Executive Summary (영문)

English Title

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▢ Background

The definition of clinical practice guidelines is "statements that included recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options" (Institute of Medicine, 2011). This definition clearly distinguishes clinical practice guidelines from other forms of clinical guidelines (e.g., expert consensus documents, consulting, criteria, etc.), and emphasizes the evidence-based characteristics of clinical practice guidelines, such as the use of systematic review. In Korea, as a result of expert consensus bulit in 2010 using RAND method, the definition is "statements that include systematically developed recommendations from review of scientific evidence for assisting the decision-making between the public healthcare provider and patient under specific clinical situations" (Ji et al.,2010).

In order to develop trustworthy clinical practice guidelines, the application of an evidence-based methodology, such as a systematic review, is considered essential. In this regard, the development of a handbook or manual that outlines the essential processes involved in the development of clinical practice

guidelines for the effective application of evidence-based methodologies is being undertaken with domestic and international agencies (Ansari & Rashidian, 2012). To date, five types of handbooks have been developed however, the accurate status of actual utilization of these handbooks has yet to be reported. Existing handbooks have been written in an extremely condensed manner and lack of detailed explanations, as well as failing to include details on the utilization rate of tools and methods for the application of corresponding content in Korea (Korean Academy of Medical Sciences, 2011).

Moreover, it is necessary to develop a methodology that reflects the current situation in Korea, which entails a mixture of de novo and adaptation methods. In addition, grading methodologies should be formulated that reflect research and evidence from literature and epidemiological study in Korea, and that can be adapted by various academic societies when difficulties are faced during the development process. As such, our objective is to develop a handbook that will aid in developing Korean clinical practice guidelines that reflect these situations, and that will assist in the qualitative improvement of domestic clinical practice guidelines that are developed in the future.

▢ Objective

The primary objective of the present study is to produce a handbook that is appropriate for developing clinical practice guidelines in Korea, and using it to aid the qualitative improvement of domestic clinical practice guidelines developed in the future.

Detailed study objectives and important topics for the handbook's development are as follows:

1) Categorize main tasks that are essential for the guideline development through a review of practice guideline development handbooks and manuals from Korea and abroad.

2) Develop tools based on information derived from opinion survey of guideline developers.

3) Develop toolkits for developing practice guidelines.

4) Develop a GRADE handbook.
5) Develop an integration process for de novo and adaptation methods.

▢ Methods

Ⅰ. Selection and Analysis of main tasks in the Development of Guidelines

In order to select the main tasks that are essential for the development of clinical practice guidelines, existing handbooks were systematically searched and reviewed. The main tasks were selected based on the 26 tasks selected by Ansari and Rashidian (2012), among previously published studies on clinical practice guideline development from these, 15 essential tasks were selected after considering the Korean context. The analysis results of each task were used to construct the table of contents for the handbook, and the handbook contents that were selected as being in the top three for each task formed the basis of the handbook's construction.

Ⅱ. Survey of Guideline Developers

A survey was conducted of 956 developers who have experience of participating in the development of Korean clinical practice guidelines that were developed between the year 2000 and August 2014. The purpose of this study is to identify the extent of their participation in the handbook's development and use, as well as to highlight problems associated with the development process. The survey, which was conducted using Internet-based software, was conducted for eight weeks, starting on August 4, 2014. From the answers to the survey questions, values for the frequency and percentage, or median and interquartile range, were calculated and presented.

Ⅲ. Toolkit Development

It was decided that three types of toolkits (a grading tool for adaptation guidelines, a determinant tool for the development method, and an assessment tool for the acceptability and applicability of recommendations) would be

developed. A rough draft for the toolkits was created based on the view of existing handbooks and clinical practice guidelines from Korea and abroad, an analysis of existing tools, and research team meetings, followed a review of advisory meetings.

Ⅳ. GRADE Handbook Development

An internal seminar was held to review 15 issues of new GRADE guidelines that had been issued for the development of the GRADE handbook. The GRADE handbook was then developed based on content that was discussed, revised, and supplemented at an internal seminar.

