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NECA
EVIDENCE & VALUE

The National Evidence-based Healthcare Collaborating Agency (NECA) provides scientific evidences to policy makers and the general public, by analyzing clinical effectiveness and economical efficiency of pharmaceuticals, medical devices and health technologies ultimately contributing to the enhancement of public health. The Evidence and Value is a journal of NECA to develop the necessary evidences in the healthcare sector for rational decision making and efficient resource utilization.

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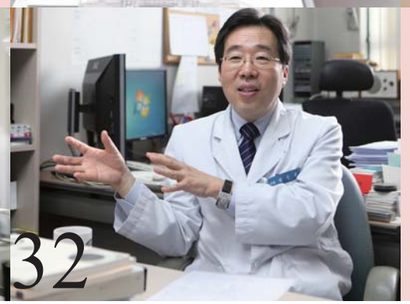
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The surrealism artist Rene Magritte had a mysterious way of thinking and his work displayed unexpected juxtapositions and paradoxes. The ideals and vision of the NECA are inspired by the work of Magritte.

What is Public Healthcare?

As with previous years, in the 2010 parliamentary inspection of administration, national university hospitals that 'concentrate on money making by ignoring public healthcare' were on the chopping block.
The point that national university hospitals are not sufficiently contributing to public healthcare has been raised every year during the parliamentary inspection of administration; issues raised include the number of multi-patient rooms, treatment of patients with medical benefits, employment of the disabled, elective treatment, and the actual state of emergency medical centers.

However, only superficial problems have been raised, and discussion on the following fundamental problems cannot be easily found. What are the objectives that must be pursued by public healthcare providers? Should only national university hospitals be responsible for public healthcare? Are private hospitals not responsible for public healthcare? Should those who are transported to emergency rooms in private university hospitals and then undergo appendectomies be considered as having received public or private healthcare services?

The logic is that national university hospitals with high numbers of treating patients with medical benefits, sick beds in rooms with 6 or more patients, and employment of the disabled, and that do not perform elective treatment are more sufficiently contributing to public healthcare than the hospitals which don't may not be representative of people who actually use hospitals. Of course, indiscriminately introducing expensive cutting-edge medical devices to create revenues to compete with private medical institutions is not the right role of national and public hospitals, their practices of unconditionally aiming to increase the number of multi-patient rooms, serve patients with medical benefits, and reduce medical expenses will make national and public hospitals incapable of providing services that are judged as satisfactory by the people.

How much do public health center and public health doctor systems that are representative public healthcare systems implemented by the government contribute to public healthcare? Although many public health doctors are assigned to private hospitals to support emergency healthcare, they actually spend most of their time bringing in more revenue for those hospitals. If public health centers that provide treatment services to financially vulnerable subjects implement free treatment in places where village clinics are concentrated, the survival of these clinics will be threatened.

In the past, when it was absolutely necessary to vaccinate and improve the hygiene in residential regions in order to prevent infectious diseases resulting from unhygienic living environments, judgments about the roles of public healthcare were not difficult. However, in an age of improved quality of life, implemented national health insurance, and 100-year envisaged life spans, defining public healthcare is not an easy task.

Sir Muir Gray of the UK defined public healthcare as being like water supplies in that the objectives and roles of public healthcare can be compared to the work required to make people confidently drink tap water at home at low cost.

If a local government does not invest in water supplies but concentrates on selling deep or mineral water, that government cannot be considered to be serving the role of a public institution properly. On the other hand, private hospitals can also be assessed as serving the function of public healthcare if they provide high quality essential healthcare at a reasonable cost.

Preventing water contamination ahead of time and maintaining and improving water quality are equally important as supplying clean drinking water. Unlike drinking water, healthcare service faces many diseases and diverse situations. To study the treatment that is best for a specific disease, and suggest the criteria required for high quality healthcare is important role of university hospitals should implement.
Judging whether certain pieces of healthcare information are right or wrong and continuously assessing whether appropriate healthcare services are properly delivered to the people are also necessary.

The healthcare market, which amounts to 70 trillion won per year, is continuously growing. Although healthcare is an area in which public interest elements are absolutely important, it certainly has sectors that can be developed into service industries that will create employment and contribute to national competitiveness. However, it is unfortunate that there are no clear criteria for the public state of healthcare; thus, policy agreements among government departments are not easily made.

There are limitations in assessing the public area of healthcare using only those roles that have been traditionally served by public healthcare, such as infectious disease control and treatment of lower income classes.
In order for healthcare to serve its intended role as a service industry axis while guaranteeing the essential healthcare for the people, the public healthcare sector should be newly defined.

Heo Dae-Seok, Chairman of the NECA

Opinion leaders' contributions to evidence-based decision making
※ The opinions expressed in this manuscript are of the author only and are not representative of the National Evidence-based Healthcare Collaborating Agency position.

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Adaptation of Clinical Practice guidelines:
Principles and Leadership in Korea

Clinical practice guidelines are currently regarded as a scientific research. It seems that as demands for developmental process transparency increase, domestic clinical guideline development groups are responding to demands. It is expected that clinical guidelines will be adapted by using more concrete methods.

1. What are clinical guideline adaptations?

Clinical practice guidelines are systematically developed tools that are used to help decision making in actual clinical settings as evidence based medicine continues to spread. A systematic search for and critical review of clinical studies should be implemented to develop evidence-based clinical guidelines. This process requires significant effort and resources.

Many clinical guidelines are being developed globally. The Guidelines International Network (G-I-N) has around 3,700 guidelines (IOM, 2011). However, quite a few of these clinical guidelines addressed the same subjects; thus, redevelopment of them would constitute duplication of effort. Accepting existing clinical guidelines rather than developing new ones in such cases is considered good practice. However, even when the same evidence has been used, recommendations may legitimately vary because of differences in population, healthcare system, and socio-cultural characteristics. Therefore, when local organizations intend to accept other clinical guidelines, recommendations should be drawn after thorough review of each guideline's suitability for the relevant region. This process is called adaptations.

Unlike de novo guidelines that use clinical trials, observational studies, systematic review, and meta-analyses as evidence, adapted guidelines use existing guidelines as the primary evidence. Fervbers and his colleagues (2006) divided adaptation guidelines into 3 types: adaptations as alternatives for de novo development, accepting guidelines of certain international organizations or foreign countries based upon the premise that those guidelines will be practiced, and revising national guidelines to fit a specific local community's needs.

Although quite a few clinical guidelines in Korea have been adapted, attention to adaptation meanings and methods has been low thus far. Upon reviewing the processes and results of guidelines adaptation in Korea, we discovered a few problems. In this document, problems raised against guideline adaptations will be examined and suggestions for improvement will be presented.

2. Issues raised in the clinical guideline adaptations

● Simple translations or adaptations

Clinical guidelines in Korea are gradually increasing. However, quite a few guidelines that are similar to foreign guidelines in structure and content have been developed at an unacceptable level. It is true that our society has been accepting of foreign guidelines in situations where attention to clinical guidelines was low and resources were insufficient. However, simple translation of foreign guidelines should be distinguished from adaptation. In cases where foreign guidelines are simply translated, approval should be obtained from the authors and the guidelines should be labeled as having been translated.

Since domestic medical studies are being developed at the internal levels and support for guidelines is now increasing, translated guidelines should not be disguised as de novo ones. Due to this problem, experts in Korea recently gathered to reach an agreement on the definition of clinical guidelines and the inclusion and exclusion criteria. According to these criteria, simple translation of a foreign guideline cannot be considered a clinical guidelines (Ji et al., 2010).

Fortunately, simple translations of foreign guidelines are gradually decreasing and cases in which the adapted guidelines are marked "adaptation" are increasing. Clinical guidelines are now considered scientific research, and as demands for development process transparency are increasing, clinical guideline development groups are responding to these demands. Clinical guidelines are expected to continue developing toward including more concrete adaptation methods.

● Adaptations or de novo development

Although adaptations are used to develop clinical guidelines in most cases, their use is inappropriate in some cases. As mentioned earlier, the process of adaptation involves accepting guidelines developed in other environments to fit our situation with the intent of not duplicating effort. Although this is good practice in cases where the content and environment of domestic healthcare services do not differ significantly from those of the guidelines' original authors, adaptations are inappropriate if these environments are considerably different from the situations in Korea. In cases of the latter, those clinical guidelines should be used for reference only.

No definite criteria yet exist for choosing between de novo development and adaptation for certain health-related subjects. Empirically, it is considered that the value of adaptation is high for acute phase hospitalization services in Korea in which there are only small differences in treatment environments from those of foreign countries. On the other hand, it is quite likely that adaptation efficiency is low in areas such as primary healthcare or mental diseases, where more significant differences in healthcare service provision systems or socio-cultural structure exist. However, this division is not absolute and may vary with a given time period or change of healthcare system.

A methodology expert who recently experienced clinical guideline adaptation suggested that since the characteristics of clinical questions were diverse even within certain guidelines, use of both de novo development and adaptation is appropriate. For instance, in cases where both the screening and the drug therapy of depression patients are addressed, if the screening inspections have large differences in healthcare systems or

Problems raised with regard to clinical guideline adaptation indicate that use of a national level unified program is necessary to improve overall capabilities and standardize the development process. It is expected that clinical guideline-related infrastructure will be well established and that through this infrastructure, evidence based healthcare will be established along with clinical guidelines.

social environments compared to those in foreign countries but the drug therapy has relatively smaller differences, different development methods may be applied. Therefore, guideline development groups should select development methods that are suitable for subjects and development plans should be made more carefully. Concrete clinical guideline content and scope should also be reviewed by several groups of external stakeholders.

● Assessment of acceptability and applicability

The core process of adaptation is assessment of source guidelines and it can be classified as assessment of the acceptability, application and assessment of evidence-based methods. According to the ADAPTE manual, acceptability and applicability assessment includes answering the following questions (ADAPTAE Collaboration, 2007):

- Does the population described for eligibility match the population to which the recommendation is targeted in the local setting (acceptable)?
- Does the intervention meet patient views and preferences in the context of use (acceptable)?
- Are the intervention and/or equipment available in the context of use (applicable)?
- Is the necessary expertise (knowledge and skills) available in the context of use (applicable)?
- Are there any constraints, organizational barriers, legislation, policies, and/or resources in the health care setting of use that would impede the implementation of the recommendation (applicable)?
- Is the recommendation compatible with the culture and values in the setting where it is to be used (acceptable and applicable)?
- Does the benefit to be gained from implementing this recommendation make it worth implementing (acceptable)?

