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Special Article

The Need for Guidelines and the Use of Economic Evidence in Decision-Making in Thailand: Lessons Learnt from the Development of the National List of Essential Drugs

Suwit Wibulpolprasert MD*
On behalf of Subcommittee for Development of the National List of Essential Drugs**

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Since 2004, the Subcommittee for Development of the National List of Essential Drugs (NLED) has embarked upon an historical evolution of applying evidence to the revision, inclusion and exclusion of medicines into and from the list. Then, the revision of the 2008 NLED was the first time in Thai history where the drug selection process in Thailand formally incorporated pharmacoeconomics. At present, the lack of a standard methodology for conducting economic evaluation is a major barrier that diminishes the potential use of economic evidence. The development of national economic evaluation guidelines by a group of national experts was subsequently endorsed by members in the Subcommittee as useful tools for future NLED revision. They emphasize that these guidelines should be applied not only to those evaluations conducted by public institutions but also by private pharmaceutical companies that often use this evidence for their marketing, or even for future requirements of economic information from industry, as complementary evidence for inclusion of health technology.

Keywords: *National list of essential drugs, Economic evaluation, Guidelines, Pharmacoeconomics*

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Rationing is inevitable for any health care system, particularly in resource-inadequate developing country settings. Practically, developing countries apply "implicit" rationing where resources are limited. There are usually neither clear decisions about which care is provided nor are the bases for those decisions clearly expressed. Market failure in healthcare can result in harmful implicit rationing due to asymmetry of information between patients and providers, monopolies and externalities. For instance, a patient's choice of physicians or hospitals is typically limited by the managed care plan's gatekeepers, so health care may be denied to those suffering from conditions of ill-health by not referring them to secondary or tertiary providers. Treatment being not withheld altogether, but delayed due to long waiting lists, at times, results in the worsening of patient conditions. In addition, most patients do not have clinical knowledge as complete as clinicians, health care can be diluted by not providing optimal treatment, as in most cases it is new and expensive.

Relying on implicit rationing may make the lives of decision-makers easier, but it is clearly not transparent and not in the best interest of patients, taxpayers and society as a whole[1]. There have recently been wider discussions and debates about explicit rationing which require clarity in definition and principles by which decisions regarding access to scarce resources are determined. Thus, definite rules/criteria are needed to ensure evidence-based decisions. Although it is impossible that all people will agree on the preset criteria to be initially applied in rationing, only using explicit evidence in decision-making

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encourages debate that will eventually support better evidence being generated.

Since 2004, the Subcommittee for Development of the National List of Essential Drugs (NLED) has embarked upon an historical evolution of applying evidence to the revision, inclusion and exclusion of medicines into and from the list. The NLED is referred to, by all three public health insurance schemes, as medicine benefit for the whole population; therefore, the process of revision of the NLED is extremely vital, as it has major implications for the whole population who are beneficiaries and the insurance funds who are the payers.

Not only drug safety and efficacy, but also the effectiveness and costs are taken into account. For example, in the revision of the 2004 NLED, there was an explicit application of cost and efficiency criteria in terms of "ISafE score" and "Essential Medical Cost Index" (EMCI)[2]. ISafE stands for Information, Safety and ease of use (namely patient adherence) and Efficacy of each medicine, and is used as the basis for computing the score. The composite ISafE score (ranging from 0 to 1) indicates the relative merit of each drug. Drugs with an ISafE score below the 50th percentile in the same group are initially excluded; those more than the 50th percentile pass the threshold of quality to be further assessed where EMCI is applied as sequential criteria, based on the cost of daily defined dose (DDD) of that medicine per ISafE score. The lower the cost of DDD per ISafE score, the higher the likelihood of it being adopted into the NLED.

Since the 2004 NLED revision, the ISafE score and EMCI have been established and applied to the revision of the NLED, though we have found some limitations. For example, these criteria cannot be used when comparing drugs with different and/or multiple outcomes, or comparing values of medications with other treatment modalities *e.g.* surgical or radiation procedures. As a result, the revision of the 2008 NLED was the first time in Thai history where the drug selection process in Thailand formally incorporated pharmacoeconomics.

