

## Executive Summary

### **Evidence Assessment on Intervention and Surgery of Non-benefit Medical Care**

- focusing on four severe diseases -

Shin S<sup>1</sup>, Park DA<sup>1</sup>, Park SH<sup>1</sup>, Lee NR<sup>1</sup>, Kim JY<sup>1</sup>, Lee SH<sup>1</sup>, Bae EY<sup>2</sup>

<sup>1</sup> National Evidence-based Healthcare Collaborating Agency

<sup>2</sup> College of Pharmacy, Gyeongsang National University

#### Introduction

Although the efforts on the benefit extension policy of National Health Insurance (NHI) have been made around benefit medical care, non-benefit medical care fees have been actually increased rapidly twice as much as benefit medical fees. The cause of this phenomenon can be given to new influx of high-priced new health technologies, no regulating price system, and absence of management system such as medical fee claims and reviewing in non-benefit item. Therefore, the appropriate decision for non-benefit medical care items could be essential for enhancing insurance benefit and efficient use of national health resource, but actually reviews of pay for the item have been mainly made by. In 2013, Ministry of Health and Welfare (MOHW) in Korea has introduced 'selective-benefit medical care' for benefit extension policy focusing on four severe disease (cancer, cardiovascular disease, cerebrovascular disease, and a rare disease). The purpose of this study is to provide the evidence relevant to policy through evidence assessment related to intervention and surgery of non-benefit items focusing on four severe diseases.

#### Method

14 items among 98 non-medical benefit items that were mainly used for the treatment of the four severe diseases(cancer, cardiovascular disease, cerebrovascular disease, and a rare disease) were selected as the final evaluation

subjects.

표 1 Evidence review procedures

	Evaluation subjects	Exception
All item	98	-
STEP 1 Whether the insurance principle meets	80	18
STEP 2 Whether four severe diseases meets	14	66
STEP 3 Evidence assessment (preliminary assessment and rapid systematic review)	Preliminary assessment: 14 <sup>1),2)</sup> Rapid systematic review: 5 <sup>1)</sup>	-

- 1) Subject items(9): Placental Tissue Implantation for retinitis pigmentosa, Transpupillary thermotherapy, Macular/foveal translocation, Percutaneous transluminal septal myocardial ablation by alcohol-induced septal branch occlusion, Transmyocardial laser revascularization, Thermocoagulation of osteoid osteoma, Cryosurgery for liver cancer, High intensity focused ultrasound for liver cancer, and High Intensity Focused Ultrasound[prostate cancer]
- 2) Subject items(5): Cryoablation for atrial fibrillation, Topical photodynamic therapy for Skin Cancer, Trans-Arterial Radio-Embolization, Photodynamic therapy, Tracheoesophageal voice prosthesis

Of 14 items, a preliminary assessment including literature review(clinical research, clinical guideline, whether insurance benefit in other countries) and consultation with clinical experts was conducted. According to the results of preliminary assessment, target items of rapid systematic review was selected. Items that clinical research lacked (low evidence) and rare domestic use demand (low societal need) considered through preliminary assessment was not selected for rapid systematic review, and otherwise rapid systematic review was conducted (Table 1). Results of evidence assessment including preliminary assessment (14 items) and rapid systematic review (5 items) was looked back by clinical experts in related fields and revised if it is needed.

## □ Results

As a results of preliminary assessment, 9 items (Placental tissue implantation for retinitis pigmentosa, Transpupillary thermotherapy, Macular/foveal translocation, Percutaneous transluminal septal myocardial ablation by

alcohol-induced septal branch occlusion, Thermocoagulation of osteoid osteoma, Cryosurgery for liver cancer, High intensity focused ultrasound for liver cancer, Transmyocardial laser revascularization, and High Intensity Focused Ultrasound [prostate cancer]) of 14 items were confirmed that the rapid systematic review is not essential. When it comes to the items that the rapid systematic review were not conducted, case-series that there was no comparison group on the research existed only or the technologies were rarely used due to the development of alternative technologies. In fact, 9 items (Table 2) were confirmed that evidence level was not changed significantly from the level reviewed when to determine whether insurance benefit or not. In other words, additional efforts of evidence generation about relative effectiveness comparing with alternative for switch to insurance benefit is not almost done after the decision to be uninsured.