It is not always easy to answer these questions. Studies in Korea that are used to identify differences in context between our environments and those in the source guidelines are insufficient. In particular, studies related to patients' viewpoints or preferences cannot be easily found. Insufficient basic research makes decision making difficult. However, since the shortage of basic research cannot be solved in the short term period, the making of reasonable decisions in a given situation is an urgent task from the development standpoint.

No matter when clinical guidelines are developed, "insufficient evidence" is a problem that must be faced every time, and clinical guideline development groups must make the best decisions in any given situation. When evidence is insufficient either in Korea or globally, expert opinions are utilized and organizations responsible for clinical guidelines enlist expert opinions and transparently implement the development process using available criteria and procedures. Therefore, to enhance the process of developing clinical guidelines to the level of advanced countries, reasonable methods of expert consensus or social consensus should be presented, and standardized procedures should be widely shared.

Meanwhile, the fact that development groups are composed of mainly experts in certain clinical areas is affecting the entire development process, and this function as a constraint of acceptability and applicability assessment. If primary healthcare doctors are excluded from the development groups that are to be mainly used by primary healthcare doctors, it is quite likely that judgments on primary healthcare will remain at superficial levels. To prevent this problem, the guideline development groups that are composed of only doctors with same clinical areas or certain positions must be avoided. Those that are responsible for policies to support clinical guidelines should encourage the creation of multidisciplinary development groups, and should consider support measures based on the premise of the foregoing when necessary.

3. Principles of clinical guideline adaptations and the need for orchestra conductor leadership

When clinical guidelines are to be developed in Korea, adaptations might first be considered. However, as reviewed earlier, developing reliable clinical guidelines via adaptation rather than translation requires considerable amounts of effort and resources.

If initial plans are slack, subjects may be changed depending on the source guideline contents, and there may be aspects that would make it difficult to consider source guideline evidence review or acceptability and applicability assessment. Besides, although collecting other clinical experts' opinions through public hearings is desirable, problems that have already been considered may be found in this process.

Based on the reflections on problems raised in the process of adaptations of clinical guidelines, we should developed reliable guidelines. This effort should begin now in earnest. Principles that must be observed without fail by guideline development groups include the following.

- Establishing concrete plans regarding the subject, scope, adaptation (development) method of clinical guidelines
- Composition of multidisciplinary development groups
- Control of conflict of interest
- Systematic review of scientific evidence
- Consideration of patient's values and preferences
- Consensus process of formulating recommendations
- External review of recommendations
- Providing suggestions for implementation of recommendations

Another problem raised during reflection of the adaptation process is that the capability to develop trusted guidelines is insufficient. If we truly want to have reliable national-level guidelines, we should improve our capabilities. However, individual research groups or societies cannot easily conduct works such as methodology standardization, and it is difficult to individually deal with problems related with implementation problems of recommendations. Therefore, a unified national-level program is necessary for the harmonization of a series of processes ranging from the selection of guideline subjects to guideline implementation. Along with the program, leadership like that of orchestra conductors is necessary to harmoniously implement complex tasks

4. Conclusion

Clinical practice guidelines are important tools that enable evidence-based decision making in the area of healthcare. As we know, evidence-based recommendations have the largest effects on decision making. Therefore, the development or adaptation of trusted clinical guidelines is very important. And the development of a unified national-level program is necessary in order to improve overall capabilities and standardize developmental processes. Evidence based healthcare will be established along with clinical guidelines.

<References>

US Institute of Medicine. Clinical practice guidelines that we can trust. Washington, DC: The National Academy Press. 2011.

Ji Seon-Mi, Kim Su-Yeong, Shin Seung-Su, Heo Dae-Seok, Kim Nam-Soon. Definition of clinical practice guidelines and criteria for the assessment of quality agreed by the RAND method. J Korea Soc Health Policy Admin 2010:20(2):1-16.

ADAPTAE Collaboration. Manual for Guideline Adaptation Version 1.0. 2007.

Fervers B, Burgers JS, Haugh MC, Latreille J, Mlika-Cabanne N, Paquet L, Coulombe M, Poirier M, Burnand B. Adaptation of clinical guidelines; literature review and proposition for a framework and procedure. Int J Qual Health Care 2006;18(3):167-176.

Planned discussion: How should evidence-based healthcare proceed?

For the second anniversary of the National Evidence-based Healthcare Collaborating Agency, Chairman Dae Seog Heo hosted a planned discussion with great scholars of this subject in the medical world to discuss the way evidence-based healthcare should proceed. During the discussion moderated by Research Fellow Sang Moo Lee, Professor Je Geun Chi and Professor Nam Sik Jung made great contributions to the development of healthcare in Korea and were liberal with their advice. Details of the meeting are included below.

- **Date and place: 2011.4.11 (Monday), Small Conference Room at the 11th floor**
- **Panelists**

Professor Je Geun Chi (former president of the Korean Academy of Medical Sciences)	Professor Nam Sik Jung (former dean of the College of Medicine, Yonsei University)
Emeritus professor of Seoul National University (Pathology)	Professor of the College of Medicine, Yonsei University (Cardiology internal medicine)
Graduated from the College of Medicine, Seoul National University	Graduated from the College of Medicine, Yonsei University
Former president of the Korean Society of Pathology	Chairman of the Board of the Korean Society of Cardiology
Former assistant director of the Korean Academy of Science and Technology	Auditor of the Korean Academy of Science and Technology
Former director of the Research Institute for Healthcare Policy, Korean Medical Association	
Chair-professor of the College of Medicine, Inje University	

Chairperson: Greetings. On its second anniversary, the NECA is holding a discussion meeting with veterans in the medical world. What do you think about institutions such as NECA that study evidence-based healthcare?

Professor Nam Sik Jung: I feel sorry that there is no culture where public research achievements are socially recognized yet in Korea. In case of the USA, advanced health care systems are being operated through evidence-based healthcare since huge amounts of clinical study expenses are provided for national health by national agencies such as NIH. The outcomes of clinical studies for long periods of time of 3–5 years are presented as evidence and the evidence is accepted as national policies. I think it is fortunate that the NECA was established in Korea so that evidence-based healthcare can be pursued but I feel sorry because its research outcomes are not properly utilized.

Assessment of existing health technology

Chairperson: The clinical trials necessary for item permission by the Korea Food & Drug Administration are conducted on small categories of patients, while drugs are used in diverse patient groups in actual healthcare sites. What do you think about the related uncertainty at sites?

Professor Nam Sik Jung: For instance, low-molecular-weight heparin has advantages such as the fact that its effect can be predicted if a certain dose is given, it involves low adverse effects to reduce blood platelet counts, and patients can inject it at home and thus they do not need to be hospitalized. For these reasons, heparin is injected into pregnant women. However, since it is currently not recognized by the insurance companies, patients must bear the expenses. Such expenses should be compensated the patients for later, if the patients raise civil complaints. Despite the fact that scientific evidence for it has already been proved, there are difficulties at sites, since there are institutional problems. In such cases, though researcher-initiated clinical studies are conducted, there are difficulties of monetary in reality. In this situation, I believe that research by the NECA should be activated further as with overseas

institutions so that research outcomes that can ultimately reduce medical expenses can be produced.

Direction of the development of new health technology

Chairperson: What do you think the evidence-based healthcare is urgently necessary?

Professor Nam Sik Jung: I think creating evidence for new health technologies or technologies placed in blind spots is more urgent than the research into health technologies that have been used for long periods of time and thus have already been verified.

Chairperson: On what areas should the NECA put emphasis on while assessing new health technologies?

Professor Nam Sik Jung: The NECA should not become obstacles to creative and original new health technologies. For instance, although there were objections against living donor liver transplantation at the beginning, as data were accumulated on this treatment method, it has become a standard treatment method and has resulted in the success of liver transplantation. There were also cases where treating the narrowed left main part of the cardiovascular system with stent insertion is proven to be as safe as existing surgical operations.

The NECA should contemplate in which phases of new health technologies the suitability, safety, and economic efficiency should be assessed.

Professor Nam Sik Jung

Chairman Dae Seok Heo

The NECA should consider the fact that such interventions may interfere with healthcare providers' originality for the development of healthcare.

When accepting new health technologies, patient safety should be an important proposition, and assessment for proving the technologies should be implemented objectively and transparently. Patient safety should be considered based on the Helsinki agreement and in the prospective studies. Therefore, not only committees to assess scientific content but also ethics committees should be included. In such cases, study data should also be monitored.

Chairperson: In the case of new health technologies, there are many problems such monetary ones. Where do you think are solutions for those problems?

Professor Nam Sik Jung: As a new health technology for valve surgery, valve replacement using catheters was developed in an advanced country and good outcomes have been reported. Since this procedure is expensive, there is no possibility for developers to provide the technology free of charge. Systems to accept these new health technologies are necessary.

Chairperson: Can coverage by an evidence development system based on the premise of the creation of evidence for public interest be an alternative?

Professor Nam Sik Jung: Since it is a system that will enable the site of treatment to quickly accept new evidence-based health technologies, I think it can be an alternative.

The NECA should become a Collaborating Agency…

Chairman Dae Seok Heo: A difficulty experienced while conducting studies over the last 2 years was that cases would occur where research outcomes could conflict with the interests of certain research groups.

Professor Nam Sik Jung: I think a society that cannot accept evidence-based research outcomes produced through scientific approaches such as economic efficiency analysis and safety analysis is not yet mature. In this situation, the role of the NECA becomes more important.

Professor Je Geun Chi: Actually what problems occurred?

Chairman Dae Seok Heo: When we concluded a certain medical practice as groundless, the medical teams that had been implementing the medical practice thus far would not accept the fact that they could be blamed for applying a groundless medical practice. In some cases, we could not easily draw a conclusion because there was disagreement between treatment specialties.

Professor Je Geun Chi: No matter how excellent NECA researchers are, it is difficult for the NECA to solve all pending social problems in the wide healthcare area. NECA should form close relationships with the medical and academic worlds.

