databases **like PubMed**, etc." (Participant 04)* *"Our guideline group will make a search for SRs." (Participant 06)* *"They did refer to the **Cochrane database**. If they find there is no clear answer for their question in the source guidelines, 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)* *"The guideline group link with organisations like the **Cochrane centre**, and all discuss very nicely to provide evidence." (Participant 09)* *"We do everything to ensure the search is comprehensive. We search for guideline has been published everywhere. For some questions we adapted, we take the new evidence around, for instance in the local context setting there might be a **new paper** that has been **published locally**, if the evidence answered the question of the local context." (Participant 10)* ***Full* de novo *search (1 participants):*** *"For experts' consensus from source guidelines, expert panel decide sometimes in addition to do a systematic search for other aggregate sources of evidence, like Cochrane reviews, and sometimes they decide to have a full de novo search for primary evidence to answer the question." (Participant 03)* ✔ ***Updating the search from source guideline(s) (3 participants):*** *"Like I said before, we conducted continuously monitoring of new evidence that relevant." (Participant 01)"*

	"In general, we may need to update the literature search if the expert panel think there are new evidence published outside the systematic reviews that particular relevant." (Participant 02) *"If it is a great guideline but its 3 years old, and since then there are new primary studies come out, they will want to look at that. If there is more up to date SR that includes additional studies, they will want to look at that." (Participant 09)* ✔ ***Experts' suggestions (3 participants)*** *"There are more experts connected with us to make more comprehensive guideline, and they do have other source of evidence. Our group starting by searching the databases like PubMed, etc. And also, experts will recommend new studies if they have one." (Participant 04)* *"Experts from our group could recommend recently RCTs apart from SRs identified from the search. But we make the process transparently reported." (Participant 06)* *"There is a committee from the national government to find some of the prestigious policy questions. We haven't been involved in any guideline for professional society or private group, we haven't been charged much for conduction reviews. The primary research we don't do. Experts will ask for relevant evidence and we will conduct the synthesis and provide to them if needed to explain or facilitate the decision making." (Participant 09)*
Question: According to your experience, how does your organisation consider implementation barriers?	
Ways to obtain the information and address it by group discussion (7 participants)	✔ ***Experts opinion, literature search, group discussion (1 participant)*** *"For the resource stratified guidelines, yes; I would say most by discussion. For example, we would include panel members who are in primary practice outside the academic medical settings, their experiences can inform what are the constrains and barriers that may impact on the implementation of recommendations. For the resource stratified guideline, we do also discussion and non-systematic environmental scan of the cost-effectiveness analysis literature. To see if the literature can influence the applicability of the implementation." (participant 02)* ✔ ***Experts opinion, literature search, group discussion (1 participant)*** *"Yes; For example, if one intervention was labelled in the US but off labelled in Germany, we asked the experts panel to assess if the evidence is really sound enough to do a such recommendation. Also, we do check the existing policies that need to be addressed. It is not systematically searchable, but it is addressed by group discussion." (participant 03)* ✔ ***Experts opinion, literature search (1 participant):*** *"Usually from the government people, they have other field angle to see how we treat disease, this is different with the way of think a clinician. But I think they based on a good tele data to make the problem understandable and solve the problem." (participant 04)* ✔ ***Experts opinion, group discussion (1 participant):***

	"We ask our panel about the feasibility of implementing a treatment and discussed within our working group by considering the context of our settings." (participant 05) ✔ ***Search, (1 participant):*** *"We only look at the cost of the intervention and look at the information available by PubMed." (Participant 07)* ✔ ***Group discussion, (1 participant):*** *"They do discuss the recommendations and to see if the recommendation is appropriate in their setting, what kind of challenging they will have when implementing the recommendations that adapted. By discussion within the guideline development group. And provide the documented acknowledge." (participant 08)* ✔ ***Literature search, Group discussion, (1 participant):*** *"We only look at the cost of the intervention and look at the information available by PubMed.* *Our group will consider at least the feasibility, and within that there will be issue of regulatory issues, ethical issues, and access issues. So, feasibility, equity and cost will be considered." (participant 09)*
Decision made after considering (2 participants)	✔ ***Modified the practice instead of changing recommendations:*** *"The source recommendations will not be change, however the practice way maybe tailored for the local context to make it applicable." (Participant 10)* ✔ ***Modified the recommendations:*** *"At least for medications, we see evidence on the use of medications, check if it's authorised to use. If it's not approved to use for any country, we won't make a recommendation to use even if there are some evidence." (Participant 01)*
Reporting the difference (4 participants)	*"We will make the notation in the summary of medication to highlight the difference." – (Participant 01)* *"If yes, advice the guideline users this is off-label in Germany and should take this into account when they inform the use for patients." – (Participant 03)* *"We described difference constrains when published the guideline, like if the medical insurance did not cover the new intervention, we will mention it." - (Participant 06)* *"And provide the documented acknowledge." – (Participant 08)*