Ⅴ. Integration Process Development

For the development of an integration manual, five manuals from Korea and 30 manuals from abroad were considered. The review process focused on the manuals that had received the top three scores for each main task. In addition, content in the practice guidelines developed to date that was related to process development was identified; this was then revised and supplemented through external review.

▢ Results

- Selection and analysis of main tasks in development of clinical practice guidelines
- Survey of guideline developers
- Toolkit development
- Handbook development

Ⅰ. Selection and Analysis of main tasks in Development of Clinical practice guidelines

Handbooks developed after 2005 and related to the development of clinical practice guidelines were systematically searched, and 35 handbooks (five from Korea, 30 from abroad) were finally selected. Handbook development tasks

selected 26 handbooks. The descriptiveness of each handbook was assessed, and the content that was considered to have been described best was "determining the level of evidence and strength of recommendation" (72.9%), followed by "operating a development group", "forming a development group", "quality assessment of evidence", "managing conflict of interest", "creating clinical questions," and "evidence synthesis and analysis," respectively. In terms of handbooks, "The Guidelines Manual" by NICE received the highest average score, at1.65 out of 2 points this was followed by "Understanding and Utilization of Korean Practice Guideline Adaptation Methods" by the Korean Academy of Medical Sciences (1.58 points), and "Clinical Practice Guideline Adaptation Manual Version 2.0" by the National Evidence-based Healthcare Collaborating Agency (NECA) clinical practice guidelines collaborating agency (1.46 points), respectively. For each task, the three handbooks that ranked the highest in terms of having the best description of task-related content were selected and used as a basis for writing each task in the integrated handbook.

Ⅱ. Survey of Guideline Developers

Among the 956 subjects contacted, a total of 139 (14.54%) responded to the survey. Of these, 107 were clinical physicians (77.0%), which made up the majority. In terms of the number of times the respondents had participated in clinical practice guidelines, once (41.7%) was the most frequent response, followed by twice (28.8%), four or more times (18.7%), and three times (10.8%). In responding to the question that asked what form their participation took when developing the most recent clinical practice guidelines, the most popular response was working staff for development (65.5%), followed by director of development, executive secretary, and administrative manager (which all equated to 11.5%). Methodology experts accounted for 4.3%. In terms of the details of actual work performed by the participants in developing clinical practice guidelines, the most common response was drafting recommendations (74.8%), followed by evidence assessment (59.7%), evidence searching (56.8%), and establishing development plans (53.2%). When "no

response" was excluded (6.5%), the lowest response rate was external review of clinical practice guidelines (25.2%). In terms of development method, 43.2% responded that they had used a hybrid method that partially integrated adaptation and de novo development, while using only adaption equated to33.1% and using only de novo development to 15.8%. The most frequently referenced manual for developing clinical practice guidelines was "The Guidelines Manual" by NICE (20.9%), followed by "Clinical Practice Guideline Development Manual" by NECA (18.0%), and "Clinical Practice Guideline Adaptation Manual" by NECA clinical practice guideline collaborating agency (13.7%). In relation to the degree of helpfulness of the handbooks referenced in the development process for each development stage, degree of helpfulness in all stages, except for the group formation stage, scored seven points (out of a maximum of nine), which was the median. On the question related to areas that need to be improved in existing handbooks on clinical practice guidelines, a nine-point scale was used, which consisted of one point for "do not need at all" and nine points for "very much needed". The items that showed the highest demand for improvement included "clear definition of terms" and "checklist that can aid decision-making on applicability of evidence". An analysis of "detailed illustration of how to develop clinical practice guidelines", "providing manuals through a variety of media", "toolkit for presenting strength of recommendation", and "need for tools that are helpful in deciding whether to use adaptation or in-house development methods" provided a median value of seven points.