When a social issue occurs, a committee is formed. In such cases, committee composition is important. Experts with databases that can be used as evidence for the issues should be employed to transparently compose and operate the committee. To this end, the NECA should find core experts in the medical world. In Korea, there is a tendency to assign committee members evenly among related societies or expert groups when composing a committee for objectivity. However, committees should be composed mainly based on persons rather than assigning evenly. The perspective to grasp issues that may be NECA's later missions is also necessary.

In the case of the US IOM (Institute of Medicine), a network consisting of numerous experts belonging to the medical sector has been composed. I know that the C in the English name NECA means "collaboration." In accordance with this meaning, please have close relationships with the medical and academic worlds and serve the role of a bridge. I hope the NECA will communicate with related societies, and I request the NECA to contribute to enhancing Korea's research capabilities with a will to do it properly rather than quickly.

What do we need to become a core research institution for establishing an evidence-based healthcare system?

Chairman Dae Seok Heo: There are cases where overseas evidence-based healthcare research institutes experienced difficulties because stakeholders raised problems, but the misunderstandings were resolved over time and, thus, they positioned themselves.

Professor Nam Sik Jung: The struggles for interests among healthcare providers are regretful. In the situation where all the damage related with the struggles is suffered by healthcare consumers, the authority of government-run research institutes is important, and this authority is created only when they are trusted by the people. Drawing evidence based on scientific data, assessing the evidence, making standards for medical practice, and broadcasting the standards are the roles of the NECA.

One more thing, it is important for NECA to be operated independently. Even if NECA receives funding from the government because it is a public institute, it should maintain independence in relation to research outcomes.

Professor Je Geun Chi: Similar overseas institutions also maintain independence from many stakeholders with which conflicts of interest may occur. In the case of the US IOM, financial sources are being diversified through its own revenues made through selling research outcome reports and donations.

The NECA is now in a process of accumulating trust. In the case of US IOM, research outcome reports have credibility related to healthcare provider credibility. Although critical research into wrong practices of the medical world may face resistance and objections presently, please accumulate trust through efforts for self-purification together with the medical world.

Chairperson: Can you present concrete examples?

Professor Je Geun Chi: The US IOM once selected study subjects that cannot be easily addressed by the medical world, such as medication errors and wrong diagnoses, and then published the research outcomes. Although the negative aspect of the medical world could be highlighted at the moment, it is accepted positively from the standpoint of the people in the mid/long run in that it provides an opportunity to improve the quality of healthcare.

One more thing I would like to request is that NECA should conduct studies with wider viewpoints so that health technology and healthcare systems in Korea can be of international standards.

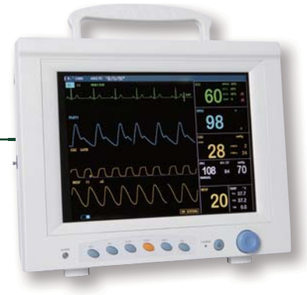
Chairman Dae Seok Heo: Reflecting on your comments today, we will make efforts so that NECA can develop into a better research institute. Thank you.

Professor Je Geun Chi

Research Fellow Sang Moo Lee

(Written by) **Worl Suk Lee,** Department of New Health Technology Assessment Research, Center for New Health Technology Assessment, NECA

Non-Invasive Cardiac Output Monitoring by Bioreactance Technology



Ⅰ. Overview

● The Non-Invasive Cardiac Output Monitoring by Bioreactance Technology is used to noninvasively measure cardiac output by attaching 4 pairs of sticker-type electrodes on the chest. Diverse cardiac output measuring methods including the thermodilution method using pulmonary arterial catheters are used as standards. The continuous cardiac output monitoring method based on arterial pressure is the most invasive. On the other hand, the bioreactance noninvasive cardiac output monitoring method, as the name suggests, is noninvasive and enables continuous measurement.

Figure 1. Monitor and electrodes for the bioreactance noninvasive cardiac output monitoring method

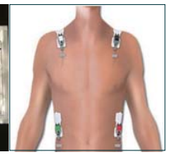


Figure 2. Electrode locations

Ⅱ. Methods

● The study was conducted by a systematic literature review. For the collection of domestic literature, 8 databases were used centering on KoreaMed. For the collection of international literature, Ovid-MEDLINE, Ovid-EMBASE, and Cochrane Library were used. Searches were conducted using "Bioreactance" and "NICOM" as keywords and were completed on September 6, 2010. A total of 425 pieces of literature were found; selection/exclusion criteria reduced that number to 246 studies. A total of 179 overlapping studies were excluded, resulting in a final of 5 studies. Literature quality was assessed using Scottish Intercollegiate Guidelines Network (SIGN) tools.

Ⅲ. Results

● The safety of the Non-Invasive Cardiac Output Monitoring by Bioreactance Technology was assessed by test-related complications and adverse effects, and its effectiveness was assessed via measurement accuracy (correlation and consistency with reference standards).

1. Safety

None of the papers selected for assessment had separately reported on safety. Since Non-Invasive Cardiac Output Monitoring by Bioreactance Technology was a noninvasive test method similar to electrocardiography, it was assessed as having no safety issues.

2. Efficacy

The accuracy of measurement was assessed via correlations and consistency with the reference standards. As reference standards, the thermodilution method using pulmonary arterial catheters (4 papers) and echocardiography (1 paper) presented in the individual papers were used. Two papers among the selected papers also presented the results of the continuous cardiac output monitoring method based on arterial pressure as a comparative test. The continuous cardiac output monitoring method based on arterial pressure is a test method that is currently registered as a "no benefit" item in the health insurance medical care benefit expense list.

A. Correlations with the reference standards: It was reported that the thermodilution method using pulmonary arterial catheters and the Non-Invasive Cardiac Output Monitoring by Bioreactance Technologyhad correlations of 0.71–0.82. The correlations between the thermodilution method using pulmonary arterial catheters and the continuous cardiac output monitoring method based on arterial pressure were 0.69–0.79; thus, Non-Invasive Cardiac Output Monitoring by Bioreactance Technology was assessed as having higher correlation with the thermodilution method using pulmonary arterial catheters than the continuous cardiac output monitoring method based on arterial pressure.

Table 1. Correlations with the reference standard

Author (year of publication)	Number of patients	Reference standard	Correlation of the intervention test	Correlation of the comparative test
Khan *et al* (2009)	47	Echocardiography	r=0.89/r=0.87	-
Marqué *et al* (2009)	29	PAC-CCO(TD)	r=0.77	r=0.69
Squara *et al* (2009)	20	PAC-CCO(TD)	r=0.77	r=0.79
Raval *et al* (2008)	111	PAC-CCO(TD)	r=0.78/r=0.71	-
Squara *et al* (2007)	110	PAC-CCO(TD)	r=0.82	-

(r: correlation coefficient; PAC-CCO: pulmonary arterial catheter-continuous cardiac output; TD: thermodilution)

B. Consistency with the reference standards: Consistency was assessed by the average value between the measured values of the 2 methods and precision (standard deviation). The bias of the Non-Invasive Cardiac Output Monitoring by Bioreactance Technology was -0.18–0.22L/min, which was smaller than the threshold of 0.52L/min defined by the researcher as a level equivalent to that of the reference standards. Precision was 0.71–0.84L/min, which was within the allowable limit of ±1 L/min defined by Van den Oever et al. (2007). The bias of the continuous cardiac output monitoring method based on arterial pressure was -0.01–0.01L/min and the precision was 0.81–0.93L/min. In conclusion, the bias and precision of the Non-Invasive Cardiac Output Monitoring by Bioreactance Technology were within allowable limits, and the method was assessed to be acceptable in clinics at a level similar to that of the reference standards.

Table 2. Consistency with the reference standard

Author (year of publication)	Number of patients	Reference standard	Bias/precision of the intervention test	Bias/precision of the comparative test
Marqué *et al* (2009)	29	PAC-CCO(TD)	-0.012	-0.012
Squara *et al* (2009)	20	PAC-CCO(TD)	0.22/0.835	0.01/0.93
Raval *et al* (2008)	111	PAC-CCO(TD)	-0.09/- , -0.18/-	
Squara *et al* (2007)	110	PAC-CCO(TD)	0.06/0.71	

(PAC-CCO: pulmonary arterial catheter-continuous cardiac output; TD: thermodilution)

The bioreactance noninvasive cardiac output monitoring method is a safe and effective test method to monitor the transition of cardiac outputs in situations such as emergency medical centers where invasive cardiac output monitoring equipment (the standard measuring method) cannot be used on patients who need continued hemodynamic monitoring.

If you scan the QR code, you will be able to see PDF files with your smart phone (depending on smart phone environment).

Ⅳ. Conclusions

● The Non-Invasive Cardiac Output Monitoring by Bioreactance Technology is a safe and effective test method to monitor the transition of cardiac outputs in situations such as those in emergency medical centers where invasive cardiac output monitoring equipment, which is a standard measuring method, cannot be used on patients who need continued hemodynamic monitoring (The Ministry of Health and Welfare notification no. 2011-17, 2011.2.16).

※ The full text of the new health technology assessment report can be read on the New Health Technology Assessment Committee home page (http://neca.re.kr/nHTA).

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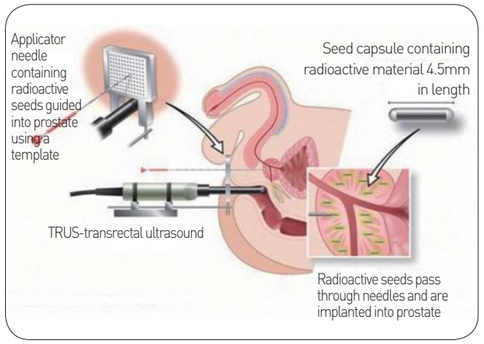
Iodine-125 Permanent Implant for Localized Prostate Cancer

Ⅰ. Overview

● Prostate cancer is the most common male cancer. With the widespread use of screening for prostate specific antigen (PSA), localized prostate cancer (stage T1-2) has shown a marked increase in Western countries. In Korea, it has shown same trend. Currently, the most common curative treatment options for men with localized prostate cancer are external beam radiation therapy, permanent implant (or it is called by 'brachytherapy') and radical prostatectomy. Each of these therapies has advantages and disadvantages, and the selection of an appropriate therapy depends on various patient factors, including the specific disease characteristics.

