Executive Summary

The system development of clinical study for conditional coverage with evidence generation

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▢ Background

The government has introduced 'selective reimbursement system' by targeting the entry with the social demands though uncertain effectiveness. If it is determined as a selective reimbursement item, that technology is covered under national health insurance with differentiated patient payment. There has been a demand for a review system that can support clinical research and research process management even for health technologies covered by health insurance and in cases requiring evidence development for medical treatments that determine that there are uncertainties in evidence for treatment effectiveness. Therefore, this study was to examine the general system that supports clinical research on health technologies that require evidence development as one of the ways for conditional coverage and as a target for selective reimbursement. Finally, we developed process management modes and detailed procedures for clinical research processes appropriate to domestic conditions.

▢ Objective

The aim of this study was to suggest a general model and related detailed procedures for clinical research support for evidence generation for domestic conditional coverage as well as policy support measures.

▢ Methods

First, criteria were analyzed for conducting domestically approved clinical research and for conducting clinical research on the temporary approval of new health technology. The Guideline for Good Clinical Practice by International Conference on Harmonization (ICH-GCP), the Nuremberg Charter, the Helsinki Declaration, and the Belmont Report were reviewed.

Second, data were collected by visiting foreign organizations and searching related web-sites for detailed case studies on operating methods for conditional coverage in major developed countries (USA Coverage with Evidence Development, Canada Field Evaluation, UK only in research, Japan advanced health service system) and on the current state of clinical research support relating to conditional coverage. Rapid reviews were conducted to obtain additional data relating to the system and to deliver policy suggestions in depth.

Third, an in-depth interview was conducted synthetically to collect various healthcare expert opinions on criteria and procedures to consider when building a system to generate corresponding evidence through clinical research.

Finally, of the criteria in the selective reimbursement system, a general model and related detailed procedures for clinical research support for evidence generation and policy support measures were suggested as a conditional coverage based on previous reports and data relating to conditional coverage in foreign countries and surveys of expert opinions.

▢ Results

Several health technologies are uncovered under national health insurance scheme even after they satisfy the health technology assessment criteria due to the lack of clarity in evidence for clinical safety and effectiveness. Therefore, criteria for selecting target technology, process administration, and funding criteria needs to be developed in determining conditional coverage for evidence generation through clinical research.

- Criteria for selecting target technology: The technologies that need additional evidence due to the lack of evidence for safety and effectiveness, health

technologies with high potential to obtain evidence within a short period, those that were generalized due to lack of evidence for safety and effectiveness, those in need of studies on relative effectiveness, those whose interest in evidence generation is low due to small business profit but is clinically needed, those that can only be provided by a high-tech healthcare provider in appropriate medical organs, and those with high potential for therapeutic changes in patients may be considered.

- Process administration: The National Evidence-based Healthcare Collaborating Agency as an independent and professional agency manages clinical research processes, provides scientific advice and requires activities to provide methodological guidance. It is necessary to construct related infrastructure and provide a performance system. Specifically, 'Steering Committee' for clinical research aimed at evidence generation is responsible for deliberating research proposals and assuming a scientific advisory role for related research. 'Research Sub-Committee and Research Support Centers' examine research proposals, verify and analyze data, conduct studies on cost-effectiveness, provide methodological guidance, and examine reports, thereby supervising the general process of clinical research for evidence generation.
- Funding: To smoothly operate a clinical research support system for conditional coverage, funding issues are key factors to consider. Principally, it is reasonable that the government should fund the study as it is in accordance with government policy support. Public research funding might be desirable but the scale of clinical research expenses may be large. Therefore, various funding sources are necessary in terms of system sustainability. Also, various stakeholders need to participate in decision process.

Ⅰ. Current state of conditional coverage in major countries

In major developed countries, various forms of conditional coverage systems are implemented according to each country's healthcare conditions. The objective of the conditional coverage system being implemented in developed countries is to verify whether the health technology can bring benefits to the applied population group through evidence generation for doubts about the health technology.

