

[ REVIEW ARTICLE ]

# An Evaluation of Clinical Economics and Cases of Cost-effectiveness

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## Abstract:

In order to maintain and develop a universal health insurance system, it is crucial to utilize limited medical resources effectively. In this context, considerations are underway to introduce health technology assessments (HTAs), such as cost-effectiveness analyses (CEAs), into the medical treatment fee system. CEAs, which is the general term for these methods, are classified into four categories, such as cost-effectiveness analyses based on performance indicators, and in the comparison of health technologies, the incremental cost-effectiveness ratio (ICER) is also applied. When I comprehensively consider several Japanese studies based on these concepts, I find that, in the results of the analysis of the economic performance of healthcare systems, Japan shows the most promising trend in the world. In addition, there is research indicating the superior cost-effectiveness of Rituximab against refractory nephrotic syndrome, and it is expected that health economics will be actively applied to the valuation of technical innovations such as drug discovery.

**Key words:** Cost-effectiveness analysis, Health technology assessments, Value of healthcare, Kidney failure, Nephrotic syndrome, QALY

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## Introduction

In order to develop and maintain a universal health insurance system, it is crucial to utilize limited medical resources effectively. Regarding the discussion of the allocation and utilization of the various medical resources from the perspective of social equity, it is expected that, going forward, health economics will be applied, and the principles and basis will be shared among the parties involved. In recent years, the adoption of “cost-effectiveness” measures that involve the positioning of health technologies within the healthcare system based on the relationship between the results gained from medical treatment and the medical resources consumed is being considered. Under this concept, as long as significant results are expected, even if the costs are slightly high, they will be permitted from the perspective of clinical economy.

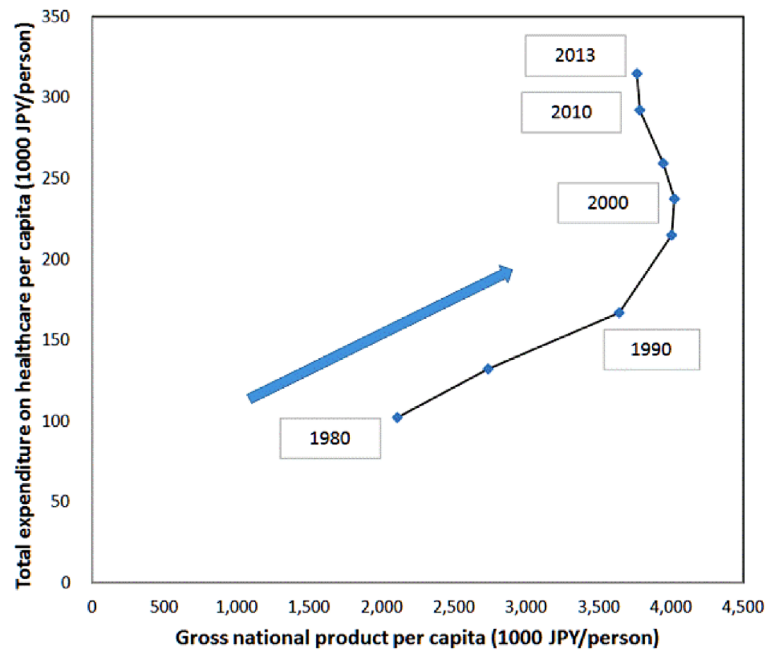
In the context of these trends, this paper organizes relevant theories, introducing reports related to the economic valuation of Japan’s clinical practice and supporting ad-

vances in terms of health economics of related areas.

## The Basic Concept of Health Economics and its Necessity

### (1) What is expected in health economics now

Medical expenses in Japan have been increasing annually. In fact, the cost of annual medical expenses more than doubled between 1989 and 2013, from 19.7 trillion yen to 40.0 trillion yen. This growth in medical expenses is due in part to an aging society, which has led to an increased demand for medical care, and partly to rising healthcare costs with advances in medical technologies and changes in the structure of disease. In contrast, the growth in the overall economy, which indirectly affects fiscal policy for healthcare, began slowing down in 1991, while the increase in gross national income peaked in 1997 at a level of 382.2 trillion yen, remaining at that level from that point. Since the total expenditure on healthcare per capita is increasing despite the downturn in gross national product (GNP) per capita, public



**Figure 1.** The relationship between the health expenditure per capita and the gross national product. (Reference 1) In order to maintain the medical system, it is necessary to maintain the balance between medical expenses and financial resources. Since fiscal policy is affected by the overall economy, Japan's sluggish economic growth rate has led to limited public funding for healthcare.

funding for healthcare has become limited, considering the balance between people who use medical services and those who pay for it (Fig. 1) (1).

To discuss the future of Japan's universal health insurance system, we must discuss in greater depth the proportion of individual payments and how to build a system that effectively utilizes the limited medical resources, within the context of the overall economic situation. In fact, it can be argued that it is necessary to introduce health technology assessments (HTAs), such as cost-effectiveness analyses (CEAs), into the medical treatment fee system in order to promote the sustainable development of a universal health insurance system even under severe economic conditions. Indeed, a previous report showed concern over the increasing financial pressure on the healthcare system in terms of expensive medical technology (2), while another report questioned the conventional way in which we make decisions regarding the cost of new medical technology and the means of paying for it without incorporating any HTA into the process (3).

