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＜ Review ＞

Cost effectiveness evaluation of health care technologies in Japan: New HTA system and the role of C2H

FUKUDA Takashi, SHIROIWA Takeru

Center for Outcomes Research and Economic Evaluation for Health, National Institute of Public Health

Abstract

Advancing medical technologies is one of the main reasons to increase medical expenditure. One possible way to consider efficiency is to evaluate cost effectiveness of medical technologies and make decisions upon the results. It is often described as health technology assessment, HTA. In Japan, introduction of HTA system was discussed since 2010. After 10 years of discussion, a new HTA system was established in 2019.

In the new HTA system, the manufacturer must submit the data first. The submitted analysis is reviewed and reanalyzed by academic analysis groups and is finalized by Center for Outcomes Research and Economic Evaluation for Health(C2H) at the National Institute of Public Health. Based on the manufacturer's submission and the C2H public analysis, the Expert Committee on Cost-Effectiveness Evaluation at the Central Social Insurance Medical Council (CSIMC) examines the scientific quality of the analysis and determines the most likely incremental cost effectiveness ratio (ICER) figure or range for the product in the appraisal process.

The target drugs and medical devices are principally selected when they are newly listed at the general assembly of CSIMC based on the predetermined selection criteria. The results of the evaluation will be used for reimbursement price adjustment, not for coverage decision. When ICER exceeds 5 million JPY per QALY, the price will be adjusted. For some diseases, such as rare or pediatric diseases and cancer, 7.5 million JPY per QALY will be used as threshold for price adjustment.

In order to implement full scale cost effectiveness evaluation, a new unit, "Center for Outcomes Research and Economic Evaluation for Health", was established in 2018 at the National Institute of Public Health.

keywords: cost effectiveness, health technology assessment, drug, medical device, Central Social Insurance Medical Council, reimbursement price, Japan

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I. Background

Advancing medical technologies is one of the main reasons to increase medical expenditure. Though new treatment technologies, including drugs and medical devices, generally contribute to better outcome of patients, some of them are very costly. This is an issue not only in Japan. In many countries health care delivery system is funded by either tax or public insurance scheme. In the system, health care budget is restricted and it is important to consider efficient use of the budget. One possible way to consider efficiency is to evaluate cost effectiveness of medical technologies and make decisions upon the results. It is often described as health technology assessment, HTA. In HTA, individual technology is evaluated by means of medical, social, ethical and economic aspects. Cost effectiveness analysis is the main tool to evaluate efficiency.

HTA system has been adopted in many countries, such as

Corresponding author: FUKUDA Takashi
2-3-6 Minami, Wako, Saitama 351-0197, Japan.
E-mail: fukuda.t.aa@niph.go.jp

UK, Australia, Canada for many years. It is also introduced in Asian countries[1]. In Japan, introduction of HTA system was discussed since 2010. After 10 years of discussion, a new HTA system was established in 2019.

II. Pilot program

Before implementing a new HTA system, a pilot program of cost effectiveness evaluation was introduced in 2016[2]. Target products were determined by the Central Social Insurance Medical Council (CSIMC) based on the selection criteria of the degree of innovation and market size. Target products were chosen among the products, for which reimbursement decisions were made between FY 2012 and FY 2015. For the pilot program, 13 products (7 drugs and 6 medical devices) were selected by CSIMC[3]. Drugs for anti-hepatitis C and PD-L1 antibody, which received much attention in the press, were included as targeted products.

The manufacturers of the target products were requested to submit economic evaluation data by the end of FY 2016[4]. Once this was completed, academic groups, including experts on clinical epidemiology and health economics, independently reviewed the data in early FY 2017. Because Japan had no official HTA agency, such as the National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK) at that time, the National Institute of Public Health (NIPH) coordinated this review process. The reviewed data were finally sent to sub-committee under CSIMC, the "expert committee of cost-effectiveness", which was established in FY2016. The expert committee had a role to perform "appraisal" of the data including a social and ethical perspective. The results of this evaluation were reflected in official prices during the next revision, from FY 2018.