Looking at the conditional coverage and the current state of operating

administration in major countries, criteria for selecting technology relating to conditional coverage with evidence development targets health technology that has insufficient evidence for 'safety and effectiveness,' which is mutually required for determining cost. In Canada and the UK, factors for 'cost-effectiveness' are also considered, and even when evidence for cost-effectiveness is insufficient, the technology is recommended as conditional coverage. On the other hand, Canada, the USA, and Japan assess not only safety, effectiveness, and cost-effectiveness but also usefulness, uncertainties in technology quality, and uncertainties in benefits to the applied population. Technology predicted to have a significant influence on the applied population has been selected as the target conditional coverage technology.

There were country-specific differences in performance methods for clinical research and evaluation methods. Especially in terms of research performance methods , researchers in the USA autonomously conduct studies, and in Japan's advanced health service system, researchers can autonomously conduct studies in corresponding authorizing institutions. The UK has been conducting an advisory mode of research performance, and Canada has been leading research in academia and research institutions. Relating to evaluation methods, both Canada and the UK conduct clinical research on the process of conditional coverage and cost-effectiveness.

In terms of funding methods, Canada and the UK are also conducting research through public aids, whereas the USA and Japan receive clinical funds from manufacturing enterprises, medical institutes, and academic institutions. Additionally, in other countries, healthcare expenses are guaranteed as conditional coverage, but under Japan's advanced health service B, technological expenses for corresponding advanced health technology are paid for out of pocket.

Ⅱ. Interviews with experts

Reflecting on the opinions of domestic healthcare sector experts, content analysis of criteria and factors to consider for primary application in each stage were conducted, and the following results were found:

(Target technology selection stage: criteria for selection and factors to consider) Of concern were cases in which additional clinical research is needed because target technology based on evidence generation for conditional

coverage lacks evidence for safety and effectiveness, additional evidence for diseases specific to Koreans is needed, disease burden is large, the technology is invasive, and the health technology is developed domestically. It was also noted that it is reasonable not to select technology performed by clinical research in foreign countries, technology developed by foreign countries, when cost for evidence generation is greater than transaction cost, technology with a narrow accommodation range, and high-cost technology as target technology. Main factors to consider during the selection process are inclusion of evaluation of cost-effectiveness, suggestion of a logical and transparent settlement process, and collaboration with an expert healthcare committee.

(Performance stage: agency and instruction for conducting the clinical research process) In the clinical research stage, process administration is important, and an agency that can professionally administer this is needed. The NECA, an independent research organization, plays an important role in administrating clinical research processes and manages half of the research process, including advice and reviews for research protocol and management of data quality. Matters to be attended to during process administration are providing regulations for punishing clinical research malpractice, providing mechanisms to obtain reliable research results, systemizing processes to write consent for participation, and strengthening the function of independent data monitoring committees.

(Other overall opinions and funding) The first alternative for funding is using government funding by default. Since the actual high material cost is responsible for manufacturer applicants as well as evidence generation, plans to pay for funding can be considered. Another alternative is to classify healthcare instruments by their characteristics and to request plans for differential support and other public funding (as funding from the national foundation R&D support and national funding, Health Technology Portal Service, Korea Centers for Disease Control and Prevention, and Korea Health Promotion Foundation support the Ministries of Finance and Economy, Science and Technology, Health and Welfare, and others). Some opinions highlighted the need for a funding mechanism from the National Health Insurance Service, which manages healthcare foundations.

Ⅲ. Development of clinical research support system for conditional coverage with evidence generating

The key performance agencies of the performance system for clinical research support for evidence generation are healthcare organizations, healthcare evaluation committees, the NECA, and the Ministry of Health and Welfare. The performance stage is largely separated into three stages: selecting target technology and implementation organizations, performing clinical research and administrating processes, and publishing results. Specifically, the performance stage was separated into five stages: target technology selection, clinical research initiation, process management during clinical research, clinical research completion, and result publication.

Doctors in the healthcare organization responsible for implementation are obligated to submit a clinical research application, gather patients, obtain consent forms, input case records, follow procedures and proposals, and write mid/final reports. When conducting research studies, doctors responsible for implementation and participating research staff may receive scientific advice and reviews from the NECA and respond to demands for procedural inspection and data.

The evaluation for selective reimbursement and medical practice evaluation committees from the healthcare evaluation committee make final reviews of the accepted target technology and play roles in verifying required documents for clinical research performance, notifying final reception, and reporting review results of acceptance from implementation organizations. When publishing results once clinical research is completed, the evaluation for selective Reimbursement and medical practice evaluation committees from the healthcare evaluation committee reconsider the reception of conditional coverage; review and decide on maintenance and transition for required payments, selective Reimbursement, coverage, and termination; report them to the Ministry of Health and Welfare; and finalize the decision at the National Health Insurance Policy Deliberation Committee.

