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Cost-effectiveness evaluation for pricing medicines and devices: A new value-based price adjustment system in Japan

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Objectives. In Japan, a new cost-effectiveness evaluation system for medicine and medical device pricing was employed in April 2019 after a trial implementation. This study describes the discussions held from April 2016 to March 2019 concerning the newly introduced system.
Methods. Using published government documents, discussions with stakeholders, and the minutes of the *Chuikyo* committee meetings, the following issues are addressed: (i) the results of the trial implementation and (ii) an overview of the newly introduced system.
Results. During the trial implementation, thirteen products were evaluated and their prices adjusted. The process of the new system—which was to be implemented in FY 2019—takes about 15–18 months to complete after listing of the target products by the National Health Insurance. The target products are selected principally based on sales volume, degree of innovation (premium), and disclosure of rationale for price setting. First, a manufacturer submits the cost-effectiveness data, which is then reviewed by the Center for Outcomes Research and Economic Evaluation for Health (C2H) in collaboration with academics. The results of the cost-effectiveness evaluation are not considered during the decision-making process concerning the product's listing. The price adjustment system is similar to value-based pricing (VBP); hence, the new system can be considered as VBP adjustment.
Conclusion. Cost-effectiveness evaluation can help promote both technological innovation and sustainability of the healthcare system. We need to create a greater capacity for enhancing this academic review system.

In Japan, the new health technology assessment (HTA) system was launched in April 2019; however, the trial evaluation of thirteen products started in 2016 and continued to 2018. Since 1992, Japan has allowed for the submission of pharmacoeconomic data for medicine pricing, and it was one of the first countries to introduce cost-effectiveness data as part of its healthcare decision making. In comparison, the Pharmaceutical Benefits Advisory Committee (PBAC) of Australia became one of the first public bodies to institute mandatory submission of such data for the Pharmaceutical Benefits Scheme (PBS) listing only in 1993 (1). However, data submission in Japan was voluntary and there was no consensus on how such data should be used. There was also no review process for the submitted data. Therefore, the Ministry of Health, Labour, and Welfare (MHLW), which is responsible for determining the prices of medicines and medical devices, did not insist on data submission, meaning that the submitted data did not influence pricing and medicine listing. Consequently, few manufacturers submitted data. Meanwhile, many other countries promoted the introduction of an HTA for medicine listing or price negotiation. In Japan, the trial introduction of cost-effectiveness evaluation[1] did not begin until 2016 (2). As an organization for official HTA process, the Center for Outcomes Research and Economic Evaluation for Health (C2H) was finally established in 2018 as a department under the National Institute of Public Health (NIPH).

Shiroiwa et al. (2) introduced the background and discussion concerning the trial introduction of cost-effectiveness evaluation in Japan. This study also emphasized the necessity of introducing HTA in the Japanese healthcare system, the role of each interest group, and the main discussion points.

Similar to the systems in France and Germany, the Japanese healthcare system is a multi-payer system. Private payers are not allowed, and all payers are public insurers. The prices of (the same brand) medicines and medical devices were constant across Japan, although they are changed over time. The MHLW regulates reimbursement prices, not ex-factory prices, thus differing from some European countries. Therefore, "price" in this study means the

[1]The phrase "cost-effectiveness evaluation" was introduced by the Ministry of Health, Labour, and Welfare (MHLW) to replace "cost-effectiveness analysis" or "economic evaluation" in the medicine and medical device pricing process. In the Japanese system, only economic efficiency is considered, which may limit the application of HTA.

reimbursement price to medical institutions, which includes wholesalers' distribution costs (no regulation of wholesalers' margin), hospitals' stock costs, VAT, and so on, but not dispensing costs. Medicines are generally paid for via a pay-for-service system, except some less expensive ones at some special hospitals. The MHLW does not apply an annual fixed-budget payment system to clinics and hospitals.

Methods

The data set consists of published documents from MHLW and discussions held with certain MHLW stakeholders, my organization (NIPH), and members of industry and academia. The introduction of cost-effectiveness evaluation was discussed at *Chuikyo*, the Central Social Insurance Medical Council (CSIMC)[2], an advisory body to MHLW. I was present at almost all the CSIMC meetings and took notes during the discussions. I also used the minutes of these meetings. As I have held another position in the MHLW related to cost-effectiveness evaluation since December 2012, my own observations were also included, although confidential information was omitted.

