Recent Advance in Clinical Practice Guideline Development Methodology

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Clinical practice guidelines (CPG) can be defined as systematically developed recommendations and related content obtained by reviewing scientific evidence, which help healthcare providers make decisions. CPG is one of the most powerful tools that helps clinicians make evidence-based decisions in practice. Methodologies in areas essential for CPG development, such as for systematic review, risk of bias (ROB) assessment, adaptation, and the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations, are rapidly developing. Therefore, they must be well-understood and applied to evidence-based CPG development. In this regard, it is necessary to learn about the updates and changed in the methodologies for CPG development. This manuscript covers the following CPG development methodologies: (1) main principles of CPG, (2) managing conflict of interest, (3) considering patient value and preference, (4) determination of key questions, (5) ROB assessment, (6) adaptation, (7) rapid guideline development, (8) living guideline development, and (9) GIN-McMaster Guideline Development Checklist.

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INTRODUCTION

Clinical practice guidelines (CPG) can be defined as systematically developed recommendations and related content obtained by reviewing scientific evidence, which help healthcare providers make decisions. CPG is one of the most powerful tools for helping clinicians make evidence-based decisions in practice.1)

As the interest in and importance of CPG increases, interest in the reliability of CPG development is also growing. This is because if the CPG recommendations are not developed in accordance with the principles of systematic review and evidence-based medicine, they may be biased and less reliable. In addition, methodologies in areas essential for CPG, such as systematic reviews, Grading of Recommendations, Assessment, Development, and Evaluations (GRADE), and risk of bias (ROB) assessment, are rapidly developing. Therefore, these methodologies must be well-understood before being applied to evidence-based CPG development.

We have focused on the following updates or changes in the methodologies for CPG development in this manuscript: (1) main principles of CPG, (2) managing conflicts of interest (COI), (3) considering patient values and preferences, (4) determination of key questions, (5) ROB assessment, (6) adaptation, (7) rapid guideline development, (8) living guideline development, and (9) GIN-McMaster Guideline Development Checklist.

The purpose of this review is to summarize the recent key updates or changes in CPG development methodology for the reference of domestic and foreign CPG developers.

REVIEW METHODOLOGY

The following documents are mainly referred to in this manuscript: handbook for clinical practice guideline developer version 1.0,2) handbook for clinical practice guideline developer version 2.0,3) health technology assessment methodology: systematic review,4) National Evidence-based Healthcare Collaborating Agency (NECA)’s guidance for assessing tools of ROB,5) and Australian government agency National Health and Medical Research Council (guidelines for guidelines).6) The key contents of the following areas were reviewed and summarized: (1) main principles of CPG, (2) managing COI, (3) considering patient values and preferences, (4) determination of key questions, (5) ROB assessment, (6) adaptation, (7) rapid guideline development, (8) living guideline development, and (9) GIN-McMaster Guideline Development Checklist.

KEY PRINCIPLES OF CLINICAL PRACTICE GUIDELINES DEVELOPMENT

CPG is valid only when it is developed using reliable and standard processes and methods. It is important to use these standards, to develop, implement, and disseminate CPGs. Several institutions and countries have announced principles of CPG development,7) and the common contents of these principles are as follows.

1. Evidence-Based Clinical Practice Guideline Recommendations (Systematic Review)
   CPG recommendations should be developed through a systematic review process, which can be conceptualized as: (1) systematic search, (2) specifying the criteria for evidence selection, and (3) specifying the strengths and limitations of the evidence.

2. Development by a Multidisciplinary Expert with Representation
   CPG should be developed by multidisciplinary experts with representing the area of expertise. CPG are generally developed by the Guideline Development Group.

3. Addressing Conflicts of Interest within the Development Committee
   COIs can affect the judgment on making recommendations; therefore, they should be declared and appropriately addressed.

4. Consideration of Patient Preferences or Values
   Patient values and preferences should be reflected in various CPG aspects. It is imperative to establish a development group that considers the values and preferences of patients.

5. Defining of the Clinical Practice Guideline Scope
   The scope of a CPG refers to the purpose of CPG development, the group of patients to whom it is to be applied, the intervention to be handled, the users of the CPG, and the CPG application environment. The scope of the CPG should be clearly defined during the planning stage.