Iodine-125 Permanent Implant is a treatment for localized prostate cancer that involves the implantation of radioactive seeds (iodine-125 or palladium-103) into the prostate gland. The radioactive seeds deliver high doses of radiation to the tumor. Only permanent implants using Iodine-125 are the subject of this application. This report summaries nHTA's assessment of the current evidence available to address the safety, effectiveness of Iodine-125 for treating localized prostate cancer.



Permanent seed implant

▪ Objective

To evaluate the safety and effectiveness of Iodine-125 permanent implant for treating localized prostate cancer compared with radical prostatectomy, external beam radiation therapy.

Ⅱ. Methods

First, we found the HTA report by MSAC (Medical Services Advisory Committee, 2005) so that we did a systematic review for the period between 2005 and August 2010. The searches were conducted via electronic databases including MEDLINE, EMBASE, HTA websites, 8 Korean medical DB. The search strategy retrieved 650 non-duplicate citations. These were screened by two reviewers using prespecified eligibility criteria. Total 41 studies (8 comparative studies, 33 case series) were included for this review. The quality of literature

Iodine-125 Permanent Implant is a treatment for localized prostate cancer that involves the implantation of radioactive seeds (iodine-125 or palladium-103) into the prostate gland.

was assessed using the tool of the SIGN (Scottish Intercollegiate Guidelines Network) and two comparative studies were '++', 4 studies were '+', and 2 studies were '

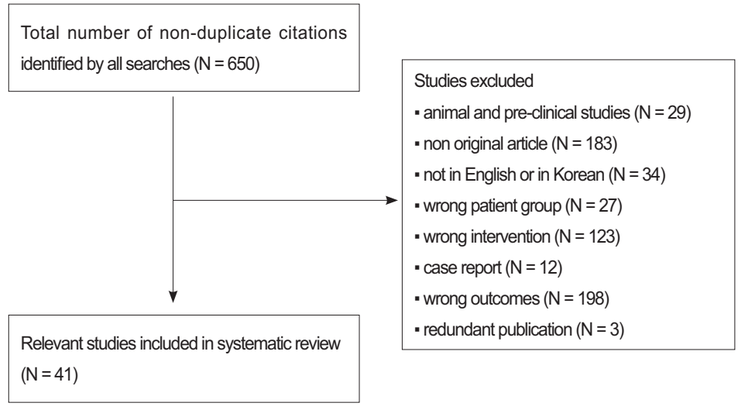


Figure 1. flowchart of study inclusions and exclusions

Ⅲ. Results

▪ MSAC's recommendation (MSAC 2005)

Following a reassessment of further evidence pertaining to the safety, effectiveness and cost-effectiveness of brachytherapy for the treatment of prostate cancer, interim public funding should continue for patients with prostate cancer meeting the following criteria: at clinical stages T1 and T2 with Gleason scores of less than or equal to 6, prostate specific antigen of less than or equal to 10 ng/mL, gland volume less than 40 cc and with life expectancy of more than 10 years; and where the treatment is conducted at approved sites.

▪ Safety

Iodine-125 permanent is comparable to or better than external beam radiation therapy, radical prostatectomy in terms of bowel and sexual function. Iodine-125 permanent result in higher rates of urinary toxicity but severe urinary toxicity did not happen and it resolved by conservative treatment. However, two case series reported that salvage therapy result in higher rates of severe urinary toxicity.

▪ Efficacy

a) Effectiveness was evaluated by biochemical disease-free survival rate. The evidence available does not demonstrate a difference in survival or disease progression between Iodine-125 permanent implant, radical prostatectomy, external beam radiation therapy in patients with localized prostate cancer. Some studies commented on the effect of risk factors (T stage, Gleason score, PSA). In case series, 5 year biochemical

we recommend that monotherapy is possible treatments for patients with low/intermediate risk group and boost therapy is possible treatments for patients with intermediate/high risk group.

disease-free survival rate of monotherapy was 91-98.2% for low risk group, 70-92.8% for intermediate risk group, 52-100% for high risk group.

Study	Patient characteristics	No. of Men	Outcome
Colberg(2007)	low risk	248	92% a
Hinnen(2010)	low risk	232	95% a
Nobes(2009)	low risk	197	98% a , c / 91% a, d
Kao(2008)	low risk	546	97.3% a/ 98.2% b
Zelefsky(2007)	low risk	319	96% a/ 96% b
Block(2006)	low risk	118	94.7% b
Khaksar(2006)	low risk	146	96% b
Colberg(2007)	intermediate risk	84	70% a
Hinnen(2010)	intermediate risk	369	87% a
Nobes(2009)	intermediate risk	144	89% a
Kao(2008)	intermediate risk	95	92.8% a / 91.3% b
Zelefsky(2007)	intermediate risk	47	90% b
			88% a
Khaksar(2006)	intermediate risk	111	89% b
Torres-Roca(2006)	intermediate risk	88	83% b
Colberg(2007)	high risk	18	52% a
Hinnen(2010)	high risk	320	59% a
Nobes(2009)	high risk	59	100% a
Khaksar(2006)	high risk	43	93% b

a : Phoenix definition (nadir + 2 ng/mL), b : ASTRO definition (three consecutive rises of the PSA level after a nadir) ,
c : brachytherapy (monotherapy), d :brachytherapy with neoadjuvant hormonal therapy
• low risk : stage T1c, T2a and PSA level ≤10 ng/mL and Gleason score ≤6
• intermediate risk : stage T2b or Gleason score of 7 or PSA level 〉10 and ≤20 ng/mL
• high risk : stage T2c or PSA level 〉20 ng/mL or Gleason score ≥8

Table 1. biochemical disease-free survival rate at 5 years

b) A comparative study, boost therapy was associated with an increase in survival in high risk group.

Treatment	No. of Men	Multivariable Analysis		
		Adjusted Hazard Ratio	95% CI	p value
Brachytherapy	221	1	reference	-
Brachytherapy + NHT	254	0.63	0.27 – 1.47	0.28
Brachytherapy + EBRT	217	0.57	0.21 – 1.52	0.26
Brachytherapy + EBRT + NHT	650	0.32	0.14 – 0.73	0.006

NHT, Neoadjuvant Hormonal Therapy; EBRT, External Beam Radiation Therapy

Table 2. biochemical disease-free survival rate at 5 years (D'Amico et al 2009)

c) There is insufficient evidence (3 case series) of salvage therapy to demonstrate effectiveness.

Ⅳ. Conclusions

● On the basis of current data, we recommend that Iodine-125 Permanent Implant (monotherapy) is a possible treatment for patients with low/intermediate risk group and Iodine-125 Permanent Implant (boost therapy) is a possible treatment for patients with intermediate/high risk group.

※ The full text of the report can be read on the New Health Technology Assessment Committee home page (http://neca.re.kr/nHTA or http://nhta.or.kr/nHTA/).

If you scan the QR code, you will be able to see PDF files with your smart phone (depending on smart phone environment).

Researchers

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(written by) Department of Health Technology Assessment Research, Office of Health Technology Assessment

The National Evidence-based Healthcare Collaborating Agency's

Educational Course on Systematic Reviews

Systematic review is a study method that is used to assess the effectiveness and safety of health technology by systematically reviewing studies related to particular study subjects and critically reviewing and summarizing the study findings to create evidence that can be used today.

Given that medical information has recently increased to the extent that individuals cannot handle it, and evidence-based medicine is emphasized outside actual treatment environments, theses systematic reviews can be essential in the process of making healthcare policy decisions and medical field.

The Department of Health Technology Assessment Research is implementing education on systematic reviews for the second time since 2010. A characteristic of this educational course is that education is implemented step-by-step using studies conducted by the National Evidence-based Healthcare Collaborating Agency and using findings of systematic reviews as actual cases. This course aims to enable students to actually implement a systematic reviews by combining theory classes with practices necessary in the individual stages of systematic reviews, including protocol preparation, searches for studies, design search strategies, assessing the quality of included sutdies(assessment of the risk of bias), and meta-analysis.

<Contents of the educational course>

Division		Schedule	Content
Systematic reviews of interventions	Lecture 1	3/28 (Mon)	● Understanding evidence-based decision-making in healthcare systems
			● Preparing protocols for systematic reviews through key questions
	Lecture 2	4/4 (Mon)	● Practice of search methods and using EndNote (Ovid interface database)
	Lecture 3	4/11 (Mon)	● Practice of search methods and surge using EndNote (Cochrane Library & PubMed, Domestic database)
	Lecture 4	4/18 (Mon)	● Assessment of the quality of studies and practice (Cochrane's risk of bias, RoBANS, and AMSTAR)
	Lecture 5	4/25 (Mon)	● Introduction to meta-analysis, data extraction, analysis, and practice (RevMan)
	Lecture 6	5/2 (Mon)	● Meta-analysis, small study effects, heterogeneity, and meta-regression
	Lecture 7	5/9 (Mon)	● Practice on evidence level and recommendation intensity using GRADE (GRADEpro)
Systematic reviews of diagnosis	Lecture 8	5/16 (Mon)	● 진Introduction to systematic reviews of diagnosis, protocol preparation, and searching
	Lecture 9	5/23 (Mon)	● Quality assessment/meta-analysis in systematic literature reviews of diagnosis

In particular, the study demand and trends this year have been reflected by recent addition of educational courses on systematic reviews of both intervention and diagnosis.

※ Inquiry: Responsible person in the Health Technology Analysis Team (02-2174-2735)

NECA

(written by) Department of Evidence Assessment, Office of Research Planning and Management, NECA

Borne for timely evidence: ‘RAPID’

Rapid
Assessment &
Production of High Quality
Information
Demanded Program

Background of establishing the RAPID program

As situations where increasing numbers of quick policy decisions are required due to changes in the forms of diseases such as novel swine-origin influenza A(H1N1), mad cow disease, and avian influenza; social issues; and subject urgency, requirements for timely best evidence are increasing. So, existing study outcomes should be quickly and systematically assessed to provide scientific evidence helpful to healthcare decision making.

However, no institution in Korea currently provides scientific evidence in a quick and timely manner for urgent healthcare-related subjects. Representative institutions and programs that implement rapid review in foreign countries include the Rapid assessment of the US Agency for Healthcare Research and Quality (AHRQ), Health Technology Inquiry Service (HTIS) of the Canadian Agency for Drugs and Technologies in Health (CADTH) in Canada, Health Evidence Network (HEN) of the World Health Organization (WHO), Rapid Review and Australian Safety and Efficacy Register of New Interventional Procedures-Surgical (ASERNIP-S) in Australia, and the Rapid Evidence Assessment (REA) of Civil service in the UK. However, there is no consistent conclusion about the definitions of the terms or implementation periods or methods.