## (2) Basic concept of health economics and its trends

Health economics as a field integrates medical science and economics. The main purpose of health economics is to analyze the healthcare system or various phenomena in clinical fields using certain economics methodologies, such as econometrics, value assessment, decision-making, and behavioral science, to help develop a healthcare system and thus improve the health and welfare of the population (4). In particular, health economics is expected to provide theories

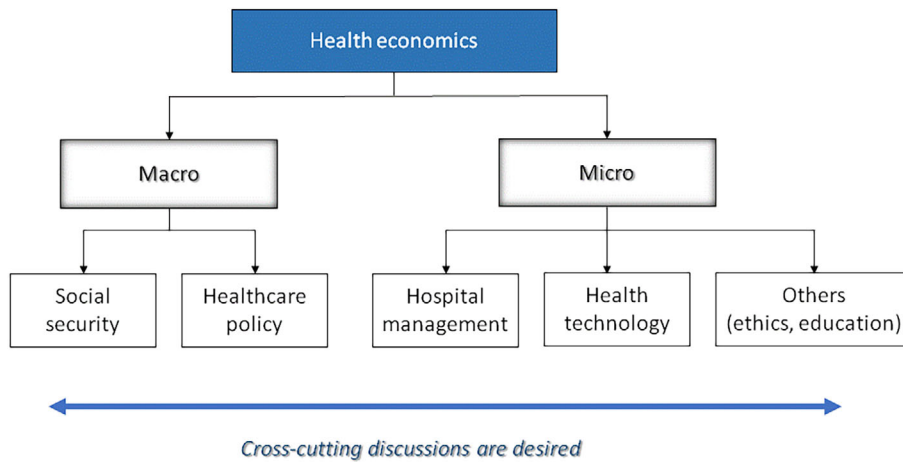
and foundational data for discussions regarding the reasonable allocation of medical resources from the perspective of social equity.

Because health economics covers a broad range of topics as a microcosm of society, the analytical method varies according to the topic. Topics are generally classified into two types: those analyzed from the macro perspective, and those analyzed from the micro perspective. Examples of macro topics are 'social security' and 'healthcare policy', while examples of micro topics are 'hospital management' and 'health technology', as well as topics such as ethics and education. However, since the socio-economics situation in developed countries has become increasingly complex in recent years, it may be argued that it is best to analyze each topic in a cross-sectional manner rather than longitudinally (Fig. 2).

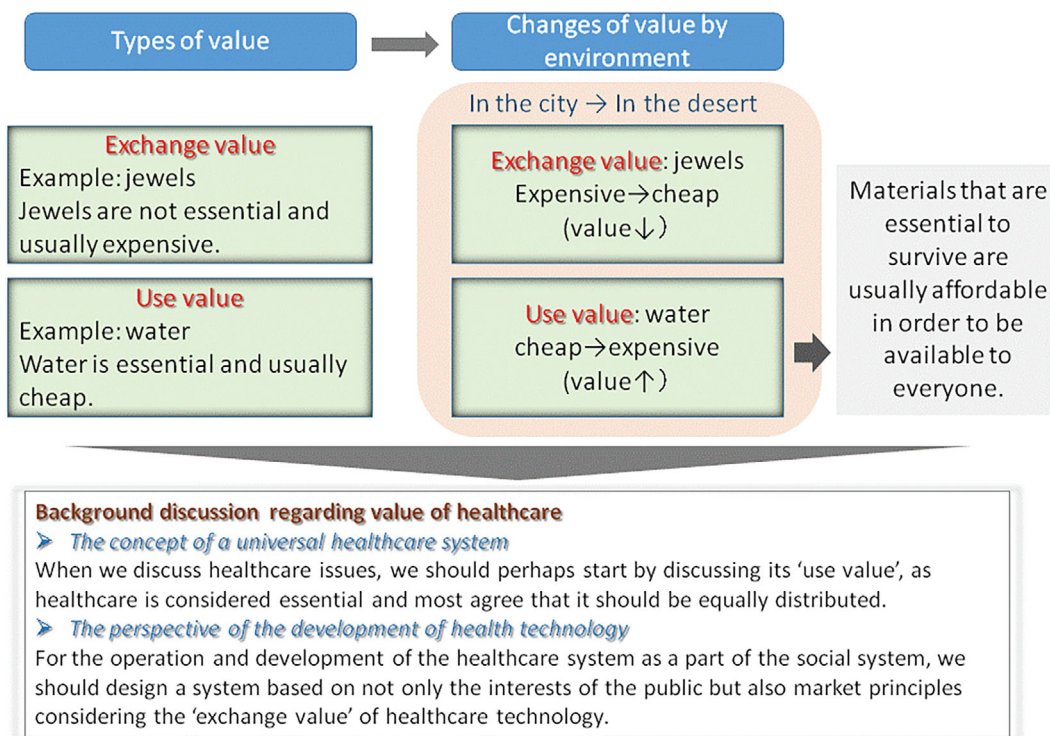
In accordance with the principle of a universal health insurance system, the healthcare system in Japan has been funded by social insurance and the public budget for more than half a century. Indeed, since the cost of medical care is largely paid by the public (social insurance and the public budget), all citizens are viewed as 'payers' in a broad sense. When discussing medical insurance as a part of the social system, we should perhaps explain the value of medical care to the final payer, that is, all of the citizens of Japan, and share the facts with them.