Given resource and research capacity constraints in health technology assessment, six groups of drugs were initially selected to require pharmacoeconomic evidence for consideration in the revision of the 2008 NLED (see detailed information about the criteria and topic selection process in Lertpitakpong *et al* 2008[3]). These included osteoporosis drugs, HMG-CoA reductase inhibitors (statin), insulin analogues, recombinant human erythropoietin, medications for treatment of Alzheimer's disease and medications for treatment of Hepatitis B and C.

During the process, the members of the Subcommittee and its Health Economic Working Group have gained more experience concerning use of evidence, and have foreseen difficulties in its future use. There is consensus that economic evaluation is useful for guiding policy decisions, but only when it is performed correctly and reported accurately. At present, the lack of a standard methodology for conducting economic evaluation is a major barrier that diminishes the potential use of economic evidence[4].

The development of national guidelines by a group of national experts, which were subsequently endorsed by the Health Economic Working Group, published in this special supplement is, therefore, welcomed by members in the Subcommittee. They approved the guidelines as useful tools for future NLED revision. They emphasize that these guidelines should be applied not only to those evaluations conducted by public institutions but also by private pharmaceutical companies that often use this evidence for their marketing, or even for future requirements of economic information from industry, as complementary evidence for inclusion of health technology, similar to that which has been practiced by the Pharmaceutical Benefits Advisory Committee in Australia[5]. Furthermore, in the draft revised drug bill in Thailand, there is a requirement for economic evaluation regarding new drugs that apply for market authorization. If passed into an act, it will further strengthen the pharmacoeconomic capacity in the country, and also emphasis the importance of the guidelines.

Not only do the guidelines ensure the use of economic evidence for the efficient allocation of scarce resources, they also increase the transparency of the evaluations undertaken by allowing audiences to assess accurately the appropriateness of the methods and the quality of the evidence used. The guidelines will improve the general quality of, and encourage comparisons between studies because the guidelines address all important methodological considerations. At this stage, it is difficult to predict the future application and contributions of economic evaluation as a tool for decision-making in Thailand. This crucial step of having standard methods established, endorsed nationally and publicized, will support the wide application and the potential contribution of economic evaluation as powerful input for policy decisions. Finally, the guidelines are an important capacity-building tool for all related sectors and institutions.

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ความต้องการแนวทางมาตรฐานการประเมินเทคโนโลยีด้านสุขภาพ และการใช้ข้อมูลเพื่อการตัดสินใจเชิงนโยบายในประเทศไทย: บทเรียนจากการพัฒนาบัญชียาหลักแห่งชาติ