6. Implementability of Clinical Practice Guideline
   The dissemination and implementation of CPG is a key part of their effectiveness, and thus, should be considered during the development of CPGs.

7. Transparency in the Development Process
   Explicitly explaining how the CPG developers evaluated the level of evidence and strength of the recommendations helps users determine the reliability of individual recommendations.

8. Appropriate Methodology of Formulating Recommendations
   The methods used to generate recommendations (voting, informal consensus, and formal consensus techniques) should be presented clearly.

9. Equity in Clinical Practice Guideline Development
   If equity factors are not properly considered in the CPG development process, it may not sufficiently address the needs of vulnerable groups,
which may subsequently widen or exacerbate health imbalances and inequalities.

10. Up-to-Date Clinical Practice Guideline
CPG must reflect the latest evidence. If there is an important evidence update that necessitates recommendation change, it should be revised.

CONFLICTS OF INTEREST

COI can be defined as a situation in which an individual’s personal interests’ conflict with the work or interests of the public or others.

1. Conflicts of Interest When Developing Clinical Practice Guidelines
COIs when developing CPGs can cause a bias in the recommendations. COIs are generally classified as financial or non-financial (organizational). Financial interests may include fees paid for service to a company (e.g., consultation payments, speaking fees), indirect payments (e.g., funding of travel), company stock, or royalties. Non-financial (organizational) interests arise if members of the development group serve as representatives of organizations with an interest in the guideline recommendations.8)

2. How to Manage Conflicts of Interest When Developing Clinical Practice Guidelines?
CPG developers should develop and implement COI policies that everyone can understand and comply with. Major components of COI policies include: (1) identifying the scope and application of the COI policies, (2) disclosure procedures for COIs, and (3) managing COIs among the CPG development group Chairman and members.8)

3. Conflicts of Interest Managing Polices
All CPG Guideline Development Group members should disclose their interests. This should include not only the steering committee and guideline panel members but also methodology experts, statistical experts, and external reviewers.

The Chairman is responsible for running COI policies and leading the development group. Ideally, independent personnel who have no financial or non-financial COIs should be selected as much as possible.

A policy for the assessment and management of COI clarifications for individuals involved in the development group must be established. A COI committee should be established within the Guideline Development Group to review declared COIs and determine if it is significant. It is recommended that the threshold and duration of the COIs be specified in advance. Significant COIs should be evaluated for ROB. If a ROB is detected, decisions such as restrictions on participation or exclusion of members may be made.9)

4. Reporting of Conflicts of Interest in the Published Clinical Practice Guideline
The final published CPG should include the declared interests and how they were managed.8)

PATIENT VALUES AND PREFERENCES

1. Patient Values and Preferences When Developing Clinical Practice Guidelines
Patient’s or consumer’s perspectives regarding the overall process, priorities, and outcomes of CPG development may differ from those of healthcare professionals. Therefore, the patient’s participation in CPG development aims to reflect the patient’s needs and concerns in the CPG. There are several ways patient values and preferences can be reflected within the CPG. Ultimately, it may be ideal for patients to participate in the CPG development process. Since consumers in Korea have little experience in participating in CPG development groups, additional literature searches or surveys should be conducted according to the stage or goal of applying patient values and preferences as an alternative to direct participation.31

2. Process of Consideration of Patient Values and Preferences
Methods that reflect patient values and preferences during CPG development involve several processes.31 First, the role of patients in CPG development should be determined. The primary role of patients is to ensure that values and preferences that differ from that of a healthcare personnel are also included during the development process. Second, a plan to reflect the patients’ values and preferences should be established. It is necessary to determine when and how patient’s values and preferences should be applied, and specific procedures and policies to carry this out. Third, the perspective of each patient should be considered. Patients can be considered as consumers. Consumers include patients, patient caregiver, consumer representatives, consumer groups, community members, and the general public. It is necessary to consider which of these viewpoints should be approached.