Ⅲ. Toolkit Development Outcome

In relation to searching for clinical practice guidelines developed using adaptation, 43 domestic and 50 foreign guidelines were collected by reviewing these, information on three types of toolkit development was obtained. In terms of clinical practice guidelines developed using adaptation, there were mostly three evidences that verified whether adaptation was used. In terms of foreign clinical practice guidelines, cases in which the word "adaptation" was clearly

indicated was most common, at 90.7%, while in relation to domestic clinical practice guidelines, cases that involved searches for clinical practice guidelines were most common, at 78%. Decisions on the adaptation method were not mentioned in 90.7% of the foreign-guideline cases and 98.0% of the domestic cases. In terms of adaptation methods used in the clinical practice guidelines collected, 27.9% of the foreign cases derived evidence only from clinical practice guidelines, or considered only the most recent version, which was the highest whereas, domestically, 36% added only the most recent version, which was also the highest. Among the other methods, cases in which one chosen guideline was adapted were most common, and there were also cases in which one guideline was selected and the most recent version added, along with cases in which domestic evidence was added to key literature and existing clinical practice guidelines.

1. Development of a checklist for choosing de novo development versus adaptation

Among the methods used to develop clinical practice guidelines—de novo development, adaptation, and hybrid development—a checklist for choosing development and adaptation was developed. Here, the hybrid method is defined as cases in which searches were conducted again on the preliminary data, or where an additional systematic review was conducted for additional key questions.

Toolkit1〉 Checklist for choosing de novo development versus adaptation

▸ De novo development must satisfy one of the criteria listed below.
① Related clinical practice guidelines (domestic or international) do not exist.
② Related clinical practice guidelines (domestic or international) do exist, but do not use an evidence-based methodology.*

▸ Adaptation must satisfy three criteria listed below.
① Existing clinical practice guidelines (domestic or international) include all key questions.
② Related clinical practice guidelines (domestic or international) were developed within the last three to five years, and there is no additional conclusive evidence (three years when evidence

expansion speed is rapid).
③ Related clinical practice guidelines, or systematic review, (domestic or international), uses an evidence-based methodology.*

▸ Hybrid development (de novo development + adaptation) must satisfy three criteria listed below.
① Existing clinical practice guidelines (domestic or international) include some key questions, but additional key questions are needed.
② Existing clinical practice guidelines (domestic or international) were developed within the last three to five years, and there is no additional conclusive evidence (three years when evidence expansion speed is rapid).
③ Related clinical practice guidelines (domestic or international) use an evidence-based methodology.*

* : Representation about systematic search of literature and clear connection between recommendation and supporting evidence

2. Development of a checklist for assessing the acceptability and applicability of recommendations

Toolkit2〉 Assessment checklist for the acceptability and applicability of recommendations

▸ Development principles
1. Use ADAPTE as the default, but supplement this using appropriate content.
2. The questions should be directed more towards the recommendation than the key question. This is because the key question and recommendation may not correspond exactly.
3. A summary of the recommended content will form the title.
4. The content on acceptability is difficult to understand. Instead, the most appropriate similarities to verify are: 1) uniformity of population group, 2) uniformity of value and preference, and 3) size of benefit from recommendation.
5. With respect to the applicability of recommendations, questions should focus on:
1) the usability of interventions/equipment, 2) essential expert skills available, 3) legal and institutional barriers.
6. Ask detailed questions first, and then ask the overall assessment question.

Recommendation acceptability assessment	CPG1	CPG2	CPG3
Population group (prevalence, incidence rate, etc.) are similar	Y/N/U	Y/N/U	Y/N/U
Value and preference are similar	Y/N/U	Y/N/U	Y/N/U

Benefit/risk from recommendation are similar	Y/N/U	Y/N/U	Y/N/U
⇒**Corresponding recommendation is acceptable**	Y/N/U	Y/N/U	Y/N/U
Notes			

Recommendation applicability assessment	**CPG1**	**CPG2**	**CPG3**
Corresponding intervention/equipment can be used if necessary	Y/N/U	Y/N/U	Y/N/U
Essential expert skills are available	Y/N/U	Y/N/U	Y/N/U
There are no legal/institutional barriers	Y/N/U	Y/N/U	Y/N/U
⇒**Corresponding recommendation is applicable**	Y/N/U	Y/N/U	Y/N/U
Notes			

3. Development of a tool for recommending grading methods for adaptations

Grading system status and determining methods were categorized using 93 adaptation clinical practice guidelines.