Results

Results of the Trial Implementation for Evaluation from 2016 to 2019

The trial implementation of the evaluation of thirteen medicines and medical devices on the market began in April 2016. By the end of March 2017, the manufacturers had submitted their analyses, which were reviewed by an independent academic group and the NIPH by September of the same year. The results were submitted to CSIMC and, based on this process, the reimbursement prices of two products—Opdivo (nivolumab) and Kadcyla (trastuzumab emtansine)—were decreased and the price of one product—Kawasumi Najuta thoracic stent graft system—was increased (Table 1)[3].

At first, the MHLW planned to officially introduce the cost-effectiveness evaluation from FY 2018 (April), just after the trial periods. However, the manufacturers opposed this strongly. Their main contention was that they were provided with few opportunities to communicate with NIPH and the experts at CSIMC. Manufactures were of course not very willing to officially introduce cost-effectiveness evaluation. As a result, the official introduction was postponed and the trial implementation was reviewed in FY 2018. After completing the reviews, detailed discussions on the official introduction resumed, with the members of the CSIMC finally reaching a consensus. The details of this consensus are presented in the next sections.

Overview of Introduced Cost-Effectiveness Evaluation System from 2019

Target Products of the New Cost-Effectiveness Evaluation System

Due to the CSIMC discussions following the submission of the trial implementation results, the new cost-effectiveness evaluation is being used initially only for the price adjustment of medicines and medical devices[4], not for reimbursement decision making[5]. The cost-effectiveness evaluation process starts after the products are launched in the market. The procedure is similar to Germany's AMNOG (3), which evaluates new products after listing. The results are reflected in the product prices after approximately 15–18 months.

The target medicines and medical devices[6] are principally selected when they are newly listed at the general assembly of the CSIMC. At the time of the introduction of the cost-effectiveness evaluation for FY 2019, the evaluation results were initially used for: (A) Adjusting premiums when the price is calculated using a "similar efficacy comparison method"[7] (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[8] is 50 percent or less) when the price is calculated using the "cost calculation method"[9].

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 percent 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; products with a small budget impact are also exempt. The selection criteria are as follows:

Category H1: Annual peak sales[10] of JPY 10 billion (USD 90 million, USD 1 = JPY 110) and over. In Japan, new products (medicines and devices) are listed quarterly. 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 (USD 45 million) to JPY 10 billion (USD 90 million). H2 category products are considered candidate targets. They are kept in reserve as candidates and the target products are selected from these candidates

[2]The *Chuikyo* is an advisory board for the reimbursement system concerning public healthcare insurance. This board consists of twenty individuals, seven of whom are representatives of healthcare payers (e.g., public insurers), seven are healthcare providers (e.g., three members from the Japan Medical Association [JMA]), and six are third parties (e.g., academics and representatives of public interest).

[3]Details concerning the analytical methods and results were not disclosed.

[4]Manufacturers insisted that the cost-effectiveness evaluation should be treated as supplemental information for existing pricing rules and opposed strong influence on the entire price. This may be one reason for the smaller influence on the price adjustment, compared with other countries.

[5]CSIMC, particularly members of a healthcare provider, strongly opposed the limitation of access to medicines and medical devices for economic reasons.

[6]In Japan, medical devices are categorized into three types. Of these, only "Special Treatment Materials (STM)" (e.g., pacemaker, artificial joint, and stent) are targeted for this evaluation. The official price of each STM is determined by the MHLW, although the costs of the other two types are reimbursed, including doctors' fee (e.g., MRI, CT, and intraocular lens).

[7]The official pricing of new medicines in Japan is determined using similar efficacy comparison or cost calculation methods. In the case of medicine pricing, the similar efficacy comparison method is applied when similar medicines have already been listed in terms of efficacy and pharmacological properties. The daily price of the new medicine is set at the same price as that of the comparator. If a new medicine is evaluated and found to be innovative, the MHLW adds a premium that ranges between 5 and 120 percent of the comparator's daily price. This premium is called the usefulness or innovativeness premium.