**Table 2 Summary of preliminary assessment (9 items)**

Subject	Results
Placental Tissue Implantation for retinitis pigmentosa	1) Placental Tissue Implantation for retinitis pigmentosa is only confirmed in the experimental research phase when treatment was developed, not nearly implemented in clinical practices.
Transpupillary thermotherapy	1) It is confirmed that transpupillary thermotherapy is rarely used in this country. In particular, a possibility of side effects is large in comparison with the effect, therefore, replaced by other treatments.
Macular/foveal translocation	1) In cure choroidal neovascular membrane, macular/foveal translocation is not high frequency of use. With high risk of severe side effects, macular/foveal translocation is a difficult skill to be required a long training period.
Percutaneous transluminal septal myocardial ablation by alcohol-induced septal branch occlusion	1) Percutaneous transluminal septal myocardial ablation have reduced the frequency of its use in the overseas as well as domestic, and not reported long-term follow-up results. In previous studies, even higher insertion rate of PPM than the surgery is reported.
Thermocoagulation of osteoid osteoma	1) Thermocoagulation of osteoid osteoma is not a lot of treatment. 2) Thermocoagulation of osteoid osteoma is not inferior compared to the conventional surgery in the symptomatic improvement period, the recovery period of daily life, length of hospital stay,

Subject	Results
	<p>recurrence or complications after surgery in osteoid osteoma. Especially, in the case of tumor nidus growing in small and hard cortical bone, as surgical resection is not possible in many cases, thermocoagulation of osteoid osteoma is reported as a safe treatment effectively.</p> <p>3) For the evaluation based on the tumor, high-quality studies compared with conventional surgery are needed.</p>
Cryosurgery for liver cancer	<p>1) For liver cancer patients who surgical resection is unable to be used, Cryosurgery for liver cancer is able to be used but rarely used in domestic fields. As thermocoagulation is insurance benefit, cryosurgery for liver cancer is not commonly used.</p> <p>2) Clinical effectiveness can be expected in terms of pain relief of patients, but applicable indications are limited.</p>
High intensity focused ultrasound for liver cancer	<p>1) Due to the high cost of treatment, this technology has been rarely used in domestic fields.</p> <p>2) When used only one technology, or in combination, curative and palliative therapy effect can be expected, and it is believed that there are no serious safety problems.</p> <p>3) As critical evidence that present an important basis for this technology have written intensively in a country where the development of device has been made, questions for the reliability of evidence are raised, and the device currently in use has not received FDA approval in the US. Most of the evidence has been made in China where device was developed. Subsequently, additional evidence may be also necessary to check.</p>
Transmyocardial laser revascularization	<p>1) This technology is rarely used in domestic and overseas.</p> <p>2) The level of evidence based on the U.S. Clinical Guidelines (ACC/AHA) dropped, a strong recommendation that NICE's guidance also prohibits the use of the technology has been proposed.</p>
High Intensity Focused Ultrasound [prostate cancer]	<p>1) This technology is a method to treat localized prostate cancer, while minimizing side effects possible to occur due to cancer surgery or radiation therapy.</p> <p>2) The long-term observation is necessary since based on the lack of such a large RCT and, so far, it is mentioned as the experimental treatment by clinical guidelines.</p>

The results of rapid systematic review on the 5 items (Cryoablation for atrial

fibrillation, Topical photodynamic therapy for skin cancer, Trans-Arterial Radio-Embolization, Photodynamic therapy, Tracheoesophageal voice prosthesis) was summarized in Table 3. When it comes to all 5 items, the quality of evidence comparing with alternatives is not high and is too insufficient to conclude for the relative effectiveness of all the items. Further, in the case of some items (Trans-Arterial Radio-Embolization and Photodynamic therapy), evidence for economic efficiency was checked for health insurance benefit.

**Table 3 Summary of rapid systematic review (5 items)**

Subject	Results
Cryoablation for atrial fibrillation	<ol style="list-style-type: none"> <li>1) Radiofrequency ablation are not suitable to conduct for arrhythmia injury and disease, cryoablation for atrial fibrillation is used to target to be difficult to expect the effect, but not very frequently used.</li> <li>2) As a result of rapid systematic review, in every study, the arrhythmias that target contain a wide variety and the quality is also not high, respectively.</li> <li>3) Although various outcome variables such as death, stroke, QOL, and symptom related variables were not reported in studies, cryoablation for atrial fibrillation was not as effective for some injuries and diseases such as PSVT as radiofrequency ablation.</li> <li>4) Based on the review, it is difficult to conclude the safety and effectiveness of medical technology definitely. To consider indications and subject of application, it is necessary to weigh the advantages and disadvantages depending on characters of medical technology.</li> <li>5) A high-quality prospective studies are needed that report the main outcome variable for each arrhythmia injury and disease in order to evaluate against cryoablation for atrial fibrillation and radiofrequency ablation in the future.</li> </ol>
Topical photodynamic therapy of skin cancer	<ol style="list-style-type: none"> <li>1) Since there are a variety of treatment alternatives, although all of the selected studies are relevant to RCT, in analyzing by the type of skin cancer, approximately two or three studies can be available.</li> <li>2) Topical photodynamic therapy for skin cancer is the most prevalent surgical therapy that shows 2 years standard relapse</li> </ol>