FORMING KEY QUESTIONS

1. Forming Key Questions When Developing Clinical Practice Guidelines
The key questions are based on the determined scope of the CPG. It is the process of identifying questions at the core of systematic reviews and CPG development. Key questions play an important role in the following CPG development processes: (1) determining the type of evidence needed; (2) establishing a basis search strategy; (3) synthesizing evidence and framing evidence analysis; and (4) formulation of recommendations.31

2. Processes of Forming Key Questions
A list of key questions is developed through several processes.31 First, the possible key questions within the scope of the CPG should be listed. The existing CPGs, brainstormed ideas of guideline panels, systematic review of the disease, and current opinions from related aca-
Bias can be defined as a systematic error in the research process causing the estimated result to deviate from the true value. ROB evaluation focuses on the study design and is determined by the degree of bias that undermines the validity of the results. ROB assessment when developing CPG should be carried out in the following order: (1) design classification of the selected literature, (2) determination of evaluation tools suitable for the research design, and (3) ROB evaluation. The research design is typically classified using the revised version of the DAMI (Design Algorithm for Medical Literature on Intervention) tool developed in Korea.

2. Selection of the Risk of Bias Evaluation Tools
ROB evaluation tool selection should be determined based on several factors. First, when developing CPG with adaptation using the systematic review, AGREE II (https://www.agreetrust.org/) is available. The minimum quality level of the existing systematic review should be checked using the AMSTAR2 (https://amstar.ca/Amstar-2.php) or ROBIS tool (Risk of Bias Assessment Tool for Systematic Reviews; https://www.bristol.ac.uk/population-health-sciences/projects/robis/robis-tool/). When developing CPG using a de novo systematic review, it should be evaluated using the RoB ver. 2.0 (https://methods.cochrane.org/risk-bias-2). If the evaluation range is expanded to non-randomized studies, RoBANS (https://abstracts.cochrane.org/2011-madrid/risk-bias-assessment-tool-non-randomized-studies-robans-development-and-validation-new) and ROBINS-I (https://methods.cochrane.org/ia/risk-bias-non-randomized-studies-interventions) should be used. If the list of key questions includes diagnosis or prognosis, QUADAS2 (https://www.bristol.ac.uk/population-health-sciences/projects/quadas/quadas-2/) or QUIP2 should be used.

3. Risk of Bias Evaluation Process
Once the ROB evaluation tool is selected, the actual evaluation process begins. ROB evaluation involves the following three processes: (1) collection of information, (2) conduction of ROB evaluation, and (3) presentation of the evaluation results. Most sources for ROB evaluation are published papers. However, the very high rate of “uncertainty” (25%–57%) of ROB evaluation results, suggests that published papers alone may be insufficient. Therefore, clinical trial registers or protocols that provide more detailed information regarding the method are helpful. Clinical research reports and regulatory documents can also be complementary. The ROB assessment should be performed independently by at least two individuals, and the resolution process for inconsistencies should be defined in advance. ROB evaluators should have content or methodological expertise (or both). An intensive and standardized training program should be developed for ROB evaluators. It is recommended to conduct a pilot evaluation of three to six documents and to share the results with all members. The ROB evaluation should be presented using a forest plot.

ADAPTATION

1. Adaptation Methodology for Clinical Practice Guideline Development
Adaptation can be defined as “a systematic approach to using or altering CPGs developed for specific cultural and institutional situations to other medical situations.” Adaptation can replace or supplement the de novo CPG development methodology. The three representative adaptation models are the ADAPTE, CAN-implement, and GRADE-ADOLOPMENT frameworks. The ADAPTE framework which was proposed by the ADAPTE collaboration, was the first methodology to be proposed. Currently, it is the most commonly used methodology in Korea. CAN-implement is a supplementary tool that provides the tools or support needed to implement the ADAPTE frameworks.

2. The GRADE-ADOLOPMENT Framework
This framework was developed by the GRADE Group for the development of 22 national CPGs in Saudi Arabia. This framework was developed by the GRADE Group for the development of 22 national CPGs in Saudi Arabia. For this model to operate, the existing CPG must have a GRADE Evidence to Decision (EtD) table for each recommendation; an EtD table should be created if it does not exist. At the consensus meeting, the contents of the EtD table should be appropriately reviewed to determine the direction and strength of the recommendations. The original CPG should have a well-documented summary of the findings for individual recommendations to allow appropriate decision-making.