## (3) Relationship between innovative technology and the universal health insurance system

The value of a specific commodity can be classified according to its characteristics. For example, water, which is



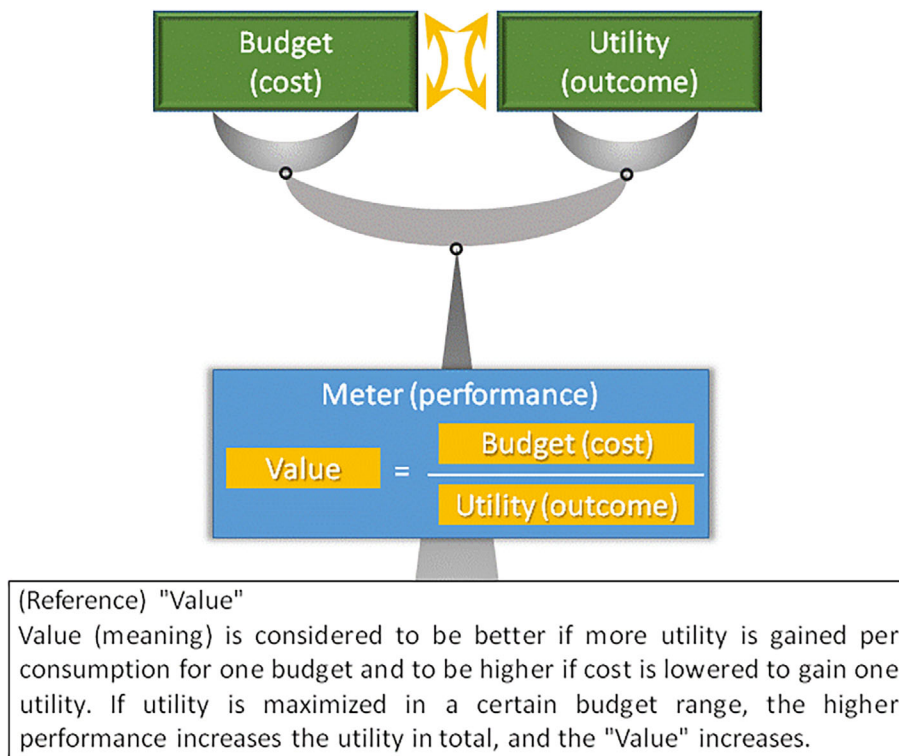
**Figure 2.** The basic concepts of health economics and its framework. (Reference 4) Health economics is the method used to discuss the appropriate distribution of health resources.



**Figure 3.** Conception of the value assessment in the quasi-public healthcare system: The balance of the valuation of technical innovations and the guarantee for all patients to have access. (Reference 5) The public medical marketplace needs a system based on a consideration of both use value and exchange value.

essential for human survival and is generally affordable, has a 'use value'. In contrast, jewels, which are not essential and are generally expensive, have an 'exchange value'. In short, value is determined according to availability and necessity and may change depending on the situation (Fig. 3) (5). Throughout the history of civilization, it has been crucial to develop a favorable environment for all inhabitants to access essential materials such as water and food equitably and at an affordable price; this is essential as a fundamental element of a community.

The medical marketplace differs from other markets in that it deals with health and life, which are precious and cannot be replaced by anything. In addition, this marketplace has the characteristic of information asymmetry because a high degree of specialized knowledge and skills are required in the medical field (6). When we discuss healthcare issues, we should perhaps start by discussing its 'use value', as healthcare is considered essential, and most agree that it should be equally distributed. Therefore, in many countries, the healthcare system has been developed, to a



**Figure 4.** The concept of economic performance: One of the methods used to discuss the economic value of healthcare. (Reference 7) 'Value' in social activities is determined by the balance between the capital investment and its returns. If you pay a certain amount of money to use a certain service (function), its value is determined by the performance, which is equal to the amount of service (function) divided by the cost. For the consumption of one budget item, the greater the result, the higher the value. In the medical fields, the amount in terms of 'restoration of health' is used as the index of the 'function'.

greater or lesser extent, under the initiative of the public institutions, and Japan's healthcare system is no exception.

However, advanced medical care often requires so much investment that not all people can receive it. Therefore, for the operation and development of the healthcare system as a part of the social system, we should perhaps design a system based on not only the interests of the public but also market principles considering the 'exchange value' of healthcare technology.