สุวิทย์ วิบุลผลประเสริฐ ในฐานะประธานคณะอนุกรรมการพัฒนาบัญชียาหลักแห่งชาติ

ตั้งแต่ปี พ.ศ. 2547 เป็นต้นมา คณะอนุกรรมการพัฒนาบัญชียาหลักแห่งชาติ ได้ริเริ่มให้มีการประยุกต์ใช้หลักฐานทางวิชาการเพื่อทบทวนและคัดเลือกยาเข้าบรรจุในบัญชียาหลักแห่งชาติ ต่อมา ในปี พ.ศ.2551 มีการปรับปรุงบัญชียาหลักแห่งชาติ และนับเป็นครั้งแรกในประเทศไทยที่กระบวนการคัดเลือกยาได้นำเอาข้อมูลการประเมินความ คุ้มค่าทางการแพทย์มาใช้อย่างเป็นทางการ ในปัจจุบันประเทศไทยยังขาดมาตรฐานของระเบียบวิธีวิจัยสำหรับการ ประเมินความคุ้มค่าทางการแพทย์เป็นอุปสรรคที่สำคัญต่อการใช้ประโยชน์จากการประเมินความคุ้มค่าทางการ แพทย์สำหรับการตัดสินใจเชิงนโยบาย ดังนั้นคู่มือการประเมินเทคโนโลยีด้านสุขภาพจึงถูกพัฒนาขึ้นโดยกลุ่มผู้เชี่ยวชาญระดับประเทศ ซึ่งต่อมาได้รับการรับรองจากคณะอนุกรรมการพัฒนาบัญชียาหลักแห่งชาติว่าเป็น เครื่องมือที่เป็นประโยชน์สำหรับการปรับปรุงบัญชียาหลักแห่งชาติในอนาคต และยังเน้นว่าแนวทางในคู่มือ เล่มนี้ควรนำไปประยุกต์ใช้สำหรับการประเมินความคุ้มค่าทางการแพทย์ ไม่เพียงแต่ในหน่วยงานภาครัฐเท่านั้น แต่ควรนำไปใช้ในหน่วยงานภาคเอกชน เช่น บริษัทยาที่ต้องใช้ข้อมูลเหล่านี้เพื่อทำการตลาด หรือในอนาคตหน่วยงาน ที่เกี่ยวข้องในภาครัฐอาจร้องขอให้บริษัทเอกชนต้องเสนอข้อมูลการประเมินเทคโนโลยีด้านสุขภาพเพื่อใช้สำหรับ การพิจารณาคัดเลือกเทคโนโลยีให้อยู่ในชุดสิทธิประโยชน์ในระบบประกันสุขภาพ

Special Article

Making Sensible Rationing: The Use of Economic Evidence and the Need for Methodological Standards

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Thailand was increasingly facing budget constraints when a comprehensive package of services was provided literally free to the whole population; therefore rationing is inevitable. 'Good value for money' is among the popular criteria in priority setting as it offers a sensible basis to compare marginal benefits with the resources spent across interventions. The majority of cost-outcome studies in Thailand were subject to bias as they relied on low-quality evidence. The methods applied also varied greatly. This hampers comparisons across studies. The first ever national guideline was developed by experts from different institutes to propose the most practical ways of conducting health technology assessment on the basis of economic principles in the Thai context. This paper also draws lessons from a transparent process involving key stakeholders in selecting technologies to be assessed given time and resources constraints. Finally, it is hoped that these tools and methods will be applicable for Thailand to facilitate comparisons of different studies in order to better inform policy decisions in a transparent manner.

Keywords: *Rationing, Economic evaluation, Guidelines, Health technology assessment*

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Although the research and development of new health technology† has produced great benefits to society, access to these innovations is often hampered by intellectual property protection, lack of health personnel, inadequate and non-functioning healthcare delivery systems, and unaffordable costs, especially among the poor in developing countries where a large portion of health expenditure is paid out of pocket by the households. Fiscal constraints are common problems facing governments and Ministries of Health in the developing world.

As a result, not only are governments and agencies responsible for adopting new health technologies, health insurers must also be held socially accountable in ensuring access to essential health services for needy populations and their insurance members by defining health benefit packages[1-3] and taking into account the fiscal capacities of governments and insurance agencies. In view of resource constraints in poor settings, health benefits should be prioritized by the magnitude and a profile of the burden of disease on the population as well as guided by evidence regarding cost-effectiveness. However, the ultimate goal of health insurers should not be comprised only of cost containment, but also the maintenance and improvement of the health status of the population covered by their insurance schemes[4]. Therefore, governments and health insurance managers have become increasingly interested in the application of economic evaluation, as one of several tools, to consider the costs and benefits associated with a given health technology, either current or new ones[5-7].

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† Health technologies here covers the whole range of goods and services including for example, medicines, vaccines, diagnostic, medical devices, therapeutic and other public health interventions aiming to improve health of the population.