3. Selection of the Adaptation Methodology
The GRADE-ADOLOPENT framework is preferred over the ADAPTE framework in Korea for the following reasons: (1) it is free from copyright issues; (2) it increase loyalty to CPG development; (3) it facilitates structured interactions and deliberations among the panel members during meetings; and (4) it is relatively easy to determine the evidence and recommendation levels in adaptation.
RAPID GUIDELINES

Rapid guidelines can be developed in urgent situations, such as the outbreak of new infectious diseases or occurrence of disasters. In such cases, rapid medical treatment guidelines are required.20)

1. Type of Rapid Guidelines
The World Health Organization has suggested two types of rapid guidelines: (1) emergency or rapid response guidelines developed when an emergency occurs in the public health sector and needs a short-term response and (2) revising, updating, and supplementing relevant sections in already established rapid response guidelines.3)

2. Rapid Review
To develop rapid guidelines, human and financial resources need to be increased, which may not be easy to implement in real life. To develop rapid guidelines quickly, the scope of rapid guidelines or generating evidence process can be simplified. Guidelines are rapidly reviewed by allowing modification of the literature review process and shortening the development process. However, to ensure reliability of the recommendations, the essential factors should be maintained in the guidance development stage. However, there are no standard guidelines for the factors that are essential for the development of rapid-care guidelines. Based on the development checklist of the 2014 GIN-McMaster treatment guidelines, 21 principles for each of the 18 topics organized by Morgan et al.21) are available.

LIVING GUIDELINES

1. Living Systematic Reviews
Based on systematic reviews, living guidelines can be maintained to include the latest recommendations and provide timely and necessary recommendations. A living systematic review (LSR) refers to a continuously updated systematic review20); the existing systematic literature reviews are kept up-to-date by procuring new research evidence through a continuous search. LSR should be performed in the following situations: (1) clinical questions are important for decision-making, (2) existing evidence levels are low, and (3) new evidence is highly likely.21)

2. Living Guideline Methodology
The entire set of medical guidelines should be regularly updated over a specific period of time (e.g., 3 years).20) The ultimate goal of living guidelines is to provide reliable information to decision-makers in a timely manner, which has been enabled by the introduction of LSR.20) The essential elements of living guidelines are as follows: (1) LSR, (2) living summary table, (3) living guideline committee, (4) living peer-review process, and (5) publishing, spreading, and budgeting for the living guidelines. For the successful maintenance of the living guidelines, careful judgment on updating the recommendations is needed. If the guidelines are frequently updated owing to low judgment criteria, it will cause problems in the spread and implementation of the recommendations.3)

GIN-MCMASTER GUIDELINE DEVELOPMENT CHECKLIST

The GIN-McMaster guideline development checklist (hereafter referred to as the checklist) is a tool developed to elucidate factors that should be considered in various processes when developing clinical care guidelines in a checklist format. This checklist was developed in 2014 by a collaboration between the Guideline International Network and McMaster University.21) This checklist consists of 18 topics and 146 items. The 18 topics are as follows21): (1) organization, budget, planning and training; (2) priority setting; (3) guideline group membership; (4) establishing guideline group processes; (5) identifying target audience and topic selection; (6) consumer and stakeholder involvement; (7) conflict of interest considerations; (8) PICO (Population, Intervention, Comparator, Outcome, and Time) question generation; (9) considering importance of outcomes and interventions, values, preferences and utilities; (10) deciding what evidence to include and searching for evidence; (11) summarizing evidence and considering additional information; (12) judging quality, strength or certainty of a body of evidence; (13) developing recommendations and determining their strength; (14) wording of recommendations and of considerations of implementation, feasibility and equity; (15) reporting and peer review; (16) dissemination and implementation; (17) evaluation and use; and (18) updating

RECENT ADVANCES IN METHODOLOGIES FOR CLINICAL PRACTICE GUIDELINE DEVELOPMENT

In summary, the newly proposed parts of Korea’s CPG development methodology are as follows: (1) The main principles of CPG development in Korea have been summarized and presented. (2) In the development of clinical care guidelines, the principles and detailed guidelines for COI management have been presented. (3) The patients’ values and preferences should be considered in the development of clinical care guidelines. (4) The development process of key questions and the ROB evaluation process have been clearly presented and applied. (5) A new adaptation methodology, the GRADE-ADOPTION, has been introduced. (6) Rapid and living guidelines development have been introduced, and the necessity of which was highlighted by the coronavirus disease 2019 situation. (7) The GIN-McMaster guideline development checklist was introduced.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.
REFERENCES