[8]Many manufacturers are not willing to reveal their detailed actual costs (due to confidentiality) when they do submit their cost calculations. This situation was criticized by some as lacking transparency. The MHLW therefore introduced the concept of a "disclosure level" of cost calculation. If there is insufficient evidence for more than half of the total costs, the profit rate is also decreased based on the results of the cost-effectiveness evaluation.

[9]If there is no appropriate comparator, the cost calculation method (or cost plus method) is used. The cost is calculated by adding up the costs of manufacturing, administration, marketing, profit, and VAT. From FY 2018, a premium (5–120 percent of all costs) may be added to the costs based on the degree of innovation, safety, and efficacy.

[10]Manufacturers must submit predicted annual peak sales (JPY) for price setting. Peak sales are defined as the maximum amount of sales achieved in one fiscal year.

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Table 1. Results of Trial Implementation

Generic name	Population	Subpopulation	Comparator	ICER (cost per QALY)
Medicines				
Sofosbuvir	Chronic hepatitis C GT2	IFN-naive	Follow-up	B
		IFN-experienced		B
	Compensated cirrhosis C GT2	IFN-naive		B
		IFN-experienced		B
Ledipasvir and Sofosbuvir	Chronic hepatitis C GT1	Y93/L31 wildtype	Daclatasvir and Asunaprevir	C
		Y93/L31 mutant	Follow-up	A
	Compensated cirrhosis C GT1	Y93/L31 wildtype	Daclatasvir and Asunaprevir	C
		Y93/L31 mutant	Follow-up	A
Ombitasvir, Paritaprevir, and Ritonavir	Chronic hepatitis C GT1	Y93/L31 wildtype	Daclatasvir and Asunaprevir	C
		Y93/L31 mutant	Follow-up	A
	Compensated cirrhosis C GT1	Y93/L31 wildtype	Daclatasvir and Asunaprevir	D
		Y93/L31 mutant	Follow-up	A
Daclatasvir and Asunaprevir	Chronic hepatitis C GT1	Y93/L31 wildtype	Follow-up	B
		Y93/L31 mutant		B
Nivolumab	Nonsmall cell lung cancer	Nonsquamous	Docetaxel	F
		Squamous		F
	Renal cell cancer		Everolimus	F
	Melanoma		Dacarbazine	E
Ado-trastuzumab emtansine	Breast cancer		Chemotherapy only	D
Medical devices				
Stent graft	Distal aortic arch aneurysm		Open surgery	A
Deep brain stimulator (DBS)	Parkinson's disease, essential tremor, and dystonia		Nonrechargeable DBS	A
Autologous cultured cartilage	Traumatic cartilage defects and osteochondritis dissecans for knee joints		Drug therapy	G
Transcatheter aortic heart valve	Aortic stenosis	High-risk patients	Open surgery	B
		Inoperable patients	Standard treatment	B

A: dominant; B: ICER is less than JPY 5 million (USD 45,000)/QALY; C: ICER is from JPY 7.5 to 10 million (USD 68,000–90,000)/QALY; D: ICER is JPY 10 million (USD 90,000)/QALY and over; E: ICER is JPY 11.25–15 million (USD 100,000–140,000)/QALY; F: ICER is JPY 15 million (USD 140,000)/QALY and over; G: impossible to analyze.

based on their peak sales twice a year, considering the number of selected products and the process capacity.

In the case of technologies that are exempt from evaluation, when the actual sales exceed the category criteria above (e.g., due to the addition of a new application), they are also included in categories H1 or H2 as target products.

Category H3: The CSIMC can select target products if their prices are significantly high (the specific threshold is not given) or if new clinical data that could influence the cost-effective evaluation becomes available. For example, it is possible that no superiority is confirmed in the actual clinical setting or better outcomes are shown after the completion of the cost-effectiveness evaluation. C2H can submit the recommendation of candidate products for re-evaluation to CSIMC.

Category H4: Products with premiums listed before the implementation of the policy and whose annual actual sales (not predicted peak sales) exceed JPY 100 billion (USD 900 million). 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. Further, CSIMC can also select products for category H4 based on the same criteria as those of category H3.