Several European countries apply an economic evaluation method when defining health services for public health insurance coverage; however, this practice has only been formally adopted in the UK, the Netherlands and Sweden. The application and methodology also differ from one country to another[8]. A review of the use of economic evaluation of pharmaceuticals in 13 European countries demonstrates that this evidence is mandatory as part of the applications for inclusion into public reimbursement schemes. This is particularly required in the case of innovative products or in situations where the manufacturer is seeking a premium price[9]. Apart from this requirement, these countries employ a range of mechanisms for encouraging the use of pharmaco-economic assessment including reference-based pricing, local formulary discussion, communications with prescribers, and the development of clinical practice guidelines development.

In the Asia and Pacific region, South Korea recently introduced economic evaluation in priority setting of healthcare services. Japan, Hong Kong and Singapore are progressing rapidly towards a government requirement of cost-effectiveness evidence as part of the approval process for new pharmaceuticals[10]. Apparently, there is a capacity to generate and apply economic evaluation in these countries to accommodate policy concerns regarding cost-escalation in the health sector.

Thailand, a lower, middle income country, has been increasingly facing budget constraints when a comprehensive package of services was provided literally free to the whole population through 3 major public insurance schemes: one for public sector employees, one for private sector employees and one for the residual population. In view of technological advancements and finite resources, policy makers, hospital administrators, and professionals realized the fact that it is impossible to cover all interventions in the benefit package; rationing is inevitable and is better applied sooner rather than later[4]. To gain public confidence and trust, the use of a well-structured and rational approaches are required. 'Good value for money' is among the popular criterion in priority setting as it offers a sensible basis to compare marginal benefits with the resources spent across interventions.

A review of economic evaluation literature relating to Thailand reveals inadequate resources and capacity in conducting domestic assessments[11]. It was found that the majority of cost-outcome studies were subject to bias as they relied on low-quality evidence. The methods applied also varied greatly. This hampers comparisons across studies. One cannot make a good judgment on whether the differences in incremental cost-effectiveness ratio reflect the real differences in costs and/or differences in outcomes or differences in the study methods applied. This calls for standardization of methodology when conducting economic evaluation.

Though high quality economic evaluations alone may not convince the public when recommending or not recommending a particular intervention, given that societal values, political and ethical dimensions which interplay in the decision processes, one still requires rigorous tools and methodology for economic evaluation; otherwise, it is difficult to defend yourself when being challenged.

Highlights in this special issue

This special issue emphasizes economic evaluation and its application in the health sector. With regard to the former, 11 articles aim to provide all concerned parties with methods and critical issues, which can be taken as guidance when there is a need to assess the costs and outcomes of particular health interventions. As chapters in the first-ever national guideline, these review papers were developed by experts from different institutes to propose the most practical ways of conducting health technology assessments on the basis of economic principles in the Thai context. These concerted efforts respond to the call for standardized tools and methodologies in conducting health-economic evaluation in a country where necessary information is usually limited.

To illustrate the health technology assessment experience in Thailand, this paper draws lessons from a transparent process involving key stakeholders in selecting technologies to be assessed given time and resources constraints. Such participatory approaches can ensure ownership and downstream policy decisions by users and trust-building between users and Technology Assessment Agencies.

Other papers give the audience a flavor of how cost assessment and economic evaluation have been applied in the country. These include, for example, studies of the economic cost of injuries due to interpersonal and self-directed violence, cost-effectiveness of initiating anti-retroviral treatment using Efavirenz- and Nevirapine-based regimens, and cost-utility of the use of recombinant human erythropoietin in chemotherapy induced anemic patients. Above all, it is vital that these assessments were not merely academic

exercises, but fed into policy-decision processes. This requires a national platform to establish the importance of health technology assessment, including economic evaluation.

Finally, it is hoped that these tools and methods will be applicable to for Thailand and also adapted by other developing countries to facilitate comparisons of different studies in order to inform better policy decisions in a transparent manner. It is noted that not only producing and applying these tools, but also strengthening and sustaining institutional capacities, to generate the evidence and effective interfaces between evidence and decisions, are equally important.