In March 2018, based on the cost effectiveness results, prices of the two of the target products were reduced, though actual reduction rate were not disclosed.

However, 7 products out of 13 in the pilot program, analysis results submitted by manufacturers and reanalysis group were markedly different, even though both analyses followed the guideline. Major reasons for the discrepancy were; difference of the scope (eg. target population, comparator), difference in the selection of data used in the analyses (eg. data sources, definition of the target patients group). Because it was a pilot program, it was decided to verify the reasons of the discrepancy in order to consider a more rational analysis. For this purpose, analyses as a verification were performed in 2018.

In the same year, intensive discussion toward full implementation of a new HTA system was made in CSIMC.

III. The new HTA system

1. Target products of the new cost-effectiveness evaluation system

Due to the CSIMC discussions following the submission of the pilot program, the new cost-effectiveness evaluation is being used initially only for the price adjustment of drugs and medical devices, not for reimbursement decision making[5]. The cost-effectiveness evaluation process starts after the products are launched in the market. The results are reflected in the product prices after approximately 15–18

Table 1 Selected products as of December 2020

ID	Brand name	Generic name	Category	Designated day
C2H1901	Trelegy	Fluticasone, Umeclidinium, Vilanterol	H1	2019/05/15
C2H1902	Kymriah	Tisagenlecleucel	H3	2019/05/15
C2H1903	Ultomiris	Ravulizumab	H1	2019/08/28
C2H1904	Breztri	Budesonide, Glycopyrronium, Formoterol	H5	2019/08/28
C2H1905	Trintellix	Vortioxetine	H1	2019/11/13
C2H1906	Coralan	Ivabradine	H2	2019/11/13
C2H2001	Noxafil	Posaconazole	H1	2020/4/8
C2H2002	Cabometyx	Cabozantinib	H1	2020/5/13
C2H2003	Enhertu	Trastuzumab Deruxtecan（Genetical Recombination）	H1	2020/5/13
C2H2004	Zolgensma	Onasemnogene abeparvovec	H3	2020/5/13
C2H2005	Entresto	Sacubitril Valsartan	H5	2020/8/19
C2H2006	Enerzair	Indacaterol, Glycopyrronium, Mometasone	H5	2020/8/19
C2H2007	Rybelsus	Semaglutide (Genetical Recombination)	H1	2020/11/11

months.

The target drugs and medical devices are principally selected when they are newly listed at the general assembly of the CSIMC (Table 1). At the time of the introduction of the cost-effectiveness evaluation in 2019, the evaluation results are initially used for:

(A) Adjusting premiums when the price is calculated using a "similar efficacy comparison method" (i.e., "new drug price" = "existing drug price" + "premium"), and

(B) adjusting the premium and regulated constant profit rate for manufacturers (the latter is adjusted only if the disclosure level is 50% or less) when the price is calculated using the "cost calculation method".

Pediatric products, or products intended for designated intractable and rare diseases as defined by Japanese law, are exempt from the evaluation. Moreover, in the case of (B), if the disclosure level of the product is more than 50% and no premium is added, the product is exempt from cost-effectiveness evaluation.

However, not all products that satisfy the above conditions are selected as targets; only products with a large budget impact are seleced. The selection criteria are as follows:

- Category H1: Annual peak sales of JPY 10 billion and over. In Japan, new products (drugs and devices) are listed 4 times in a year. Products from category H1 are selected at the time of their listing and the cost-effectiveness evaluation process starts.
- Category H2: Annual peak sales from JPY 5 billion to JPY 10 billion. H2 category products are considered candidate targets. They are kept in reserve as candidates and the target products are selected from these candidates based on their peak sales twice a year, considering the number of selected products and the capacity for evaluation.
- Category H3: The CSIMC can select target products under some conditions such as significantly high cost of the product.
- Category H4: Products with premiums listed before the implementation of the policy and whose annual actual sales exceed JPY 100 billion. The criteria for categories H1 to H3 are meant for products newly listed after the start of the cost-effectiveness evaluation, and the criteria for H4 are intended for existing, older technologies.
- Category H5: In this final category, the drugs and devices similar to the target products selected for evaluation are included. Such products are not individually evaluated but their prices will be adjusted in the same manner as the similar product already targeted.