In this respect, timely evidence suitable for the situation in Korea should be provided and appropriate methodology and standards with balanced qualities of evidences should be prepared.

Therefore, the National Evidence-based Healthcare Collaborating Agency established the RAPID program in order to provide the best available and timely evidence for urgent healthcare-related subjects required by the people and policy decision makers. The program will be introduced as follows.

Introduction of the RAPID program and its implementation processes

The Rapid Assessment & Production of High Quality Information Demanded Program (RAPID) is a program that provides the best evidence in a timely manner when it is urgently required. The process of implementing RAPID is as follows (Figure 1).

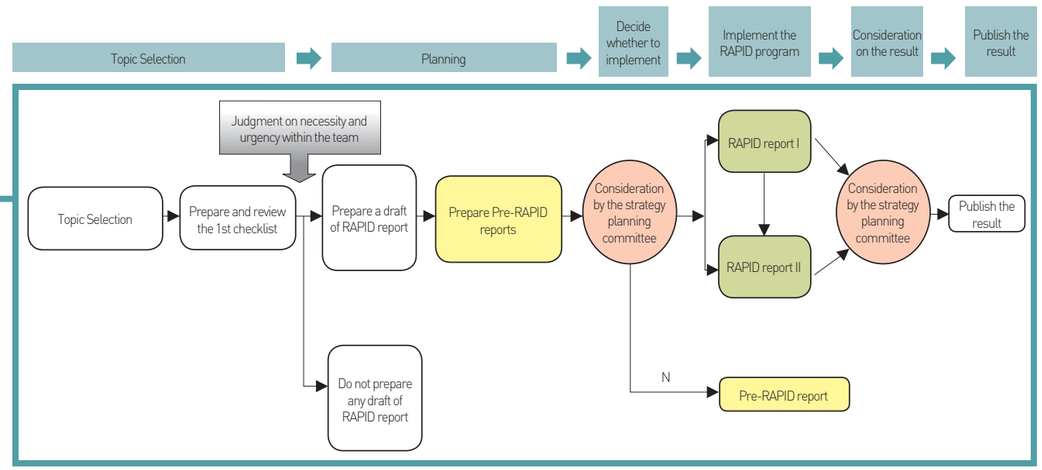
First, the subjects are selected. When requested by governmental or related agencies, when drawing internal study subjects, or when drawing urgent subjects in the process of surveys of demand for study subjects, planned reports are prepared considering the categories, necessity, urgency, possibility of implementation, and expected study effects.

Second, based on the planned reports, the agency’s Strategy Planning Committee determines whether to implement RAPID.

Third, subjects dropped in consideration are closed with pre-RAPID reports and in the case of bills accepted in deliberation; RAPID reports are prepared through rapid and scientific literature review according to the internal RAPID program operation policy.

Fourth, reports on implemented RAPID programs are deliberated again by the agency’s Strategy Planning Committee to provide the results to demanders.

Figure 1.Process of the RAPID program



RAPID characteristics

RAPID is implemented in accordance with subjects or situations without being restricted by methodology rather than adhering to traditional systematic review, and reports are prepared based on literature evidence and expert opinions.

Reports presented through RAPID include reports prepared using either abstract or full literature reviews.

The difference of RAPID from the existing systematic review is its timeliness and rapid nature. Its characteristics are as follows (Figure 2).

Figure 2 Characteristics of the RAPID program

Plans to use RAPID and the expected effects

Results obtained using RAPID can rapidly provide the best available evidence in a short time based on scientific evidence to the people, experts, and policy makers for urgent healthcare-related subjects that can be used as evidence for determining policy.

However, since RAPID reports are prepared with 2 conflicting values in mind (timeliness and quality), this fact should be taken into consideration.

RAPID: Rapid Assessment & Production of High Quality Information Demanded Program, a program that provides the best evidence in a timely manner when evidence is urgently required.

(written by) **Sung Hee Oh**, Office of Health Technology Assessment, NECA
(supervised by) **Jeong Hoon Ahn**, Senior Director Research Fellow, Office of Clinical Outcome Research, NECA

In order to enhance people's interest and understanding of the economic evaluation in the area of healthcare, the Economic Evaluation Team of the National Evidence-based Healthcare Collaborating Agency is planning to periodically review major journals such as Pharmacoeconomics and Value in Health and introduce recent trends and new concepts of economic evaluation methodologies.

Review of the transferability of other countries' model-based economic evaluations

Several countries utilize economic evaluation in the healthcare decision-making process, policy makers of various countries have come to seriously consider whether model-based economic evaluations implemented in foreign countries can be applied to their countries. Accordingly, checklists have been developed to assess the transferability of the results of economic evaluation in health care by many scholars in the area of healthcare. Boulenger et al.(2005) defined "transferability" in healthcare as "When potential users of economic evaluation intend to use a study already implemented in environments to which they belong, they can use the data, methods, and results of a given study if they can assess their applicability to their setting and they are applicable to that setting." In accordance with this definition, Essers et al. (2010)[1] presented processes to apply model-based economic evaluations to other countries in the following 3 stages through an example of processes to review whether a model-based economic evaluation for Herceptin (component name, trastuzumab), an assistant remedial agent for HER2-positive early breast cancer implemented by NICE in the UK, can be applied in The Netherlands.

Stage 1: Assess transferability

Economic evaluation studies in a certain country should be assessed to see whether it can be applied to other countries and, to this end, tools developed in published studies can be utilized.

First, the Transferability Decision Chart, presented by Welte et al. (2004)[3], is composed of general and detailed transferability criteria. Studies that are excluded by the general criteria have low transferability; thus, it can be seen that conducting new studies can be more appropriate than transferring them. Transferability factors that must be corrected for applying studies conducted in other countries can be identified through the detailed exclusion criteria.

Second, the checklist developed by Boulenger et al. (2005)[2] is composed of 42 questions related to study subjects, methods, effects, and discussion. For each question, the state is measured by giving 1 point to "yes," 0.5 point to "partially," and 0 points to "no." The scores for all the questions are added up to assess transferability and find transferability-limiting factors.

Third, the checklist by Urdahl et al. (2006)[4] assesses items related with "the viewpoint of analysis, definition of regions, transparency of reports on the details of models, suitability of data sources, and uncertainty of parameters" of economic analysis in order to review how studies conducted in other regions or viewpoints can be transferable.

Stage 2: Adapt factors that limit transferability

If factors requiring correction are found, they become factors that can limit transferability. Therefore, Essers et al. (2010)[1] examined whether it was feasible to adapt this factor based on existing knowledge estimating relationships between different environments and then adapted and used them if possible. For instance, regarding the 'medical costs-discount rates' in detailed cost informations of UK model-based cost–effectiveness analysis, they judged the relationship between the UK and Netherlands as being 'low-moderate' and adapted the medical costs-discount rates based on 'Price index figures-Phamacoeconomic guideline'.

Stage 3: Estimate country-specific cost effectiveness

Stage 3 is the process to assess the applicable country(setting)-specific cost-effectiveness based on the variables and models corrected in Stage 2. Uncertainty is also estimated through one-way sensitivity analysis and probabilistic sensitivity analysis.

Essers et al. (2010)[1] believed that applying the model-based economic evaluations from other settings to certain countries through assessing the transferability could shorten the benefit appraisal processes for new health technologies. However, to transfer model-based economic evaluations implemented in different countries or settings, transparency of methodologies and outcome reports of given studies is required. It should be possible to access the healthcare data sources of the country to which the models could be applied. Precise assessment of model-based economic evaluations should also be supported. If these conditions are not met , the process to bring the outcomes of studies conducted in different settings also requires a considerable amount of time and effort. In relation to transferability, the ISPOR Economic Data Task Force emphasized that when transferring model-based economic evaluations implemented in different settings, identifying limiting factors was most important, and remarked that those developing national guidelines for economic evaluations should think carefully about the need for local data or methods.

Therefore, to enhance the transferability of economic evaluation models implemented in different environments, transferability should be basically considered from the process of developing economic evaluation guidelines, and processes to review the transparency of the models to be applied using appropriate transferability assessment tools are essential. Furthermore, when transferability-limiting factors are adapted, although cost conversion between countries has been frequently addressed in the area of traditional economics and can be utilized diverse conversion indexes such as the Purchasing Power Parity, for converting effects such as utility between countries, we should be cautious because of differences in race or sociocultural value systems.

This manuscript has been prepared based on the paper of Essers et al. (2010).

1. Essers B, Seferina S, Tjan-Heijnen V, Severens J, Novák A, Pompen M, Oron U, Joore M. Transferability of model-based economic evaluations: the case of trastuzumab for the adjuvant treatment of HER2-positive early breast cancer in the Netherlands. Value in Health 2010;13(4):375-80.

2. Boulenger S, Nixon J, Drummond M, Ulmann P, Rice S, de Pouvourville G. Can economic evaluations be made more transferable? Eur J Health Econ 2005;6:334-46.

3. Welte R, Feenstra T, Jager H, Leidl R. A decision chart for assessing and improving the transferability of economic evaluation results between countries. Pharmacoeconomics 2004;22:857-76.

4. Urdahl H, Manca A, Sculpher M. Assessing generalisability in model-based economic evaluation studies. A structured review in osteoporosis. Pharmacoeconomics 2006;24:1181-97.

(Written by) **Ji Yu Song** (Photo) **Sang Young Yun**

The Department of Outcomes Research is responsible for evidence between the 2 large pillars–evidence and value–that constitute the National Evidence-based Healthcare Collaborating Agency. The womanpower of the 9 individuals who are using careful analysis to create new evidence suitable for our situations is dazzling.

NECA: a Mecca of Outcome research to provide evidence

On a shiny spring day, laughter flowed unceasingly among the 9 women gathered in the meeting room. In the National Evidence-based Healthcare Collaborating Agency, where people are striving hard to establish a public nature and identity in which scientific evidence and social value are considered, those who work day and night in order to create evidence are the very members of the Department of Outcomes Research that boasts woman power.

The Department of Outcomes Research that works with the sense of a mission to create the best evidence for healthcare is a team that makes evidence when evidence of health technology or policies more suitable for situations in Korea is necessary or when new evidence is necessary because there are no data for medical teams to apply as evidence in treatment sites.