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หลักการประเมินทางเศรษฐศาสตร์การจัดสรรปันส่วนอย่างสมเหตุสมผล โดยใช้ข้อมูลทางเศรษฐศาสตร์และความต้องการมาตรฐานในระเบียบวิธีการศึกษา

วิโรจน์ ตั้งเจริญเสถียร, ภิรมย์ กมลรัตนกุล

ประเทศไทยซึ่งกำลังเผชิญกับปัญหาด้านงบประมาณที่มีอยู่อย่างจำกัด ภายใต้ชุดสิทธิประโยชน์ที่รัฐกำหนดให้ประชาชนสามารถเข้าถึงโดยไม่เสียค่าใช้จ่าย ดังนั้นการจัดสรรปันส่วน หรือการกำหนดลำดับความสำคัญ จึงเป็นสิ่งที่ไม่สามารถหลีกเลี่ยงได้ เกณฑ์การพิจารณา "ความคุ้มค่า" เป็นหลักเกณฑ์ที่ได้รับความนิยมเป็นลำดับแรก ๆ ในการนำมาใช้เพื่อจัดลำดับความสำคัญ เนื่องจากเป็นหลักการพื้นฐานที่เปรียบเทียบผลลัพธ์ที่เพิ่มขึ้นกับทรัพยากรที่ใช้ไปในมาตรการนั้น การศึกษาด้านต้นทุนและผลลัพธ์ในประเทศไทยส่วนใหญ่ ยังมีอคติข้อมูลที่นำมาใช้ยังด้อยคุณภาพ วิธีการศึกษามีความหลากหลาย ซึ่งเป็นอุปสรรคต่อการเปรียบเทียบการศึกษาเหล่านั้น คู่มือเล่มนี้เป็นแนวทางการประเมินเทคโนโลยีด้านสุขภาพสำหรับประเทศไทยเล่มแรก ซึ่งได้รับการพัฒนาขึ้นโดยผู้เชี่ยวชาญจากหลายสถาบัน โดยเสนอแนะแนวทางที่เป็นไปได้ในทางปฏิบัติสำหรับการประเมินเทคโนโลยีด้านสุขภาพหลักการพื้นฐานทางเศรษฐกิจภายใต้บริบทของประเทศไทย คู่มือเล่มนี้ยังพัฒนาขึ้นด้วยกระบวนการที่โปร่งใส ผ่านการมีส่วนร่วมของผู้มีส่วนได้ส่วนเสียสำคัญ ในการจัดลำดับความสำคัญของเทคโนโลยี ท้ายที่สุดหวังว่าคู่มือเล่มนี้ จะถูกนำไปประยุกต์ใช้ในการศึกษาในอนาคตสำหรับประเทศไทย

Special Article

Making Health Technology Assessment Information Available for Decision Making: The Development of a Thai Database

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In Thailand, there is an attempt to develop the Thai HTA database in order to improve the accessibility and usefulness of HTA information. At present, the database is available online at www.db.hitap.net. The database includes 1) economic evaluation studies i.e. cost-minimization analysis, cost-effectiveness analysis, cost-benefit analysis, and cost-utility analysis, 2) outcome assessment studies i.e. randomized controlled trials, and 3) quantitative measured quality of life studies. All HTA studies related to the Thai context, and published in either Thai or English from 1990 onward, are eligible for inclusion in the database. In addition, there is a quality evaluation for each economic evaluation study which will help readers, who have limited knowledge about the method, to understand and make appropriate use of the information in their own settings. This may also raise awareness among researchers, who will conduct economic evaluation studies in the future, to adhere to the standard methodological guidelines because the quality evaluation was developed based on the national guidelines published in this supplement journal.

Keywords: *Health technology assessment, Database, Economic evaluation*

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Health technologies, including pharmaceuticals, medical devices, procedures, and health prevention and promotion, at both individual and community levels are an important part of health care systems, and form a significant proportion of health expenditure worldwide. Health technology assessment (HTA) is, therefore, considered as an important tool for assisting decision makers in appraising whether a particular health technology is effective, appropriate and efficient[1].