Subject	Results
	<p>in BCC, when compared to cryotherapy, this technology have similar effects. The difference among 5-FU, photodynamic therapy and cryotherapy in relapse rate in BD is not meaningful. When it comes to subjective cosmetic results, the photodynamic therapy is reported to be superior in all types of skin cancer.</p> <p>3) When it comes to safety, the typical side effect of this is burning sensation and pain that are shown in photodynamic therapy with the higher frequency but are temporary.</p>
<p>Trans-Arterial Radio-Embolization</p>	<p>1) Trans-Arterial Radio-Embolization is mainly being conducted on metastatic liver cancer patient or primary liver cancer patient on whom it is unable to conduct surgical resection and local treatment.</p> <p>2) As a result of rapid systematic review on Trans-Arterial Radio-Embolization, compared to Trans-Arterial Chemo-Embolization or chemotherapy treatment, there is a similar safety to Trans-Arterial Chemo-Embolization or chemotherapy treatment in the case of within 30 days of treatment related death rate and occurrence of side effects and complications. Effectiveness as well, it had been reported that when it comes to the median value of survival time, Trans-Arterial Radio-Embolization was longer. However, high topical treatment effects and low rate of the progress of the disease in certain study had been also reported.</p> <p>3) The study to compare and evaluate Trans-Arterial Radio-Embolization and Trans-Arterial Chemo-Embolization (or chemotherapy treatment) were not much. Furthermore, since the subjects included in each study were different and indicator presenting results was also unmatched, the quantitative integration is impossible.</p> <p>4) When considering the very high treatment cost, it is necessary to find more evidence for economic efficiency in order to switch to insurance benefits.</p>
<p>Photodynamic therapy (Barrett's oesophagus, esophageal cancer)</p>	<p>1) Photodynamic therapy can be used in the treatment of the early esophageal cancer and Barrett's Oesophagus, but since incidence of these diseases is not high enough, number of use in domestic is low.</p> <p>2) Unlike EMR that is available in most hospitals, Photodynamic</p>

Subject	Results
	<p>therapy can be only conducted very few hospitals because of the factors such as technology, equipment, and high cost of drugs.</p> <p>3) As a results of the rapid systematic review to Photodynamic therapy against esophageal cancer and Barrett's Oesophagus, there were few comparative researches itself for the clinical effectiveness and safety. Furthermore, there were various kinds of comparator in each study, while the quality of study was low.</p> <p>4) When considering the current domestic use, if for example high cost, and based on the evidence level, whether to switch to insurance benefits or not will be considered through a review of economic efficiency in the future.</p>
Photodynamic therapy (Lung cancer)	<p>1) Photodynamic therapy can be used in the treatment of lung cancer that surgical resection is not possible.</p> <p>2) As a result of the rapid systematic review to Photodynamic therapy against lung cancer, there were few comparative clinical researches itself. Furthermore, there were various kinds of comparator in each study, while the quality of study was low.</p> <p>3) Effectiveness and safety of this treatment may be considered, but this treatment itself is not relatively frequent due to the high cost of photosensitizer.</p> <p>4) When considering the current domestic use, if for example high cost, and based on the evidence level, whether to switch to insurance benefits or not will be considered through a review of economic efficiency in the future.</p>
Tracheoesophageal voice prosthesis	<p>1) It is known as the best treatment to keep the voice function by partial resection as the early diagnosis of laryngeal cancer, furthermore, the frequency of use of tracheoesophageal voice prosthesis is not high due to the development of other therapies such as chemotherapy and radiation therapy besides the laryngeal surgery.</p> <p>2) As a result of the rapid systematic review, tracheoesophageal voice prosthesis that is one of the voice rehabilitation methods that are needed for patients who received total laryngectomy, the voice rehabilitation methods and outcome variables were different in each study, also the quality of study was not high.</p>

Subject	Results
	3) Although each study result was different in aspects such as phonetic indicators, function, success rate, and quality of life, overall, tracheoesophageal voice prosthesis could be considered to be a not inferior alternative to other voice rehabilitation methods. In order to compare between voice rehabilitation methods, high-quality prospective studies with a more standardized research plan are needed.

## □ Conclusions

The matters of concern of researches and policies have revolved around reviews on insurance benefit items until now. However, when considering the balloon effect that the speed of rising cost of the non-benefit items is much faster than that of the insured items, there is a limit of benefit extension policy without management mechanisms for non-benefit items. Therefore Ministry of Health and Welfare (MOHW) in Korea has introduced 'selective benefit medical care' for benefit extension focusing on four severe disease and tried to overcome it.

In this study, evidence assessment (preliminary assessment and rapid systematic review) with HTA approach was conducted for supporting benefit extension policy. As a result of reviewing in this study, in fact, the non-benefit items can be also confirmed, which are already replaced by other techniques. Moreover, because of the part that decision was not made based on HTA results under the existing systems, there are items used without sufficient evidence. When considering the selective benefits plan of the four severe diseases that 14 items would be classified as the selective benefits. Therefore, when classifying as the selective benefits items, this study could be used as evidence of the relevant policy-making, furthermore, this study approach could be applicable to other field.

**Key Words: Non-benefit Medical Care, Intervention and Surgery, Evidence Assessment**