In considering the grading methods, clinical practice guidelines that used in-house system accounted for 9.3% and 4.0% for international and domestic, respectively, while≥ 90% of clinical practice guidelines used grading systems from other organizations. The method most often used in domestic and foreign clinical practice guidelines was GRADE (foreign: four cases, domestic: eight cases), followed by USPSTF and NHMRC for foreign clinical practice guidelines (with three cases each). The grading methods used in 93 adaptations clinical practice guidelines were most often decided upon after looking at evidence or evidence tables (foreign 62.8%, domestic 62.0%).

Toolkit3〉 Development of a tool for recommending grading methods for adaptations

▸ First stage: Selection of grading system

If an in-house grading system is available, that system can be used. If there is no in-house grading system, an appropriate system to be applied to the corresponding practice guidelines must be selected. The grading system that is referenced or used the most can be used.

▸ Second stage: Preparing strength of evidence decision

In reviewing the strength of evidence in the original practice guidelines, examine whether the strength of evidence system used is suitable to be translated to the new guidelines. Next, if translation is difficult, use an evidence table or evidence document to directly decide the

strength of evidence.

▸ Third stage: Decide the strength of evidence

Strength of evidence is authorized according to the content prepared during the second stage. Authorization can include subjective areas, and is given after agreement is reached by two or more people. Afterwards, recommendations should be made to the clinical practice guidelines development team in order to enable them to reach a decision through consensus meetings.

▸ Fourth stage: Decide recommendation grades

Once the strength of evidence based on recommendation grades has been decided, most cases decide the recommendation grade as-is however, some cases may require additional criteria to be reviewed in order to determine the final recommendation grade. First, a decision must be made on whether the recommendation grade can be translated. If it can, the strength of evidence does not need to be translated hence, the second and third stages can be omitted. If it cannot be translated, the grade should be determined according to additional considerations based on the strength of evidence decided in the second and third stages.

Ⅳ. Handbook Development Outcome

The 26 tasks in the clinical practice guideline development process selected through review of existing handbooks were categorized into three stages: planning, development, and finalization. The planning stage includes main tasks such as topic selection, forming a clinical practice guidelines development group, establishment of development plan (and selection of development method), designation of scope, and creation of clinical questions.

The development process was divided into the methods of de novo, adaptation, or hybrid, and described accordingly. For this, a new definition was needed for the integrated development process. Within the development process, main tasks include searching for evidence (guidelines), compilation of evidence (guidelines), determining strength of evidence, and providing recommendations.

In the finalization stage, the tasks are focused on external review, publishing, revision and updating, and dissemination and implementation. A separate section was dedicated to GRADE methodology.

▢ Conclusions

In the present study, we integrated the development of a clinical practice guidelines manual and adaptation manual published by NECA in 2011 and created a revised handbook that incorporates a process to allow for the integration of new development and adaptation methods that consider the development environment in Korea. Moreover, after selecting and reviewing tasks mentioned as part of the evidence-based development methodology process in extant handbooks, these tasks were arranged and described for clinical practice guideline practitioners to use at each stage. In order to ensure their applicability to real-world scenarios, sample cases from existing guidelines were added, and the newly revised GRADE handbook from the GRADE working group (which contains the GRADE methodology that is receiving increasing attention and utilization by developers), along with recently published works from journals and academic societies, were referenced to create the handbook for practitioners to refer to.

The handbook is intended to be used by those with experience of developing clinical practice guidelines, or medical staff interested in new development. There are plans to revise and amend the handbook by collecting opinions from practitioners and academic societies.

It is hoped that the handbook will be used in practice, and referenced for all future activities associated with the development or revision of clinical practice guidelines. Further, it is expected that this handbook will ultimately contribute to enhancing the quality of patient care through its use in future development and expansion of high-quality clinical practice guidelines dedicated to an evidence-based methodology.

Key words

trustworthy clinical practice guideline, comprehensive development handbook, evidence-based method, toolkit development