To summarize, the public medical marketplace should provide established and widespread treatment at affordable prices, but at the same time, it is necessary to guarantee high prices for innovative or specialized technology. In short, the public medical marketplace needs a system that is based on the consideration of not only the 'use value' but also the 'exchange value'.

## Basic Concept of Cost-effectiveness and Important Points

### (1) Basic cost-effectiveness methods

Attempts have been made for years to discuss the value of healthcare mainly by researchers and policymakers overseas; however, it seems that due to diverse concepts and the

difficulty of quantification, no concrete developments have been made thus far. However, concern about the sustainability of healthcare systems in the context of the population dynamics of an aging population and changes in economic conditions due to the impact of globalization is a phenomenon common to developed countries whose relevant systems have matured. In this context, some studies have attempted to apply cost-effectiveness methods and discuss the economic value of healthcare, even to a small degree (Fig. 4) (7). For example, if we consider that "value equals performance", this means that the greater the results obtained by the consumption of one budget item (e.g. the utility), the better the value, and the lower the cost required to achieve a given result, the higher the performance. If we maximize the utility within the scope of the budget, regardless of the value type, then the higher the performance, the better the results (utility, etc.), thereby increasing the so-called value.

CEAs are an evaluation method that can be used to consider the positioning of health programs in systems from the perspective of health economics. A CEA selects test values commonly utilized in clinical practice as effectiveness indicators, generally considering "cost / effectiveness" as units, and the smaller the value, the higher the performance. Although this is not strictly organized, CEA is also the general term for cost-effectiveness, and when the methods are classi-

**Table 1. Primary Methods for Healthcare Technology Assessment (Reference 4).**

Type of Analysis	Characteristics and advantages	Disadvantages
Cost-benefit analysis: CBA	Outcomes are measured in monetary units, as this analysis is for resources. It permits a direct comparison between the incremental cost and its incremental outcomes.	The valuation of outcomes in monetary units is difficult, as valuing human life may be viewed as unethical.
Cost-effectiveness analysis: CEA	Outcomes are measured in natural units, such as years of life saved and decreased morbidity. Its outcomes are commonly used in general practice, so they are acceptable for physicians and payers.	It is difficult to establish comparisons between different diseases due to differences in the measure of primary effectiveness.
Cost-utility analysis: CUA	Outcomes are measured in quality-adjusted life years (QALY), which combines the benefits of the survival and quality of life as a measure of effects. It can simultaneously compare results among different diseases.	In some situations, the sensitivity is low due to the measurement method. The value of QALY is more likely to be lower with the elderly than with younger subjects.
Cost-minimization analysis: CMA	By comparing the cost of two or more alternatives that have identical outcomes, this analysis identifies the least-expensive alternative. It is easy to understand.	It is difficult to compare different diseases due to differences in the measure of primary effectiveness. The definition of cost included should be discussed deeply.

A CEA is usually used to compare each intervention for the same disease or under the same condition. A CUA is usually used to analyze the allocation of limited medical resources.

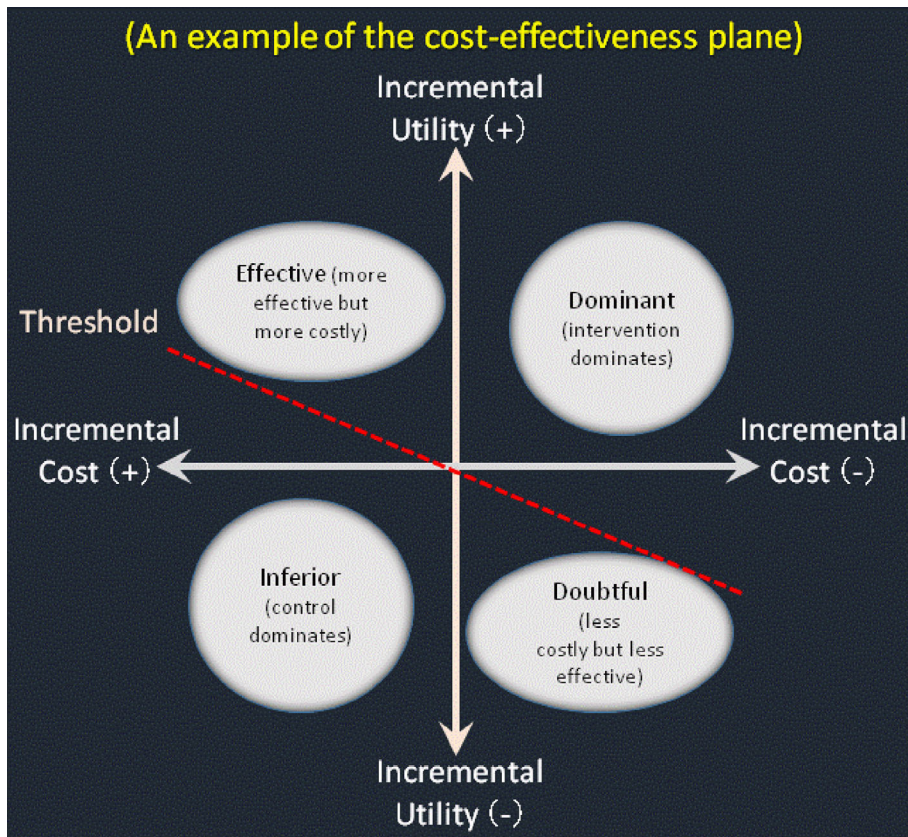
fied in detail, depending on the type of result selected (patient outcomes, benefits, etc.), cost-utility analyses (CUAs) and cost-benefit analyses (CBAs) may also be applicable (Table 1) (4). In the healthcare area, utility is treated as a part of the health-related quality of life (HRQOL), and measures based on preferences that include patient satisfaction are utilized. On multiplying this by the years of life, we obtain the measure ‘quality-adjusted life-years’ (QALY). Benefit is a method of converting acquired results, such as health improvements, into monetary units.