2. Price adjustment system based on cost-effectiveness

The CSIMS decides the reimbursement price adjustment of products using the results of the cost-effectiveness evaluation[6]. In the case of products evaluated using the similar efficacy comparison method, only the premium (part of the whole price) is adjusted. In contrast, both the profit rate and the premium are adjusted if the cost calculation method is applied (the profit rate is adjusted only for products with a profit rate of 50% or less).

When additional benefits to a comparator can be proven, an incremental cost-effectiveness ratio (ICER) is calculated by using quality adjusted life year (QALY) as common outcome measure. The adjustment rate is determined using the ICER interval and the premium or profit rate. 5 million JPY per QALY is used as reference value. When the result shows that ICER is beyond 5 million JPY per QALY, the price of the product should be adjusted. 7.5 million and 10 million JPY are also reference values. The price is adjusted stepwise with those reference values.

In the case of oncology, pediatric, and designated intractable and rare disease products, the reference value is increased by a factor of 1.5. The factor is based on the consensus of the CSIMC.

Finally, if price is reduced based on the calculation above, the cost/QALY may fall below JPY 5 million (or JPY 7.5 million) as a result of the adjustment, and it may be over-adjusted for manufacturers. In this case, the reduction stops at the threshold price. In addition, the maximum reduction rate is limited to 10%–15% of the entire price before adjustment. Such safeguards may be put in place when the premium rate is high.

3. Process of cost-effectiveness evaluation

The target products are selected after the CSIMC decides the listing. If a product is selected for cost-effectiveness evaluation, the manufacturer must submit the data within nine months from selection. During the first 3–6 months, the analysis framework (including the target population, comparator, etc.) should be determined based on preliminary consultations with the Center for Outcomes Research and Economic Evaluation for Health (C2H) at NIPH. The submitted analysis is reviewed by academic analysis groups and is finalized by C2H within 3–6 months. Based on the manufacturer's submission and the C2H public analysis, the Expert Committee on Cost-Effectiveness Evaluation examines the scientific quality of the analysis and determines the most likely ICER figure or range for the product in the appraisal process. This result is then reported to the CSIMC general assembly and the prices may be adjusted. The entire process takes 15–18 months.

IV. Role of C2H

Health technology assessment is often used to decide coverage of medical technologies under the public scheme or reimbursement prices. For this purpose, analyses must be made from a fair and neutral perspective. HTA agencies are publicly funded in most countries. For example, NICE in UK is a non-departmental public body funded by the government. In Australia, Pharmaceutical Benefit Advisory Committee (PBAC), as a committee in the government, plays the main role of HTA. In Japan, no HTA agency has been existed. In order to implement full scale cost effectiveness evaluation, a new unit, "Center for Outcomes Research and Economic Evaluation for Health", was established in 2018 at the National Institute of Public Health. Abbreviation is "CORE2-Health" or "C2H". The main role of C2H is assessment of the products which are selected by CSIMC (Figure 1). As mentioned earlier, manufactures are responsible for submitting cost effectiveness analysis of the product. C2H reviews the results and perform reanalysis when necessary. Before manufactures start their analysis, it is important to discuss framework of analysis between manufactures and C2H. Because capacity of C2H is limited, assessment of the products are jointly worked with contracted research teams at universities. This structure is similar to the NICE in UK and academic groups. In order to provide reasonable analyses, C2H issues guidelines for analysis based on discussion in a research group funded by MHLW (Figure 2). C2H also provides information on evaluation methods, including preliminary consultation process for manufacturers.