Category H5: In this final category, the medicines and devices similar to the target products selected for evaluation are included. Such products are not individually evaluated but are treated in the same manner as similar products already targeted.

Table 2 shows the products selected for cost-effectiveness evaluation in December 2019 and the categories.

Price Adjustment System Based on Cost-Effectiveness

The MHLW adjusts the reimbursement price of products using the results of the cost-effectiveness evaluation described in the previous section. In the case of products evaluated using the similar efficacy comparison method, only the premium (part of the

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Table 2. Selected Products for Cost-Effectiveness Evaluation from December 2019

ID	Generic name	Manufacturer	Category	Designated day	Status
C2H1901	Fluticasone, Umeclidinium, Vilanterol	GSK	H1	05/15/19	Under evaluation
C2H1902	Tisagenlecleucel	Novartis	H3	05/15/19	Under evaluation
C2H1903	Ravulizumab	Alexion	H1	08/28/19	Under evaluation
C2H1904	Budesonide, Glycopyrronium, Formoterol	Astrazeneca	H5	08/28/19	No analysis[a]
C2H1905	Vortioxetine	Takeda	H1	11/13/19	Under evaluation
C2H1906	Ivabradine	Ono	H2	11/13/19	Under evaluation

[a]The same results with C2H1901 will be applied.

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 percent or less).

First, the target product is evaluated from the perspective of additional benefit as a selected major outcome(s) (e.g., effectiveness, safety, or QOL) using systematic reviews. If the product has no additional benefits compared with a similar product (referring to the cost-effectiveness analysis), a so-called cost-minimization analysis should be performed.

Only if additional benefits to a comparator can be proven, can an incremental cost-effectiveness ratio (ICER) be calculated. The adjustment rate is determined using the ICER interval and the premium or profit rate (Figure 1). The Japanese reference value 5 million (USD 45,000) per QALY is frequently cited in academic research. According to the CSIMC discussion, the value is justified by (a) empirical survey of willingness-to-pay (4) (b) GDP per capita, and (c) cost per QALY threshold in other countries (Figure 1). Further, MHLW uses different premium and profit rates for different categories. The actual decreased price is calculated by the multiplying adjustment rate by the range of price adjustment (premium, profit rate, or both). For example, a medicine with a 10 percent premium (JPY 110) is not cost-effective when compared with a similar drug (JPY 100). According to the results of the cost-effectiveness evaluation, the adjustment rate is .4 (the method for determining the adjustment rate is described below) and the price of the product is decreased by JPY $10 \times (100 - 40$ percent), or JPY 6.

As a more complicated example, if the ICER interval of a cost-calculated product (JPY 110) with a 10 percent premium (JPY 10) is JPY 8 million per QALY, the adjustment rate for the premium is .4 and that of the profit rate is .67. The product loses 60 percent of its premium and 33 percent of its profit rate, that is $10 \times .6 + 100 \times 14.6$ (profit rate) $\times .33$ or JPY 10.8, using the cost-effectiveness evaluation.

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, not based on the scientific discussion. For both normal and special products, the price reduction stops when the ICER reaches JPY 5 million (or 7.5 million). As previously mentioned, the products indicated as meant only for pediatrics or intractable and rare diseases are exempted from the evaluation. However, when products for special populations, such as the pediatric population, have other indications for adults, they are not exempted from evaluation and cost-effectiveness for pediatric population is evaluated.

Finally, if the 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 overadjusted for manufacturers. In this case, the reduction stops at the threshold price. In addition, the maximum reduction rate is limited to 10–15 percent of the entire price before adjustment. Such safeguards may be put in place when the premium rate is high.

Process of Cost-Effectiveness Evaluation

The target products are selected after the CSIMC decides the listing. The MHLW routinely adds new products to its quarterly reimbursement list. If a product is selected for cost-effectiveness evaluation, the manufacturer must submit the data within 9 months from the 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 C2H. The submitted analysis is reviewed by academic analysis groups[11] and is finalized by C2H (at the NIPH) within 3–6 months. Based on the manufacturer's submission and the C2H public analysis, the Expert Committee on Cost-Effectiveness Evaluation[12] examines the scientific quality of the analysis and determines the most likely ICER figure or range for the product (the appraisal process). This result is then reported to the CSIMC general assembly and the MHLW adjusts the price of the product based on the cost-effectiveness evaluation. The entire process takes 15–18 months[13] (Figure 2).