Appendix 04. Identified adaptation methodologies

Question: Could you please describe the adaptation process or which framework or methods your organisation used for guideline adaptation?	
Adaptation Frameworks	**Quotes**
ADAPTE 2010	*"We used ADAPTE 2010 and supplement with GRADE system for assessing the level of evidence."* (*Participant 04)*
ASCO endorsement/adaptation methodology	*"We used a mixed method, some of them from ADAPTE methodology. We have published a paper on our methods and I´ll be happy to provide that, I think it may explain better than I do." (Participant 02)*
DynaMed methodology	*"We are using Dynamed methodology which is GRADE-based, you could find it in Dynamed website." (Participant 01)*
CCO endorsement protocol	*"We used to use more ADAPTE before, and now we are slowly covering to GRADE. For our group we do have an overarching CCO endorsement protocol, but I also use GRADE-ADOLOPMENT as it has more details" (Participant 05)*
GRADE-ADOLOPMENT	
ACP guideline development methods	*"We use others methodology of adaptation, which is call ACP guideline development methodology, you could find the information published." (Participant 07)*
Pilot adaptation Framework	*"The BMJ paper described the framework developed at that time by NICE and piloted it in our setting". (Participant 08)*
ACA framework	*"We have highlighted the methods in South Africa, and published this resource, and I could give you the references to this methodology. In some cases, questions could either be adopting" (Participant 10)*
DELBI	*"We do have a national version of the AGREE II instrument, which called DELBI, that is complemented with four specific questions to consider when it comes to guideline adaptation. Most group of our country did not use the whole ADAPTE instrument, but rather consequently used the four questions in DELBI." (Participate 03)* *"We use the DELBI to assess the guideline methodology quality. But when group adapting, they use question 30-34 to inform their process." (Participate 06)*
Adaptation Experience	*"I am trying to think the process. They don't have a standardised guideline development or adaptation protocol in the country. A lot of kinds of process will be in a national process and there will be a specific health questions and PICO. Then we will be asked to conduct SR, and then what we do have in that particular process is that the SR would including first to look at what guidelines are out there, and then we will look at what SRs are out there before we conduct our systematic review. If there is a guideline of good quality, those are the recommendations" (Participant 09)*

Details of newly identified methodology and organisations:

1. DynaMed editorial methodology [3]: DynaMed is a clinician-focused tool designed to facilitate efficient and evidence-based patient care. They review the medical literature daily and updates their CGs. However, Dynamed also adapts CGs when those retrieved reflect relevant differences with the original one.
2. American Society of Clinical Oncology (ASCO) CG endorsement/adaptation methodology [4]: ASCO is a scientific society that provides CG endorsement and adaptation for those resource constrained settings.
3. American College of Physicians (ACP) guidance statement [5]: ACP is a medical-specialty society that develops CG statements when CGs are controversial and finally achieve the adoption or adaptation.
4. Cancer Care Ontario's (CCO) endorsement protocol [6]: The CG development program of the CCO provides CG endorsement/adaptation of high-quality CGs from other authorized institutions.
5. German Instrument for Methodological Guideline Appraisal (DELBI) [7]: The Association of the Scientific Medical Societies in Germany (AWMF) developed DELBI to provide CGs as well as adaptation approval and registration in Germany. Guideline adaptation groups (GAGs) in Germany also use DELBI to inform their adaptation process.
6. Piloted adaptation Framework [8]: The Indian Ministry of Health and Family Welfare raised a call for adaptation process and piloted the adaptation framework developed by NICE in India context.
7. Adopt–Contextualise–Adapt (ACA) framework [9]: Based on a long-term partnership with the International Centre for Allied Health Evidence (iCAHE), one health centre in Philippines developed the ACA framework for practising CGs adaptation with adopt (no modifications from source CGs), contextualized (tailored for target context), and adapt (modified the evidence and recommendations) components.

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Table 1. Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No Item	Guide questions/description	Page (No.)
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	Page 5
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	Page 5
3. Occupation	What was their occupation at the time of the study?	Page 5
4. Gender	Was the researcher male or female?	Page 5
5. Experience and training	What experience or training did the researcher have?	Page 5
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	Page 5
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Page 5
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	Page 5 and 10
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Page 5
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	Page 5
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	Page 5
12. Sample size	How many participants were in the study?	Page 6
13. Non-participation	How many people refused to participate or dropped out? Reasons?	Page 6 and 21 (Figure 1)
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	Page 5
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	Page 5
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	Page 6
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Page 5
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	Page 5
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	Page 5
20. Field notes	Were field notes made during and/or after the interview or focus group?	Page 5
21. Duration	What was the duration of the interviews or focus group?	Page 5
22. Data saturation	Was data saturation discussed?	Page 6
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	Page 5
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	Page 5

25. Description of the coding tree	Did authors provide a description of the coding tree?	Page 5 and 16-20
26. Derivation of themes	Were themes identified in advance or derived from the data?	Page 5
27. Software	What software, if applicable, was used to manage the data?	Page 5
28. Participant checking	Did participants provide feedback on the findings?	Page 5
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number	Page 15 and appendix 2
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Page 6-8 and 15-20
31. Clarity of major themes	Were major themes clearly presented in the findings?	Page 6-8
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Page 6-8

Resources from: Allison Tong, Peter Sainsbury, Jonathan Craig, Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups, International Journal for Quality in Health Care, Volume 19, Issue 6, December 2007, Pages 349–357.
Also see from: https://www.equator-network.org/reporting-guidelines/coreq/