Insurance benefits from the Ministry of Health and Welfare are agencies for publishing requirements for target technology, organizations, and operators; for announcing recruitment of prospective clinical research organizations; and for notifying selection of implementation organizations. Additionally, after the acceptance period for clinical research is terminated, extension of an additional acceptance period must be announced in the result publication stage (Fig.1).

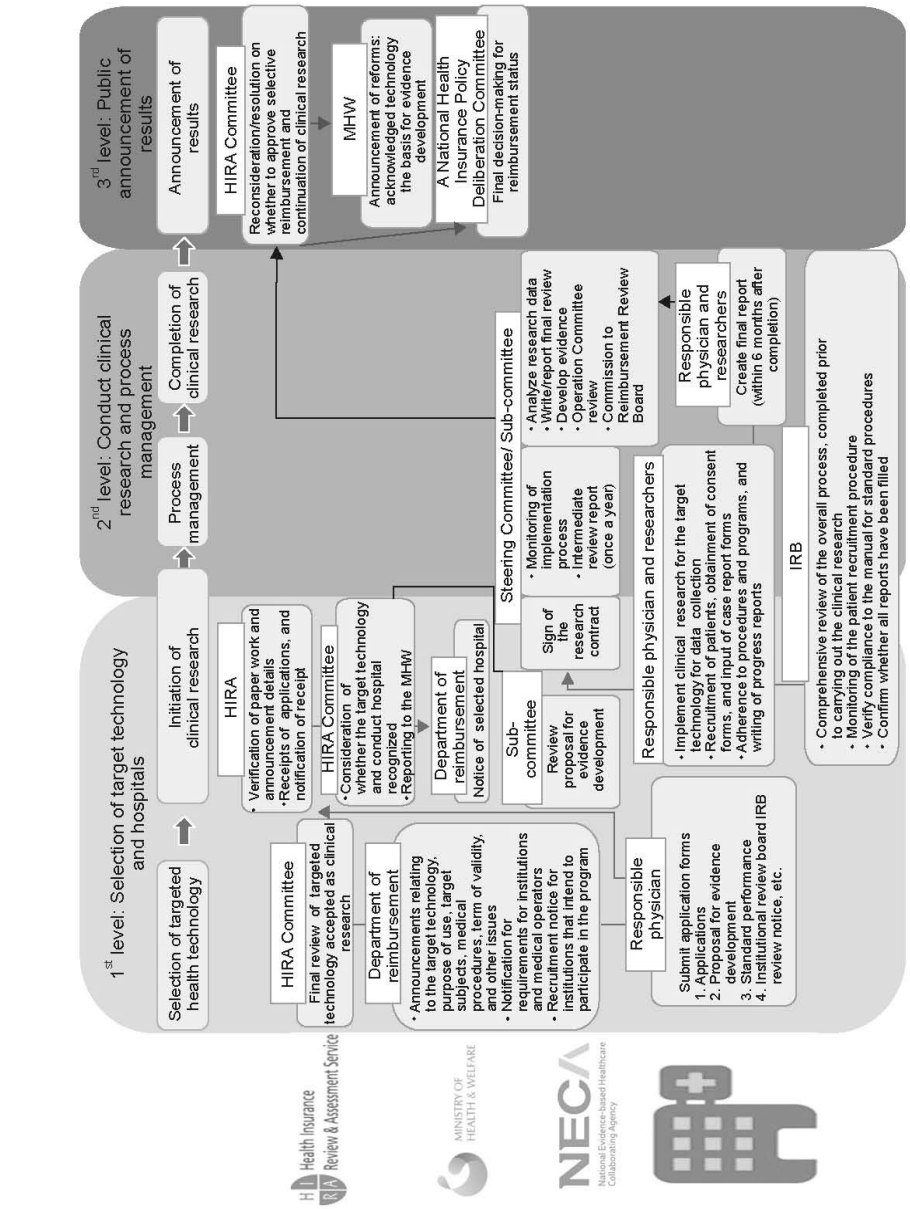

Fig 1. General support system model of clinical research for conditional coverage with evidence development