In addition, there is also the incremental cost-effectiveness ratio (ICER), a concept that can be utilized in health technology assessments, where the increased costs are compared with the incremental increase in effects. ICER (Fig. 5) is generally expressed as the “incremental increase in cost / incremental increase in effect”, and the concept is as follows: when comparing health technologies, even if the cost increases, if there is a greater increase in effectiveness, the so-called performance (balance of cost and effectiveness) will improve. For example, if technology A has a higher cost than technology B but a smaller effect, it will be “inferior” to technology B, whereas if technology A has a lower cost than technology B with a larger effect, it will be “superior” (8). If the ICER value is superior, the technology in question is recognized as having a higher health economy than the comparison technology, and this becomes a basis for promoting patient access. Taking the cardiovascular area as an example, these methods have been laid out in the “ACC/AHA Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures” (9) overseas and in the “Guidelines for Rehabilitation in Patients with Cardiovascular Disease (JCS 2012): The Future of Cardiac Rehabilitation from the Health Economics Viewpoint” in Japan (10).

## (2) Requirements for utilizing and cultivating health technology assessments

The basic concept of cost-effectiveness in the broad sense has developed in the areas of determining social policies and the control of management resources (1). In other words, it is characterized by know-how cultivated in a contract society and through management activities and has been utilized in social consensus building and decision-making. In the 1950s, cost-effectiveness began to be applied in research in the healthcare area in Europe and North America (11). At the time, many reports discussed CBAs, but from around the late 1970s, there began to be an increase in reports discussing CEAs, and since then, development of both analytical methods has progressed. We can therefore see that cost-effectiveness is a relatively new concept in the healthcare area.

With the introduction of CEAs, it is important that the development of innovative, new health technologies be promoted, and if these are exceptional technologies, care should be taken to ensure that patient access is not obstructed. This also involves discussing the investment-versus-return for those who created the healthcare innovations, and one option is to conduct an insurance valuation that is in line with the results of the CEA if the results are good. This requires the development of a health economics prediction model based on limited information about new technologies (such as their efficacy and safety from clinical trials) as well as the consideration of methods for securing and allocating the financial resources mentioned in the beginning of this paper. In other words, in addition to organizing a system to promote the fluidity of the allocation of resources among disease areas and the subjects providing them, we should also be discussing, although difficult, the state of social resources (such as the scale of health insurance finances) that support the advancement of healthcare. Having a well-balanced dis-



**Figure 5.** The concept of the incremental cost effective ratio (ICER): The result of the cost-effectiveness analysis is shown in four quadrants. (Reference 8) The cost-effectiveness threshold represents the additional cost that must be imposed on the system to forgo one QALY of health through displacement; the cost-effectiveness threshold depends on a person's willingness to pay for an improved quality or length of life.

cussion of both of these aspects is essential for the progress of HTA (Fig. 6) (12).