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There are two distinct operational cultures within a health care system that could limit the use of HTA information in decision making. On one hand, decision-makers, including policy-makers at national and hospital levels, are often working in a very tight timeframe. They rarely wait for evidence before making their decisions. On the other hand, academics seeking a research result prefer to work within longer timeframes. They like to ensure that they conduct a perfect study. HTA will have a limited impact on policy if it is not available at the right time for making decisions. For example, by the time HTA data are available or published, it is often too late to include the information in the coverage decision because the new technology has already become established. This is also an

important barrier to subsequent changes based on HTA data, because once a technology or intervention has become standard practice, restricting its use becomes much more difficult.

Two ways to improve the availability of information for decision-making are suggested here. First, it is recommended that HTA should be planned and used in a systematic manner rather than on an a*d hoc* basis. It is possible for HTA studies to be conducted and used routinely as a source of information, for example, for the pharmaceuticals listed on the Pharmaceutical Benefit Schedule in Australia[2], or they can be used with a clear and planned timeline for evaluations as is the practice by NICE in England and Wales[3]. Second, if HTA information is to be introduced for decision-making at every level, having access to reliable HTA data for competing health technology is very important. The latter recommendation is also in line with the development of HTA databases in many settings[4].

During the past decades, although there has been an increasing number of HTA studies related to the Thai setting[5], a limitation of the Thai HTA database limits the accessibility of the information and, subsequently, the use of HTA in decision-making. As a result, searching for HTA information becomes a time-consuming procedure. Many HTA studies have been published in grey literature such as theses, dissertations, conference proceedings and research reports and that makes it more difficult for the reviewers. In Thailand, there is an attempt to develop the Thai HTA database in order to improve the accessibility and usefulness of HTA information. This is a collaborative project between the Ganesh SAP Research Unit, the Silpakorn University and the Health Intervention Technology Assessment Program (HITAP) with support from the Health Systems Research Institute, the Thai Health Promotion Foundation, and the Bureau of Policy and Strategy, Ministry of Public Health.

At present, the database is available online at www.db.hitap.net. The database includes 1) economic evaluation studies *i.e.* cost-minimization analysis, cost-effectiveness analysis, cost-benefit analysis, and cost-utility analysis, 2) outcome assessment studies *i.e.* randomized controlled trials, and 3) quantitative measured quality of life studies. All HTA studies related to the Thai context, and published in either Thai or English from 1990 onward, are eligible for inclusion in the database. The database will be updated regularly. In addition, one of the most important initiatives of the database is that there is a quality evaluation for each economic evaluation study which will help readers, who have limited knowledge about the method, to understand and make appropriate use of the information in their own settings. This may also raise awareness among researchers, who will conduct economic evaluation studies in the future, to adhere to the standard methodological guidelines because the quality evaluation was developed based on the national guidelines published in this supplement journal.

Lastly, given a better HTA infrastructure *i.e.* the methodological guidelines and the HTA database, we hope that proper policy and strategies can be developed to improve the allocation and use of health technology instead of the imprecise, inconsistent and unaccountable practices of prioritization which still exist in the Thai health care system today.

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การส่งเสริมให้มีข้อมูลการประเมินเทคโนโลยีด้านสุขภาพสำหรับผู้กำหนดนโยบาย: การพัฒนาฐาน ข้อมูลสำหรับประเทศไทย