Even though C2H provides public analyses and reports to subcommittee of CSIMC, C2H does not perform appraisal. Appraisals and decisions are made in CSIMC. After the final decision is made for a product, C2H will open its report to public.

Because capacity for evaluation is limited, it is important to increase the number of experts. C2H contributes to develop a training program as well.

A new HTA system has just started in Japan. C2H is willing to provide good information for decision makers for efficient use of medical technologies.

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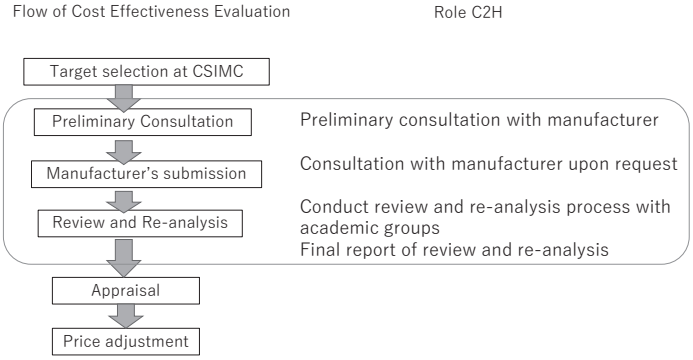

Figure 1 Flow of cost effectiveness evaluation and the role of C2H

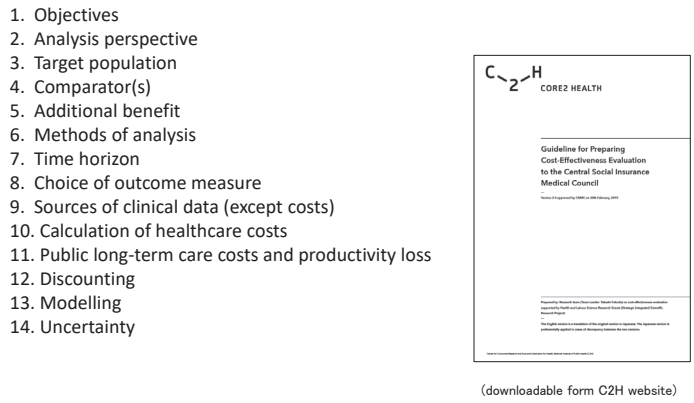

Figure 2 Guideline for Preparing Cost-Effectiveness Evaluation to the Central Social Insurance Medical Council, Version 2.0

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＜総説＞

日本における医療技術の費用対効果評価
―新 HTA 制度と C2H の役割―

福田敬，白岩健

国立保健医療科学院保健医療経済評価研究センター

抄録

医療技術の進歩は医療費増加の一つの要因となっている．効率的な医療提供を推進するための一つの方策は，医療技術の費用対効果の評価を行い，その結果に基づき意思決定する方法である．一般に医療技術評価（HTA）と呼ばれる．日本ではHTA導入の議論が2010年頃にスタートし，約10年の議論を経て2019年に制度化された．

新HTA制度では，まず製造販売業者がデータを提出する必要がある．提出されたデータについて国立保健医療科学院保健医療経済評価研究センターおよび学術グループがレビューを行う．この結果に基づき中央社会保険医療協議会（中医協）の費用対効果評価専門組織が分析の科学的妥当性を検討し，増分費用効果比（ICER）の段を確定する．

分析対象となるのは中医協において新規に保険収載される医薬品および医療機器で，一定の条件を満たすものが選定される．分析結果は保険償還の可否ではなく，償還価格の調整に用いられる．ICERが500万円/QALYを超えるものについて価格調整の対象となるが，希少疾患や小児特有の疾患および抗がん剤については750万円/QALYを超えるものが対象となる．

このような費用対効果評価制度を実施するために，2018年に国立保健医療科学院に保健医療経済評価研究センター（C2H）が設置された．

キーワード：費用対効果，医療技術評価，医薬品，医療機器，中央社会保険医療協議会，償還価格，日本