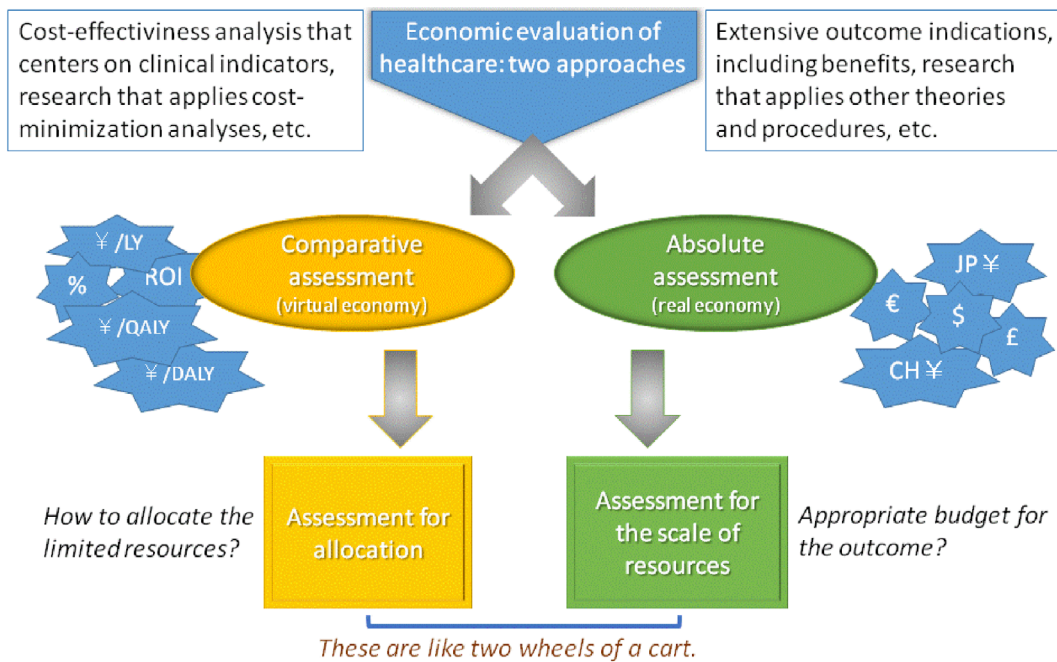
As mentioned earlier, as cost-effectiveness itself has a history that has developed in the context of contract societies in other areas, in order to fully express the capabilities of the evaluation tool, it will likely be important to continue to foster an environment that ensures the transparency of system operations, negotiations based on data, and logical decision-making mechanisms, as well as adjusting responsibilities and rights. However, we should also consider the national character of Japan, its values, and the history and principles of the universal healthcare system (mutual aid, self-aid, public aid), as well as the characteristics of healthcare, which handles the highly indefinite and irreversible aspects of life and health. Going forward, there are expected to be further developments in the consideration of system design with consideration of such things as the declining birthrate and aging of the Japanese society. In this context, the trial adoption of cost-effectiveness evaluations for pharmaceutical products and medical devices was started in Japan in fiscal year 2016, and we should consider the measurements of effectiveness and their scope of application that are suited to our country, as a system that sets an example for the rest of the world.

## Examples of Health Economy Assessments

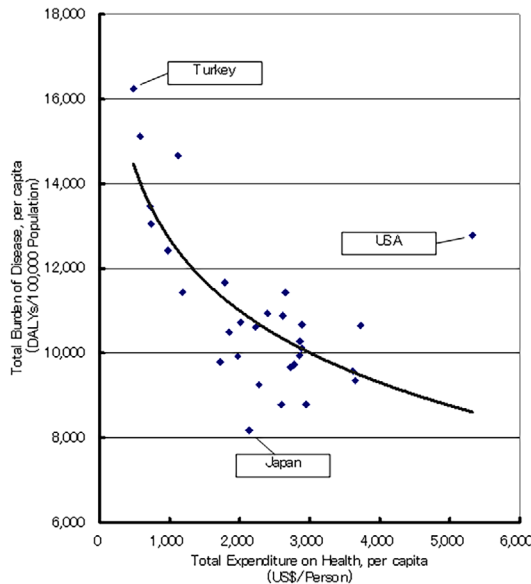
### *(1) Examples of the assessment of the economic performance of healthcare systems*

Japan is a global leader in terms of the economic performance (ratio of the consumption of healthcare finances to the medical treatment results gained through them) of its healthcare system and the comparison of a country's total healthcare expenditure versus disability-adjusted life years (DALY), which is a measure for estimating a country's disease burden developed by the World Health Organization (WHO) and the World Bank. Some reports suggest that Japan should expand its relevant resources in keeping with the country's health economic value (Fig. 7) (13). The argument is that it is important to promote discussions of the price standards and investment of capital that are in line with the value generated by healthcare services for the future development of the healthcare area in Japan.

For example, at present, the total healthcare expenditure per person in Japan is 2,100 (USD/person), while the DALYs per population of 100,000 is approximately 8,100 (DALYs/100,000 population). As Japan's disease burden is the



**Figure 6.** For the advancement of healthcare, both allocation of limited resources and total healthcare expenditure resources should be considered. The evaluation on an absolute scale is as important as a comparative assessment for the progress of health technology assessments. In other words, when conducted evaluations on a comparative scale using clinical indicators, such as a cost-effectiveness analysis or a cost-minimization analysis, it is also important to conduct evaluations on an absolute scale using benefit as the outcome so that we can discuss the state of social resources (such as the scale of health insurance finances).



**Figure 7.** An international comparison of the relationship between total expenditure on health and total burden of disease. (Reference 12) This figure shows the economic performance of the healthcare system in each OECD country. The dots at the lower left represent good cost-effectiveness, while those in the upper right represent lower cost-effectiveness.

lowest of all OECD countries and its medical expenditure is also low, the economic performance of Japan's healthcare system is understood to be good. In other words, if meas-

ured against the average value for the economic performance of target countries, even if healthcare expenditure per person is expanded to approximately double, or close to US standards, Japan's economic performance is still expected to rival that of leading developed countries. Incidentally, it is said that the poor improvement of the disease burden in the US, which has the largest average medical expenditure per person, is due to the impact of the US healthcare system, which is based on the free market. This tends to lead to the biased consumption of healthcare resources, thereby bringing down the overall average standards.