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เพื่อเพิ่มการเข้าถึงและใช้ประโยชน์จากงานวิจัยที่เกี่ยวกับการประเมินเทคโนโลยีด้านสุขภาพ คณะผู้นิพนธ์ได้พัฒนาฐานข้อมูลสำหรับประเทศไทย ซึ่งปัจจุบันสามารถสืบค้นได้จาก www.db.hitap.net โดยฐานข้อมูลดังกล่าวประกอบด้วย 1) งานวิจัยด้านการประเมินความคุ้มค่าทางการแพทย์ ทุกวิธีการวิเคราะห์ ได้แก่ ต้นทุนต่ำสุด ต้นทุนประสิทธิผล ต้นทุนผลได้ และต้นทุนอรรถประโยชน์ 2) งานวิจัยด้านการประเมินผลลัพธ์ เช่น การทดลองแบบสุ่มที่มีกลุ่มเปรียบเทียบ 3) งานวิจัยด้านการวัดคุณภาพชีวิต ทั้งนี้ฐานข้อมูลดังกล่าว รวบรวมงานวิจัยการประเมินเทคโนโลยีด้านสุขภาพ ในบริบทของประเทศไทย ที่ตีพิมพ์ทั้งภาษาไทยและภาษาอังกฤษ ตั้งแต่ปี พ.ศ. 2533 เป็นต้นมา นอกจากนี้ยังมีการประเมินคุณภาพงานวิจัย ซึ่งช่วยให้ผู้อ่านที่มีความรู้จำกัด เกี่ยวกับระเบียบวิธีวิจัย สามารถเข้าใจและนำข้อมูลจากงานวิจัยไปประยุกต์ใช้อย่างเหมาะสมต่อไป และอาจกระตุ้นให้นักวิจัยที่จะทำงานวิจัยด้านการประเมินความคุ้มค่าทางการแพทย์ยึดถือเป็นมาตรฐาน ตามคำแนะนำในคู่มือการประเมินเทคโนโลยีด้านสุขภาพสำหรับประเทศไทย

Special Article

Thai Health Technology Assessment Guideline Development

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Health Technology Assessment (HTA) is a comprehensive form of policy research that provides information on the consequences of the application of health technology. It is used primarily to guide health care resource allocation decisions. In Thailand, there is increasing impetus to use HTA information to allow more explicit and transparent health care priority setting. A previous study indicated that serious attention needed to be given to the quality of reporting and the use of information in the analyses. These problems could be reduced by setting up standard guidelines for conducting HTA to stimulate the provision of standardized, reliable and good quality information for policy makers. Nevertheless, Thailand has not yet set up such guidelines. This may lead to low quality evaluations. Therefore, the objective of this article was to describe the rationale for guideline development, supporting principles, guideline development process, sources of information, and future challenges for HTA.

Keywords: *Health technology assessment, Rationale, Guideline development*

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"In this world nothing can be said to be certain, except death and taxes

……..and scarcity of resources"

Alan Maynard adding on the famous Benjamin Franklin statement; our certain fate: rationing in health care (1998)

Rationales for guideline development

There are insufficient resources to provide all patients in all circumstances with the best possible healthcare. The growing health needs of an aging population and acceleration in technological development in the area of health is producing an ever-increasing demand on limited health resources. This is particularly crucial in developing country settings where resources are very limited. Health Technology Assessment (HTA) is a comprehensive form of policy research that provides information on the consequences of the application of health technology. It is used primarily to guide health care resource allocation decisions[1,2].

In Thailand, there is increasing impetus to use HTA information to allow more explicit and transparent health care priority setting. However, the systematic review of literature relating to Thailand conducted by Teerawattananon et al[3] revealed a number of methodological flaws with prior HTA publications. The review highlighted that serious attention needed to be given to the quality of reporting and the use of information in the analyses. In addition, it demonstrated a large variation in methods used which made it very difficult to compare results between studies. These problems could be tackled and reduced by setting up standard guidelines for conducting HTA. Thailand, however, has not yet set up such guidelines and this may lead to low quality evaluations. If HTA information is useful for making health care technology policy only when performed correctly and reported accurately, these findings clearly depict information barriers that would diminish the use of HTA information when used to assist in health decision-making processes.

The lack of a uniform methodology in conducting HTA can be seen as a major weakness that

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diminishes its ability to assist in the health decision-making process[4-10]. Methodological guidelines are, therefore, a way to stimulate the provision of standardized, reliable and good quality information for the target audiences[11-15]. These guidelines will increase the transparency of studies by allowing readers or users to assess precisely what the analysts have done and whether the method was appropriate. These guidelines will also help to ensure standards that enable comparisons across health care interventions because the difference in, for example, a cost-effectiveness ratio is likely to reflect true differences between the interventions being evaluated rather than differences in study methodologies.