As explained by Principal Researcher Sun Young Jung, the Department of Outcomes Research conducts outcome research for study subjects that have high social value but have insufficient evidence; thus, evidence should be created.

Creating optimal evidence for healthcare

When evidence must be created, the Department of Outcomes Research conducts outcome research that measures, compares, and assesses outcomes in diverse aspects such as clinical effects, patient satisfaction, and expenses to concentrate on creating suitable and valid data. In particular, in order to create good quality study data, this team develops survey forms and questionnaire tools and is responsible for quality control, such as monitoring the data collection and outcome analysis stage. Furthermore, in outcome research using secondary data sources, this team is responsible for overall processes of designing studies, grasping the health technology to be studied, defining outcome indexes, analyzing risk factors for bias correction, establishing plans so that valid evidence can be made, and collecting and analyzing data.

In the case of our studies, many outcomes are obtained through long-term follow-ups. However, since most studies should be finished in a year and the people who need evidence cannot wait forever, it is difficult to obtain necessary data at a correct time with necessary methods due to temporal restraints.

As indicated by Deputy Research Fellow Jin Won Kwon, the most difficult part is data sourcing. Therefore, this team is seeking various methods to overcome the difficulties as well as making continuous efforts for contemplating and developing the newest outcome research methodologies. In particular, in overall processes of outcome research to create primary data sources or those using secondary data sources, multidisciplinary approaches in collaboration with related clinical experts are essential. To this end, the team members aspire to establish an outcome-based research system to create optimal evidence based on cooperation and communication.

Beautiful women who bloom with good results

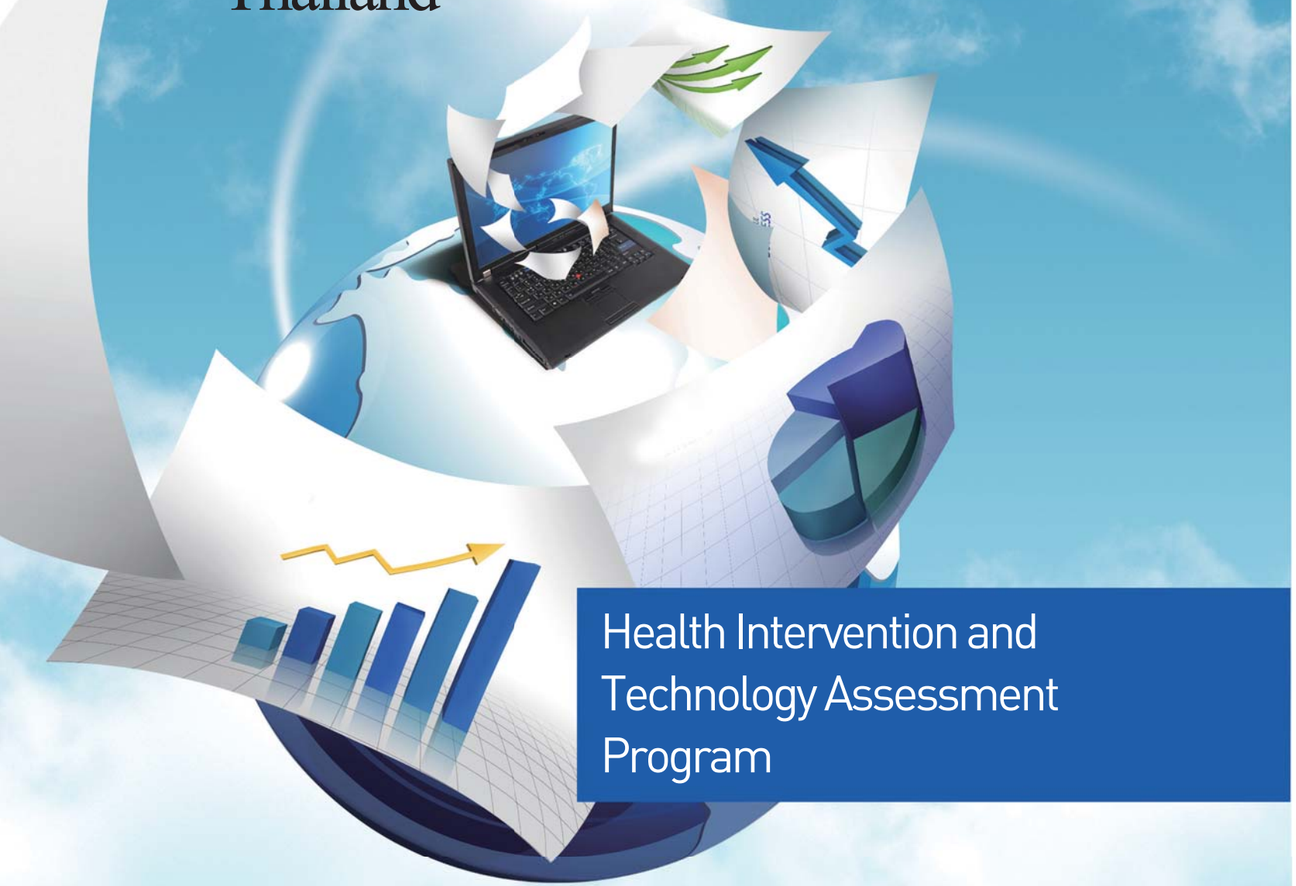
Despite many difficulties and challenges, the Department of Outcomes Research conducted 16 studies for around 2 years after the establishment of the NECA. Representative studies include "Disease burden of seasonal influenza and effectiveness of seasonal influenza vaccination in Korea," "Long-term Safety and Stability of refractive surgeries in myopia," "Long-term Safety and Stability of refractive surgeries in myopia," "Health technology assessment for effectiveness and safety of human placental extracts," and studies for public interest such as "Societal consensus formation regarding the withdrawal of meaningless life-sustaining treatment." In particular, "A study of early stomach cancer treatment using endoscopic submucosal dissection" is a long-term, 7-year study of which 5 years is remaining.

The team consists of 9 women: Team Leader Hyun Joo Lee, who is responsible for these works; Senior Researcher Min-Kyung Hyun; Responsible Researcher Ji Eun Choi; Researcher Jong Hee Kim; Researcher Jung Im Shim; Researcher Eun Ju Lee; and Researcher Na Rae Lee. This group's members refer to themselves as the famous Korean girl group, "Girls' Generation." These members say that their largest reward is that they can grasp facts that people do not know well, share these facts, and focus all of their energy on outcome research to create evidence that reflects the reality of Korea today.

When I asked them what their hope was, they said it was "becoming the first public institution outcomes research team in Korea." The team members frequently burst into laughter when one of them speaks. However, with keen eyes and sharp analytical skills, they allow no errors in their work. Since every one of them is an excellent entertainer, they are self-confident and can produce good results if all 9 of them work together. It really seems like they can be considered the "mecca" of the NECA.

(Written by) Yot Teerawattananon MD., PhD.
Leader of Health Intervention and Technology Assessment Program (HiTAP)

Using research to gain health and allocate resources sensibly in Thailand



Health Intervention and Technology Assessment Program

Statement of the problems

Thailand has devoted an increasing proportion of its national resources to healthcare over the last three decades due to the increasing availability of high-cost innovations, a fast ageing population and the introduction of the universal health coverage. In addition, there was an alarming irrational use of technologies, which resulted in a growing demand for evidence-based recommendations regarding the appropriate use of health resources and technologies.

Although some academic units had been conducting health technology assessment (HTA) for a number of years, these projects were short-lived or not successfully linked to policymaking. Furthermore, decision makers lacked understanding of, trust in, and incentives to use the results from HTA in policy and practice. Also, limited research capacity to produce timely, policy-relevant and high-quality HTA was a major obstacle.

Approaches for problem-solving

With the mission of addressing the abovementioned challenges, the Health Intervention and Technology Assessment Program (HITAP) was formally set up in 2007. The programme was initially funded by the Thailand Health Promotion Foundation, the Health Systems Research Institute and the Ministry of Public Health, with the aim of evaluating the medical, economic, social, and ethical implications of development, diffusion, and use of health technology in a systematic, transparent, unbiased and robust manner. A comprehensive scope for HTA was adopted since inception, including not only pharmaceuticals, vaccines, medical devices and procedures, but also public health interventions, health policies and the health system itself.

In HITAP the main research agenda is set annually during a consultation with key stakeholders from different organizations, who are invited to suggest research topics. Through participatory and deliberative processes, the top priority topics are selected to conduct HTA and feed into policy decision making. Although a systematic and well-planned prioritization of research topics is established, HITAP is flexible to respond to urgent requests from policymakers when they are facing challenging policy questions, in order to create a close link with and hold accountability to them.

HITAP has devised robust and context-specific methods for conducting HTA, which are available for the scrutiny of policymakers, professionals and the public. HITAP does not only evidence synthesis and policy analysis, but also primary research, such as household surveys, observational and experimental studies. An essential part of HTA is to ensure participation of all relevant stakeholders, so that the final recommendations can be acceptable for all parties. Pertinent policymakers, professionals, academics, industry, civil society organizations and citizens are identified and invited to participate for scoping of the research questions and validation of the research inputs. As a result of inviting stakeholders to participate in the HTA processes, understanding and trust of methods and policy relevancy of research are ensured.

HITAP strategies for research dissemination have been carefully devised as they play a crucial role in enhancing evidence utilization in policy and practice. Key principles of effective communication with stakeholders, including sincere dialogues, tailor-made messages and appropriate channels have been introduced in every step of studies. Mainly, research findings are presented to and discussed with relevant stakeholders in policy and technical meetings. As many studies conducted by HITAP are made upon requests from national health authorities, the researchers obtain opportunities to discuss the proposals and findings with respective decision-making committees. Besides, concerned parties can visit HITAP's website to follow up the progress and results of particular projects. Research reports are distributed in hard copy to hundreds of organizations and individuals throughout the country. In some instances, public forums on certain policies are convened by HITAP in collaboration with its alliance. Public media such as newspapers, magazines, television and radio are important channels through which HTA information is conveyed to the general public.