For the above reasons, Japan's universal healthcare system is expected to have significant economic value when considered globally, and given Japan's changes in population demographics and economic conditions that are happening ahead of other developed countries, Japan's drive to rebuild its healthcare system going forward is likely to draw international interest.

## (2) Examples of the assessment of the economic performance of health technologies

When we consider the area of kidney failure, recently there have been some papers related to cost-efficiency. Traditionally, in research in this area, the vital prognosis, kidney function, and cardiovascular events have been used as indicators of efficacy. Recently, however, the measurement of the effects from the recipient's perspective (preference and satisfaction) have been drawing attention. One of these

**Table 2. Cost-effectiveness by Utility and Cost in Patients on Maintenance Hemodialysis (MHD) (Reference 14).**

Parameter	All Subjects	Glomerulonephritis	Diabetic nephropathy	Others
<b>Utility (QALY)</b>				
Mean±SD	0.75 ± 0.21	0.73 ± 0.17	0.68 ± 0.23	0.83 ± 0.22
Median	0.73	0.71	0.60	1.00
p value		*	**	
		**		
<b>Cost (\$10,000 US year)</b>				
Mean±SD	4.52 ± 0.88	4.53 ± 0.88	5.11 ± 1.07	4.11 ± 0.41
Median	4.33	4.41	4.35	4.19
p value		**	**	
		**		
<b>Cost-effectiveness (\$10,000 US/QALY)</b>				
Mean±SD	6.88 ± 4.47	6.82 ± 4.07	8.17 ± 5.28	5.46 ± 2.74
Median	5.87	6.09	8.11	4.44
p value		**	**	
		**		
<b>Dialysis time (hours per intervention)</b>				
Mean±SD		4.35 ± 0.50	4.19 ± 0.39	4.08 ± 0.43
95% CI (two sample population mean)		0.16(0.01, 0.28)	0.11(-0.01, 0.23)	
			0.27(0.16, 0.37)	
<b>Biochemistry</b>				
<i>Cr (mg/dL)</i>				
Mean±SD		9.93 ± 2.11	9.47 ± 2.39	10.97 ± 3.24
95% CI (two sample population mean)		0.45(-0.78, 1.70)	1.50(-0.09, 3.09)	
			1.04(-0.29, 2.38)	
<i>BUN (mg/dL)</i>				
Mean±SD		67.09 ± 15.62	69.43 ± 16.92	72.43 ± 12.38
95% CI (two sample population mean)		2.34(-4.87, 9.56)	2.99(-4.20, 10.20)	
			5.34(0.02, 10.65)	
<b>Age (years)</b>				
Mean±SD		63.59 ± 12.30	63.78 ± 4.27	51.78 ± 14.08
95%CI (two sample population mean)		0.18(-1.88, 2.26)	12.00(9.19, 14.81)	
			11.81(8.63, 14.99)	
			*: $p < 0.05$ , **: $p < 0.01$	

These values were analyzed by distinguishing between the primary disease for end-stage kidney disease (ESKD), glomerulonephritis, diabetic nephropathy, or others, in the first four weeks of observation.

international measures of efficacy is the aforementioned QALY, which can simultaneously assess both the years of life (quantitative merit) and quality of life (qualitative merit). In Japan, there are several clinical studies being conducted that use QALY as a measure of effectiveness. In an observational study of cost-effectiveness that followed 29 patients with end-stage renal disease receiving outpatient maintenance dialysis for a period of 36 months, it was reported that the medical expenditure required to achieve 1 QALY was 6.88±4.47 (10,000 USD) (Table 2) (14). The cost-effectiveness results were particularly good for elderly patients, and this is also expected to have a significantly positive social and economic impact to improve the medical sys-

tem and better meet the needs of the progressing aging of society. However, it has also been revealed that the cost-effectiveness was significantly poorer for groups with diabetic nephropathy as the underlying disease than for those with glomerulonephritis (8.17 ± 5.28 vs. 6.82 ± 4.07,  $p < 0.01$ ), decreasing by approximately 20%.