The C2H was established for the official evaluation process in 2018 as a department of the NIPH. Three universities were selected for the academic analysis groups.

Revision of the Cost-Effectiveness Evaluation Guidelines

The official cost-effectiveness evaluation guidelines (Guidelines for Preparing Cost-Effectiveness Evaluation to the CSIMC) were revised and approved by the CSIMC general assembly (5). The second edition of the guidelines follows the same principles as the original (6), but contains some revisions concerning the results used for price adjustment.

First, regarding the comparator, the concept of "most replaced" played a significant role in the first edition; when a technology is newly introduced in the clinical setting, the listed old technology (standard or most commonly used therapy) is replaced by the new technology. This applies to the discussions on listings but not to those concerning price adjustment, as a

[11]An academic analysis group is selected by the C2H considering conflicts of interest and feasibility of the analysis.

[12]The identities of the members of the expert committee are not disclosed except the chair person.

[13]If the manufacturer's submission is acceptable and requires no revision by C2H, the process has to be completed within 15 months.

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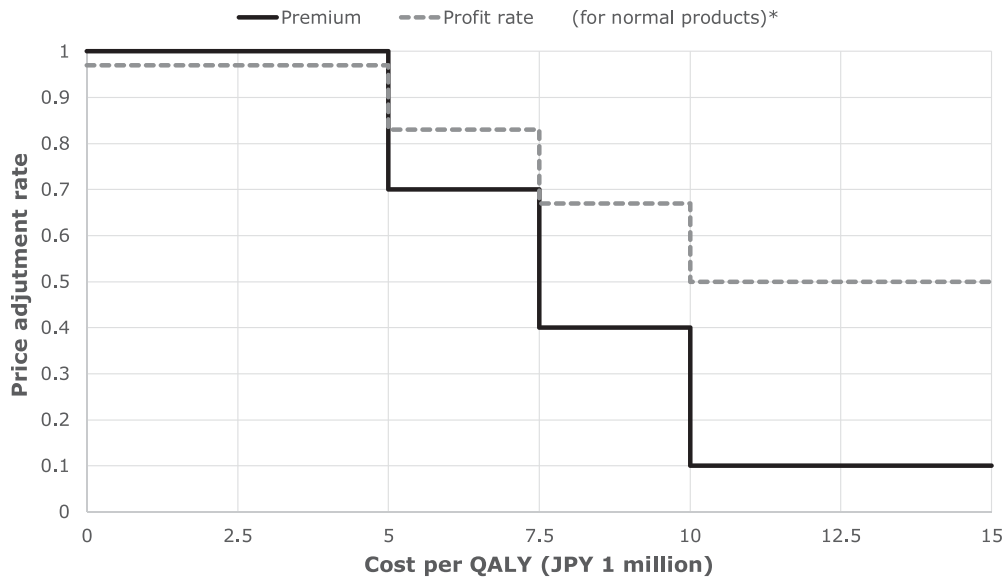

* Reference value is determined as follows;

Type of disease	Range of cost per QALY		Adjustment rate (premium)	Adjustment rate (profit)
	Lower limit	Upper Limit		
Normal	Dominant		Possibility of price increase *	
	JPY 0	JPY 5 mil (USD 45,000)	1	1
	JPY 5 mil (USD 45,000)	JPY 7.5 mil (USD 68,000)	0.7	0.83
	JPY 7.5 mil (USD 68,000)	JPY 10 mil (USD 90,000)	0.4	0.67
	More than JPY 10 mil (USD 90,000)		0.1	0.5
Oncology, pediatric, and designated intractable and rare diseases	Dominant		Possibility of price increase *	
	JPY 0	JPY 7.5 mil (USD 68,000)	1	1
	JPY 7.5 mil (USD 68,000)	JPY 11.25 mil (USD 100,000)	0.7	0.83
	JPY 11.25 mil (USD 100,000)	JPY 15 mil (USD 140,000)	0.4	0.67
	More than JPY 15 mil (USD 140,000)		0.1	0.5