In the relatively short period in which HITAP has been active, the impact of its works is already noticeable. HITAP's works have assisted the authorities in developing or re-designing policies that have resulted in evident health gains for the society and important cost savings. For instance, during the time of active promotion of the human papillomavirus vaccine, an evaluation of strategies to prevent cervical cancer concluded that the most cost-effective strategy was to improve accessibility to screening and not to adopt the vaccine, because the vaccine protection duration is still uncertain and its price was too high for the vaccine to become cost-effective in Thailand. The recommendations were promptly adopted by the responsible authorities, resulting in a significant increase in screening coverage from 20% in 2006 to 70% in 2010. It is estimated that this improvement could avert 1,500 new cervical cancer cases and 750 women deaths annually and save 6 million international dollars per year from treating the advance cancer cases. Meanwhile, the industry decided to adjust down the vaccine price according to HITAP's recommendations, despite the vaccine is not reimbursed by the public health plan yet. Another example is HITAP's role in solving the social debate regarding the feasibility and value for money of a new drug regimen for prevention of mother-to-child HIV transmission, in which research recommendations were implemented nationwide and an estimated 101 paediatric HIV infections are currently saved annually.

The success of HITAP in translating its research outputs into effective policies is partly based on the organization's strict code of conduct, which precludes accepting benefits from the private sector, for example. Its neutral position, as an autonomous research institute, has also facilitated the adoption of its recommendations by decision makers. In order to overcome the limited number of HTA researchers available, HITAP recruits young and committed staff to work closely with experienced researchers, and has established fruitful links with the academic sector, employing scholars who act as advisors for junior staff and supervise research projects. Moreover, HITAP offer formal education to its junior staff whose commitment and capability are well demonstrated during their apprenticeship. These approaches have proved effective in attracting and retaining young university graduates. At present, HITAP employ 6 senior (PhD) staff, 36 mid-career and junior staff, and 7 administrative officers and 3 mass-media communication specialists.

Challenges

Nevertheless, these advances are not free from important challenges. Perhaps, the most prominent is the long-term sustainability of the organization, if the programme does not become institutionalized with an official mandate and support. Currently, HITAP's recommendations are not legally binding either. As a consequence, changes in health policy direction and priorities may hinder the growing status of the institute. Meeting the increasing need/demand from policy makers both inside and outside the country is another challenge, taking account of the limited number of research staff available. Although HITAP's main priority is the national policy development, building regional and international networks has been both a learning opportunity for staff and rising HITAP's reputation at international level, which will turn to support its national movement. Recent examples include working with Myanmar's Ministry of Health to develop a maternal-child health initiative or assisting WHO in informing pandemic influenza preparedness guidance with economic evidence. In conclusion, although the Thai experience in developing a formal system for evaluation of health technologies may serve as an example for similar settings, important challenges along the way need to be addressed with leadership, scientific rigour, transparency, and involvement of all relevant parties.

Links

- Health Intervention and Technology Assessment Program (HITAP) website: http://www.hitap.net/index_en.php
- Thai Health Technology Assessment Guideline. Journal of the Medical Association of Thailand 2008; 91 (2): http://www.hitap.net/backoffice/report/pdf_reports/2009-04-08_JMed.pdf
- First Step. Evaluating HITAP: 2 years on:http://www.hitap.net/backoffice/news/pdf_news/2010-03-11_FirstStep(Eng).pdf

(written by) **Dong-Uk Lee**, Director General for Healthcare Policy, the Ministry of Health and Welfare

Direction of healthcare policies
for healthy people and a safe society

Korea has enhanced the people's accessibility to healthcare by providing national health insurance. Our life expectancy is higher than that of people in advanced countries, even those with lower medical expenses (life expectancy in 2008, 79.9 years; OECD; 79.4 years). However, it is true that although high-level infrastructures have expanded quickly, the government did not faithfully control resources such as manpower, sick beds, or equipment, instead operating the health insurance system mainly with price control in mind and making only sporadic investments for expanding public healthcare infrastructure in national/public institutions.

Last March, the Ministry of Health and Welfare announced a plan to reestablish medical institutes' functions.

The goal of the reestablishment of medical institutions is to establish sustainable healthcare systems. The ministry will rectify inefficient healthcare systems and mandate that medical institutions provide high quality healthcare services at appropriate expenses. The ministry will reform related systems so that clinics can concentrate on minor ambulatory treatment, hospitals can concentrate on hospitalized treatment, and large hospitals can concentrate on educational/research functions and treating patients with advanced diseases.

First, the ministry will reorganize the charge for medical treatment and criteria for designating high-class hospitals to induce treatments and roles suitable for the functions of medical institutions by class, and promote mutual requests for treatment and returns between medical institutions, utilization of treatment information, and linked cooperation in order to enhance patients' convenience.

Furthermore, the ministry will introduce a medical institution certification system and utilize it in requirements for designating high-class general hospitals to ensure that medical institutions can utilize brand effects and induce competition between medical institutions from the standpoint of patients to reinforce the patients' rights to be provided with high-quality healthcare services.

Among others, the Medical Dispute Adjustment Act, a long-cherished hope of our people and medical personnel drastically passed by the National Assembly 23 years after its first submission, was promulgated on April 7, 2011 to make a historic foundation to establish safe treatment environments.

Instead of lawsuits that took an average of 2 years and 2 months, medical accidents can now be settled within 120 days via the Medical Dispute Mediation and Arbitration Board to greatly reduce social expenses or patients' and medical personnels' mental burdens.

Through objective investigations of medical accidents, the victims' burden of proof was minimized and a medical dispute mediation and arbitration system will be prepared so that it can be settled as a system beneficial to both the people and the medical personnel.

Although the rebate dual punishment system became effective last November, illegal rebates remain the same due to excessive competition between pharmaceutical companies. The ministry has a firm will to eradicate illegal rebates without fail in order to realize fair society without foul or privilege.

The Ministry of Health and Welfare, prosecution, police, Korea Food & Drug Administration, Health Insurance Review & Assessment Service, National Health Insurance Corporation, Fair Trade Commission, and National Tax Service will cooperate at a government-wide level to operate permanent monitoring systems and strictly treat violating practitioners pursuant to the law to do their best to establish sound order of distribution.

Furthermore, in order to reinforce support for healthcare blind spots such as the vulnerable classes, the ministry will expand multiclass healthcare safety networks to protect ordinary persons by activating donation culture in the healthcare sector, where donation rates are relatively low, through fundraising institutions dedicated to healthcare.

The ministry will introduce helicopters dedicated to emergency healthcare to be occupied by doctors and equipped with various emergency medical devices for the first time in Korea, to serve emergency patients on islands and in vulnerable regions in order to enhance the rapidness and professionalism of emergency patient transportation systems.

The paradigm of health and welfare policies is being switched toward the direction of maintaining the balance between the expansion of welfare and sustainability for the government to faithfully guarantee the people's basic health and safety.

From this viewpoint, the Ministry of Health and Welfare will form a "healthcare future committee" to prepare future blueprints and alternatives for measures to stabilize health insurance finance, measures for efficient use of healthcare resources such as manpower, and preventive health improving measures such as measures against smoking and suicide.

However, this is impossible with the government's efforts alone; the wholehearted understanding and cooperation of academia, research institutes, interest groups, non-government organizations, and the people are essential.

The ministry promises to make its best effort to sufficiently collect opinions of various classes and discuss with them ways to achieve social consensus to secure the sustainability of healthcare systems that would result in "healthy people and a safe society."

Profile

Lee Dong-Uk

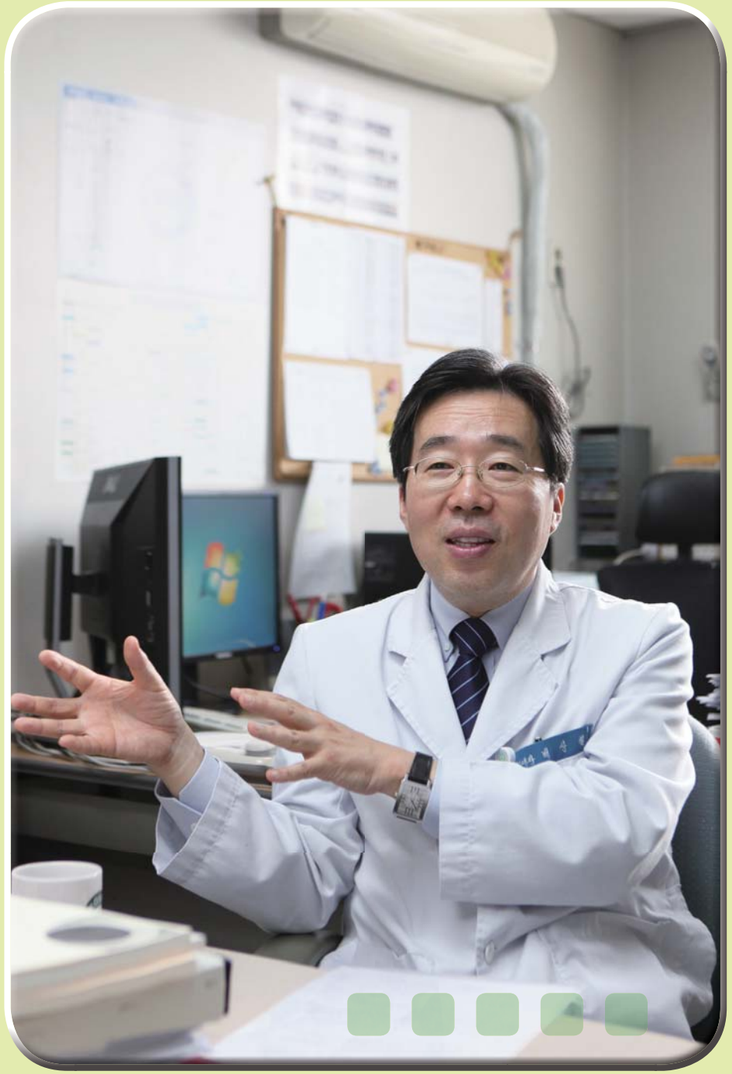
- 2002, Secretary of the minister of the Ministry of Health and Welfare
- 2005, Senior officer in charge of administration in the executive office of the President of Korea
- 2008, Director of the Department of Disabled Person Policies
- 2009, Spokesman
- 2010, Officer of Pension Policies

(Written by) **Su Hee Kim** (Photo) **Sang Young Yun**

Efforts to draw socially acceptable agreements through studies of pharmacology and pharmacoeconomics

Sang Cheol Bae, Director of Rheumatism Center, Department of Internal Medicine, Hanyang University College of Medicine

I visited Professor Sang Cheol Bae, who analyzed glucosamine jointly with the NECA last year to reveal that glucosamine was abused and not effective in preventing arthritis, which was a big issue in Korea. I look into his life concentrated on clinical studies of rheumatic diseases.