The NECA is the agency tasked with examining clinical research proposals for evidence generation, inspecting clinical research implementation procedures, and reporting mid-inspection results (once a year) and a final inspection report (within six months after clinical research is terminated). Especially, the NECA scientifically supports researchers' clinical research performance and systematically manages the process by establishing steering committees and subcommittees as well as research support centers. The steering committee reviews research proposals. Sub- committees and research support centers examine research proposals written by researchers and, being responsible for monitoring, inspecting, and analyzing clinical research data, also inspect mid-reports and final reports submitted by researchers. If it is a necessary technology, studies on its cost and effectiveness are conducted. Furthermore, research support centers provide methodological guidance to help understand research performance of clinical researchers and research methods for decision-makers (Fig. 2).

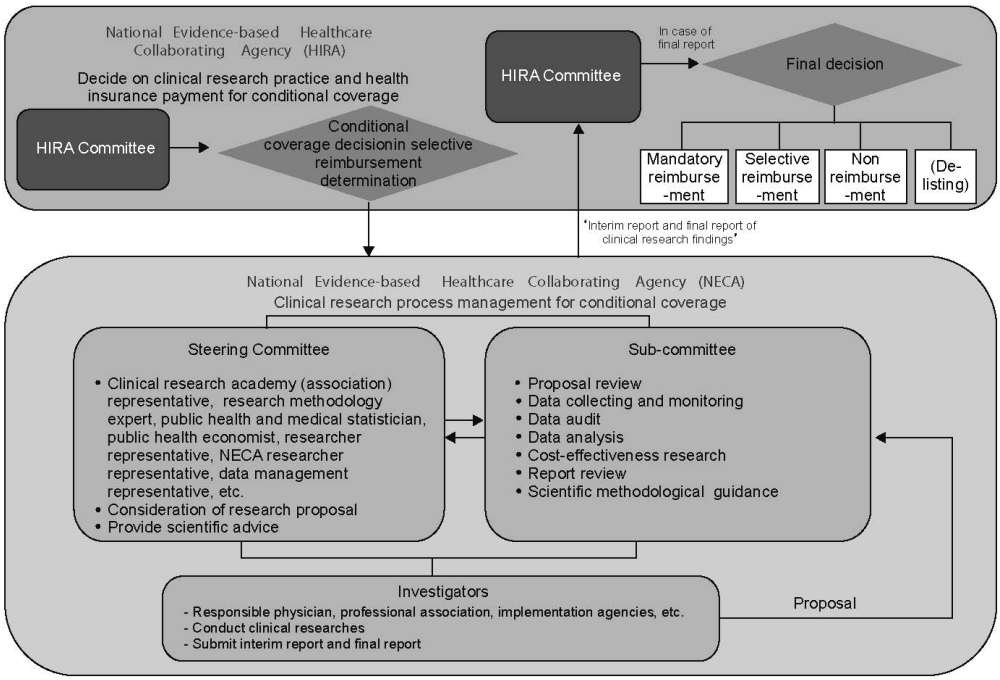

Fig 2. Process management support system model of clinical research for conditional coverage with evidence development

▢ Conclusions and Policy proposal

In terms of policies for system operation, there were three main considerations. First, criteria for selection must be explicit and specific in the target selection stage, and social impact must also be considered as well as the opinions of various stakeholders, and a mechanism for participation should be guaranteed. Second, in order to increase the credibility of evidence obtained through clinical research, the importance of process management must be acknowledged, institutions that can assume professional responsibility to provide 'scientific advice' and 'methodological guidance' must be highlighted, and building related infrastructure and providing performance systems must be supported. Additionally, it is suggested that funds be used to build not only support measures for public funds but also research foundations for medical technology development. Emerging jointly with stakeholders and governments, public research foundations made possible clinical research funding for that can contribute to public health promotion and will be a driving force in maintaining continuous clinical research for evidence generation.

In order to increase the credibility of evidence obtained through clinical research, the importance of process management must be acknowledged. Since the proposed scheme didn't collect the various opinions, the policy should be designed through the consultation of stakeholders and agencies related to actual system performed by authorities and the targeted medical technology.

Key words

selective reimbursement, conditional coverage, evidence development, clinical research support system, process management