** If a product is proven to be dominant and innovative, rather than just improved, 1.5 is used as "1-adjustment rate" (not to exceed 10% of the entire price). If the ICER is less than JPY 2 million (USD 18,000), price increases are not allowed unless the product is innovative and manufacturers can provide new evidence with high clinical effect. The "high-effect evidence" is defined using the impact factor (IF) of academic journals (15.0 and above) that publish clinical data. Further, the clinical study also has to show statistical superiority to the comparator in the cost-effectiveness evaluation in Asian populations, including Japanese patients. In this case, 1.25 is used as "1-adjustment rate" (not to exceed 5% of the entire price).

Fig. 1. Stepwise function of price adjustment rate (normal product).

new technology has already been listed and has replaced the old technology. Therefore, instead of the "most replaced" concept in the first edition, technology at the tip of the efficiency frontier (the most effective technology[14]) was used as the comparator.

Second, the difference in the parameters between groups, which may be caused by chance, is disallowed, and the same pooled value is used in both groups for model parameters. Of course, the "difference" may be accepted if it is sufficiently supported by other clinical evidence, even if there is no statistical significance. Therefore, this evaluation system first requires proof of "additional benefit" over those offered by a comparator, and cost-minimization analysis must be employed if such benefit is not confirmed.

[14]However, cost-ineffective technologies were not automatically excluded from comparator candidates. Therefore, some cases of technology at the tip of the frontier do not conform to the selected comparator.

For example, the hazard ratio of the product under evaluation is estimated to be 1.08 (95 percent CI, .76–1.41), and there is no other evidence of its superiority to a comparator. Thus, in this case, 1.0, and not 1.08, should be used for the hazard ratio of the base-case analysis, which may be contrary to the Bayesian concept. When the results of a cost-effectiveness analysis are used for listing, the decision is mainly binary (yes or no). However, in our setting, the single price adjustment rate using the cost-effectiveness analysis result is used. In such a case, it seems difficult to apply ICER based on the Bayesian concept to decision-making. Further discussion on this issue might be needed.

In the case of evaluation of technologies that have multiple indications or heterogeneous groups, various pricing methods are used in other countries (7). Section 6.5 of the official guidelines states the ICER of each group and determines the price adjustment rate for each group. Next, the weighted mean of the

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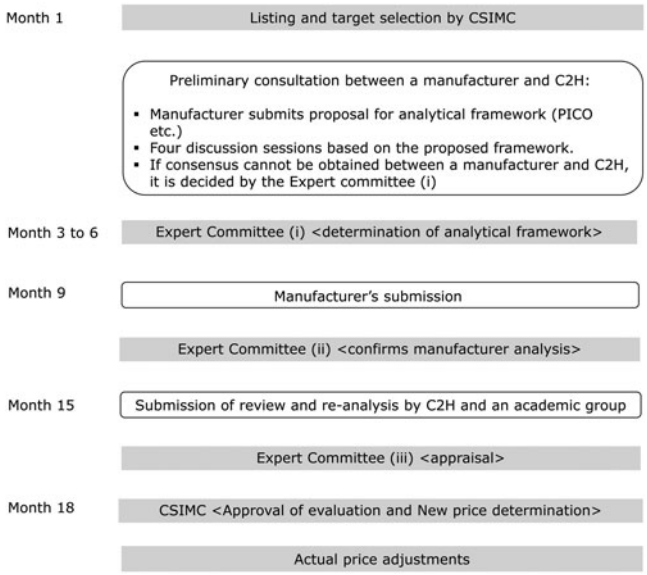

Fig. 2. Process of evaluation.

price adjustment rate considering the size of each population was calculated. For example, a product with a 10 percent premium has indications for three different indications (e.g., lung, breast, and colorectal cancer). First, three different ICERs are calculated independently for each indication (lung, breast, and colorectal cancer). Assuming the ICER is JPY 7 million/QALY for lung cancer, 20 million/QALY for breast cancer, and JPY 10 million/QALY for colorectal cancer, the adjustment rate is 1, .1, and .7, respectively (Figure 1). If the percentage of the population is .3, .45, and .25, the price is decreased by 10 percent (premium) × {(1 − 1) (adjustment rate for lung cancer) × .3 (population weight for lung cancer) + (1 − .1) (rate for breast cancer) × .45 (weight for breast cancer) + (1 − .7) (rate for colorectal cancer) × .25 (weight for colorectal cancer)} = 4.8 percent. This method is similarly applied to the sub-population in the same indication.