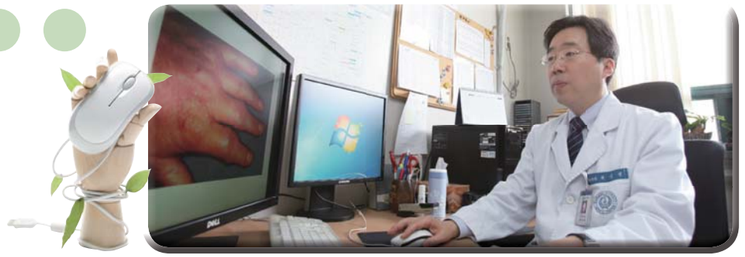
In February 2010, Director Sang Cheol Bae of Hanyang University Hospital for Rheumatic Diseases published the results of a survey of the present state of use of glucosamine and chondroitin products in Korea and the assessment of their scientific evidence conducted jointly with the National Evidence-based Healthcare Collaborating Agency.

He is a famous specialist in rheumatic diseases who was the first to introduce activated systematic clinical studies of rheumatic disease treatment in Korea.

"Rheumatic diseases are of around 100 types and cause troubles to joints, cartilages, and bones and the most representative ones include autoimmune diseases such as rheumatoid arthritis and lupus. Since rheumatic diseases are very complicated and diverse by patient depending on genetic factors and socioeconomic environments, clinical studies conducted through patient cohort analysis are important."

Last year, he analyzed glucosamine products jointly with the NECA through a study of the results of a survey of the present state of the use of glucosamine products in Korea. Their scientific evidence revealed that it was abused and not effective in preventing arthritis, which created a big uproar. This study was conducted through diverse methods including present state surveys, Gallop surveys, surveys of the present states of hospitals, and surveys of people's perceptions, and it revealed that rheumatoid arthritis patients, lupus patients, and even cancer patients were taking glucosamine to treat joint pain. Even children were being given these substances under the assumption that it was good for their joints.

Since many cases of glucosamine abuse were analyzed to bring this limelight, this also requires future continuous study.



Although difficult, treatment is the most rewarding

Director Sang Cheol Bae, who serves 4 roles including treatment, research, education, and administration, says that although difficult, treatment is most rewarding.

"By the nature of rheumatic diseases related with the complicated immune systems, many cases are not resolved with existing cases or specialty books only. Therefore, I would like to provide treatment without any regret by combining clinical studies through diverse patient cohort analyses with treatment."

Director Sang-Cheol, is also serving as the director of the Rheumatic Disease Clinical Study Center as designated by the Ministry of Health and Welfare, has established national rheumatic disease-related cohorts, through which he is analyzing the characteristics of rheumatoid arthritis patients in Korea through various epidemiological studies. He already succeeded in establishing cohorts of around 5,000 patients to create the evidence necessary for treating patients. Cohort studies composed this way will become important evidence for studies of genetic epidemiology and drug genetics for customized medicine in the future.

Having studied diverse areas including epidemiology, statistics, drug economics, healthcare quality control studies and medical ethics to obtain a degree in clinical epidemiological economics (MPH) from the Graduate School of Health, Harvard University in the mid-1990s, Director Sang Cheol Bae is recognized for his excellent research achievements through 189 papers published in Korea and 154 papers registered in SCI. He received "Best Clinical Research Award" from the Asia Pacific Rheumatic Disease Society in 2008 and received "HANMI Proud Doctor Award" in 2010 for his contribution to enhancing the level of overall clinical studies in Korea by developing reasonable treatment methods for rheumatic diseases and comprehensive studies of drug economics and genetics.

"Although the rate of complete recovery of rheumatic diseases has increased over the last 5 years, thanks to the development of new therapeutic agents, we should contemplate about reasonable alternatives to solve patients' economic burdens due to the high costs, the government's financial problems, and the issue of new drug production."

The road not taken

Since selecting the Department of Rheumatic Internal Medicine (an undeveloped area) instead of the Department of Cardiology Internal Medicine (which was already established when he was a resident in 1990), Director Sang Cheol Bae has been studying rheumatic diseases for 20 years.

"I would like to study healthcare services to reflect patients' thoughts and characteristics centering on research to upgrade Rheumatism Center of Hanyang University College of Medicine into a hospital with good systems. I will make the best model to satisfy patients' needs and to make them happy as well as being equipped with competitiveness in the global markets."

On the first page of his notebook is a Robert Frost poem entitled "The Road not Taken." As with his selection of the underdeveloped area of rheumatic disease internal medicine 20 years ago and the resulting great outcomes, future achievements are expected as well.

NECA news

NECA global project

Study fellows Sang Moo Lee and Jeong Hoon Ahn participated in the 1st international workshop of “Social values and health priority setting: an international comparative analysis” held in London, UK during February 17–19, 2011. The purpose of this workshop was to understand the different healthcare systems of individual countries and to share the social values and their priorities considered when healthcare-related decisions are made.

A total of 28 persons from the NICE and University College of London, UK; CMTP Center for Medical Technology Policy (CMTP), John Hopkins University, USA; NECA, Korea; Health Intervention and Technology Assessment Program (HITAP), Thailand; Haute Autorite de Sante (HAS), France; Institute for Quality and Efficiency in Health Care (IQWiG), Germany; and WHO participated in the workshop.

On the first day, there was a session for presentations of individual countries' healthcare systems and questions and answers. Fellow researcher Jeong Hoon Ahn made a presentation on healthcare systems in Korea. On the second day, there was hot discussion about future directions in which to proceed with projects, protocols, and the use of results. The issues raised through presentations of individual countries were transparency in decision-making processes, the source of responsibility, participation in decision-making processes (doctor associations, consumers, patients, etc.), clinical effects and evidence (evidence creators and methods to reflect various evidences), use of cost effectiveness (advantages and disadvantages of using threshold values and existence of legal coerciveness), selection of factors that must be considered first in equity, joint liability (joint bearing of expenses), autonomy, social value, and stages at which individual institutions participate in decision making. A direction was established to prepare a frame in this project to give answers regarding tools that may help policy decision-makers when they make decisions, matters in other systems that are desired to be known, matters that must be overcome, and the existence of social values being sufficiently sympathized by many persons.

The second workshop will be held at the HTAi conference in June 2011 in Rio de Janeiro. Many South American countries that could not participate in the first workshop indicated their intention to participate in the 2nd workshop; thus, it is expected that the international position of this project will be enhanced.

Public hearing on Clinical Practice Guideline for depression patients in primary medical institutions

The Clinical Practice Guideline(CPG) support division held a public hearing on treatment guidelines for screening depression patients in primary medical institutions on March 16 at the Cancer Institute, the College of Medicine, Seoul National University, jointly with the Clinical Research Center For Depression (Director Tae Youn Jun) through the sponsorship of the Ministry of Health and Welfare, the Korea Health Industry Development Institute, and the National Strategic Coordinating Center for Clinical Research (NSCR). Since there are many cases in which depression patients do not recognize that they are patients and visit primary medical institutes to report physical symptoms, appropriate screening tests and processes for those patients who visited primary medical institutes are necessary for identifying patients and providing effective treatment.

This public hearing was composed of theme presentations and a panel discussion on processes to develop Clinical Practice Guideline for depression patients, and Clinical Practice Guideline for depression patients for youth, adult, and elderly depression patient screening and treatment attracted a lot of attention from experts.

Commemoration of the second anniversary

The NECA commemorated its second anniversary on March 24 in the conference room. Through a congratulatory address, Director Heo Dae-Seok said, “I give a meaning to the fact that we made a first step of an evidence-based healthcare system in Korea in past years” and requested the personnel “to make efforts to establish evidence for health technology from the standpoint of the people.” He further encouraged the personnel by saying, “Please have the pride that you are leading the development of healthcare systems in that one step of the NECA will guarantee patients the right to be treated safely; provide policy decision makers with information for rational decision making; and present scientific evidence for the effects of drugs, medical devices, and health technologies etc to medical personnel.” As for future plans, he indicated his aspiration by saying, “From 2011, I will expand the role of the NECA as a public research institute such as guaranteeing the quality of healthcare from a macroscopic viewpoint and presenting sustainable growth strategies etc.”

Revised notification of the results of assessment of the safety and efficacy of new health technologies

The Ministry of Health and Welfare notified revised results of assessment of the safety and efficacy of new health technologies pursuant to item 3 of article 53 of the Medical Services Act. and article 4 of the Rules regarding the assessment of new health technologies (Ministry of Health and Welfare notification no. 2011-44, 11.4.12). The new health technologies that have been recognized for their safety and efficacy are as follows and the original text PDF notification can be viewed on the New Health Technology Assessment Committee's home page (http://nhta.or.kr/nHTA/) and the Ministry of Health and Welfare's home page (http://www.mw.go.kr).

- FAH gene mutation [base sequencing]
- PAH gene, mutation [base sequencing]
- PKD1 gene, mutation [base sequencing]
- STAT3 gene, mutation [base sequencing]
- ACADM gene, mutation [base sequencing]
- DHCR7 gene, mutation [base sequencing]
- GALC gene, mutation [base sequencing]

First half of 2011 professional educational courses on health technology assessment

The center for new health technology assessment opened the 2011 professional educational courses on health technology assessment, where trainees can learn health technology assessment related methodologies. The educational courses are composed of an “educational course on literature search” and an “educational course on systematic review” and will be divided into “basic course in the first half of the year” and “intermediate course in the latter half of the year” based on the level of lecturers so that trainees can receive education at appropriate levels. On April 6, the “basic educational course on literature searches” was implemented as full-day education combining theory and practice, and most trainees showed satisfaction with the lecture. The “educational course on systematic review” that will be implemented from May 4 will be composed of lectures on methods to extract/synthesize scientific evidence from medical/scientific literature and practices and will be implemented on every Wednesday for the month of May.

The details and schedule of the 2011 professional educational courses on health technology assessment can be identified on the column Events of the NECA tab on the NECA home page (www.neca.re.kr).