By conducting the above clinical research on health economics, several socio-economic insights have been newly gained, and they may contribute to the further advancement of the therapeutic area in question. For example, given the finding that “cost-effectiveness is poor when diabetic nephropathy is the underlying disease”, we can identify the direction of promoting prophylactic intervention for the pa-



**Table 3. a Medical Economics Analysis (pre-post CEA) Accounting for the Medical Costs of Rituximab (Reference 17).**

A. Exclusion of rituximab costs			
Items	Pre-administration	Post-administration	Difference (after-before)
Medical cost difference (points/24 months)	725,403	317,707	-407,696
(USD/24 months)	(70,155)	(30,726)	(-39,429)
Relapse difference (times/24 months)	4.30	0.27	-4.03
Pre-post CEA (points/24 months/times)			101,082
(USD/24 months/times)			(9,776)
Reference: pre-post CEA with a case in which the analysis was restricted to 17 months (points/17 months/times)			50,982
(USD/17 months/times)			(4,931)
B. Addition of costs for rituximab			
Items	Pre-administration	Post-administration	Difference (after-before)
Medical cost difference (points/24 months)	725,403	401,539	-323,864
(USD/24 months)	(70,155)	(38,833)	(-31,321)
Number of relapses (times/24 months)	4.30	0.27	-4.03
Pre-post CEA (points/24 months/times)			80,297
(USD/24 months/times)			(7,766)
Reference: pre-post CEA with a case in which the analysis was restricted to 17 months (points/17 months/times)			29,445
(USD/17 months/times)			(2,848)

The analysis was corrected for the number of months. Pre-post CEA was calculated as [medical cost (post - pre) / medical effectiveness (post - pre)] (Suppression amount for medical costs accumulated over 24 months per one-time reduction [avoid] in relapses, expressed as points per 24 months per time).

tients in question, as the socio-economic significance of preventing the exacerbation of diabetes is high. In this context, under the fiscal year 2016 medical service fee revision, a premium was newly established for the instruction of patients with renal failure as an assessment of exercise instruction for patients with advanced diabetic nephropathy. In addition, given the finding that “the cost-effectiveness for elderly patients  $\geq 65$  years of age has relatively improved”, we can reconfirm the socio-economic advantage of maintenance dialysis among elderly patients and expect it to be useful when utilized as supplementary information for selecting treatment methods and determining applicability in the clinical field.

### (3) Examples of assessing the economic performance of drug therapies

Since the beginning of 2000, the efficacy of administering rituximab against nephrotic syndrome has been discussed (15, 16), and the drug was listed in the NHI drug price listings in Japan in fiscal year 2015. Recently, the results of a CEA for adopting rituximab to treat refractory nephrotic syndrome (FRNS or SDNS) have been published (17). This study targeted 30 patients who developed and were treated for nephrotic syndrome during childhood or as an adult (male ratio: 70.0%), and the regimen for the study involved administering 500 mg of rituximab every 6 months, for a total of 4 times. In this study, the main meas-

ure of effectiveness selected was the number of instances of recurrence, and the amount billed in medical service fees (including in-patient, out-patient, and patient out of pocket) for the disease in question was used as the measure of cost. The endpoint for the health economic assessment was taken to be the CEA, and using traditional drug therapies (steroids and immunosuppressants) as the control, they compared the findings before and after the start of rituximab administration.

The results of this study were as follows: The average age of the group administered rituximab was  $29.1 \pm 11.4$  years, and the average period from the onset of the disease to the start of administration of rituximab was  $13.1 \pm 7.9$  months. When the clinical features before and after administration were analyzed, the number of instances of recurrence were  $4.30 \pm 2.76$  times/24 months before administration and  $0.27 \pm 0.52$  times/24 months after administration, with statistically significant improvement observed ( $p < 0.01$ ). In addition, the urinary protein improved from  $2.1 \pm 4.6$  g/day before administration to  $0.0 \pm 0.0$  g/day after administration ( $p < 0.05$ ). Expenditures, including other drugs before and after the administration of rituximab, were reduced from 2,923 (USD/month) to 1,280 (USD/month). After administration, expenditures were also significantly reduced for 18 months ( $p < 0.01$ ). In addition, superior results were generated for pre-post CEA (artificial ICER) (Table 3).

The above indicates the possibility that intervention in

therapies for the patients in question with rituximab may have advantages in terms of health economics compared to traditional drug therapies (rituximab showed higher cost-effectiveness than conventional treatments for nephrotic syndrome). On considering this trend from the perspective of healthcare policy, promoting the sustainability of the healthcare system and socio-economic innovation in our country will require a rational propositus for insurance prices and self-payment.

## Conclusion

Growth of medical expenditures that are not accompanied by equivalent socio-economic improvements may impede the development of the healthcare system and prevent the spread of advanced healthcare technologies. Reorganizations of the healthcare system in Japan to take into account changes in the general economy and population demographics, as well as technological innovations, need to be carried out smoothly. To this end, going forward, we will need to accumulate evidence based on health economics, such as CEAs, to promote consensus building and educational activities about the medical service fee system. However, as it is difficult to assign a single quantitative value to the diverse values associated with clinical medicine, it is also crucial to use related evidence to connect the system and physicians, thereby creating synergy with the expert opinions of healthcare professionals. For instance, as part of HTA of medical diagnoses and follow-up, the decision-making value of not performing something, in order to avoid excessive medical intervention, is worth considering along with an approach in harmony with hospital management. From the perspective of the overall optimization of the healthcare system, we expect that discussing the balance of clinical practice and economics will aid in the further advancement of healthcare in Japan.

**The authors state that they have no Conflict of Interest (COI).**

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### Authors' contributions

Takura, T contributed to the study design and interpretation.

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