Value-Based Pricing Adjustment System

In summary, the size of the price adjustment in the new cost-effectiveness system is determined by the following three factors: (a) price reduction rate (per part of the price or per premium and/or profit rate) determined by the ICER, (b) price reduction rate (for the entire price) when the cost/QALY reaches JPY 5 million (e.g., JPY 7.5 million in case of anticancer medicines), and (c) 10–15 percent of the entire price before adjustment.

The MHLW indicates that factor (a) is the principal price adjustment method, and that (b) and (c) are supplementary to prevent the reduction rate from becoming excessive. However, the actual price reduction rate is essentially determined by the weakest (or the lowest percentage) of the three rules. The adjustment method can therefore be explained as follows.

The price is reduced to the point where the ICER reaches JPY 5 million/QALY (rule [a]), and two other rules ([a] and [c]) alleviate the adjustment.

This indicates that the Japanese system is also similar to value-based pricing (VBP) (8), in which the prices of medicines and medical devices are set at a level where the ICER is below the cost/QALY threshold.

Discussion

We have taken the first step of introducing cost-effectiveness evaluation (or HTA) to the Japanese healthcare system. The discussion on the introduction began in 2012 and lasted for 7 years, until it was officially introduced. This long period of discussion was needed for reaching an agreement with stakeholders and ensuring understanding of the concept and technical terms of HTA. Technically, how to build the new concept of cost-effectiveness into the existing pricing system is a difficult problem. The pricing system has complicated but established rules and procedures.

It seems complicated to harmonize the new system with the existing, more complicated, pricing rule. However, the principal idea is essentially similar to that of value-based price adjustment (VBPA). The superficial difference in the systems of Japan and other countries (e.g., the UK) may be the result of how official prices of drugs and devices are determined. In many developed countries, prices are freely determined by manufacturers or through negotiation with public bodies, and thus, explicit rules and regulations of pricing are simpler. However, in Japan, the MHLW, and possibly also manufacturers, prefer detailed and strict calculation rules for pricing.

From my academic perspective, a simpler and clearer HTA system is more suitable. My concern is that in the case of unpredictable flaws in the system, which are sometimes obscured by complexity, manufacturers are provided with some incentive or disincentive—an undesirable consequence for the healthcare system. However, our system has to start from this point, and it is a critical step forward in the Japanese HTA system. We should continue efforts to enhance the system by collaborating with the government, academia, and manufacturers.

For improving the system, immediate discussions are needed on:

(a) The application of a cost-effectiveness evaluation to the decision-making process for listing new medicines: The Japanese system currently uses cost-effectiveness evaluation results only for price adjustment, not for reimbursement decisions. The reimbursement decision should also consider cost-effectiveness. If the stakeholders hesitate to limit the reimbursement of products, it might be better to start with optimizing the reimbursement condition using a cost-effectiveness evaluation.

(b) Expansion of target products: The current system exempts the evaluation of technologies with no premium. However, in certain cases, the comparator for medicine or medical device pricing might be different from that of the cost-effectiveness evaluation. Technologies with no premium are not always cost-effective, even when their price is similar to existing technologies; therefore, their prices should be evaluated.

(c) Target of price adjustment: The current system limits the target of price adjustment to a part of the entire price (premium and/or profit rate). There is no clear rationale for this from an academic perspective, as the size of the premium is not determined by the HTA. Some have criticized this rationale, as the premium rate or how the comparator is determined at the price setting is sometimes arbitrary and unclear. It is therefore more reasonable for a price adjustment to target the entire price or part of the price.

HTA system reform will help promote both technological innovation and sustainability of the healthcare system with transparency. Moreover, there are few economic evaluation experts in Japan with the relevant evaluation experience. We need to create greater capacity to enhance this academic review system. This is a fundamental issue for our newly constructed system.

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