The development of these guidelines reflects the need of the Thai setting to have its own HTA guidelines rather than using existing international and/or peer review journals' guidelines. There is especially true since the different settings have different limitations on resources and capacities. Also, different countries, governments and HTA agencies may decide to apply different fundamental principles to decisions, such as whether to place a greater value on efficiency or equity dimensions, whether and how to value health care costs etc.

It was decided in the first place that Thai HTA guidelines will pay special attention to the methodologies for conducting health economic evaluation (i.e., an approach used to analyze the costs and benefits of different health care interventions) because it is a relatively new discipline in Thailand and a large variation in the method used was observed. Furthermore, the current policy dialogues stress the need for institutional capacity strengthening to provide economic evaluation evidences to guide decisions on drug registrations by the Thai Food and Drug Administration, and the adoption of drugs into the National Essential Drug List. Thus, ensuring good quality economic evaluations and a standardization of the study framework are the main objectives of the guidelines, while the issues of feasibility, affordability and ethics (including equity) will be overviewed at the end of this guideline.

The principles supporting the development of the guideline

There were some prior requirements of these methodological guidelines. These requirements were driven by the desire to improve the quality and use of HTA studies in decision making on the diffusion of health technologies in Thailand. Firstly, the guidelines should address all major methodological aspects that the authors might face when conducting economic evaluation to minimize the risk of using unjustified or biased information. The guidelines should be clearly stated and allow readers to validate their study design and conduct using their recommendations. In addition, the guidelines should be well equipped for future adjustments that incorporate new academic findings and consensus, and to accommodate changes in the decision making context, whenever the guidelines are involved in the decision-making process.

Secondly, the guidelines should support the study to meet the need for informing the decision process for the allocation of health care resources, and achieve the necessary standard of economic evaluation study. The guidelines should address the main concerns of decision makers and recommend practical approaches to arrive at those outcomes. Lastly, the guidelines should facilitate the use of local information with recognition of the limitations of resources and information that are specific to the health care system in Thailand.

Table 1. Sources of information

Type of information	Sources	Reference
Formal guidelines	Australia (Common Wealth Department 1995)	21
	Canada (1997)	22
	Denmark (2001)	23
	Norway (2002)	24
	Hungary (2002)	25
	England & Wales (2004)	26
Informal guidelines	Gold et al (1996)	27
	Drummond et al (1997)	28
	Tan-Torres et al (2003)	29

The guideline development process and sources of information

At the end of 2006, the Health Intervention and Technology Assessment Program (HITAP) consulted experts from both academic and research institutions across the country to make a concrete plan for the development of the first methodological guideline for conducting health economic evaluation in Thailand. The development of this guideline began with a review of existing guidelines (Table 1) including those developed by governments and standard health economic evaluation textbooks in order to determine the similarities, differences, strengths and weaknesses of each major component. The inclusion criteria for selection of the guidelines to be evaluated were based on a subjective view of the authors on the methodological basis of the guidelines themselves and also the availability of the guidelines through library and electronic sources.

Recently, a number of previously developed guidelines have been produced in different formats. Many countries, such as Australia, Canada, Denmark, Norway, Hungary, England and Wales, have developed economic evaluation guidelines with different details but similar objectives. That is to provide a uniform methodology approach to improve the quality and standardization of health economic evaluation studies. Although many existing guidelines from other countries are available, there is still a limitation if those guidelines are applied to developing countries such as Thailand due to the limitations on resources and capacity when compared to developed countries[16-20].

Previously, a number of guidelines with different formats were proposed by the Panel on Cost-Effectiveness[30] and NICE guidelines[26]. A "reference case" was proposed which contains a standard set of methodological practices that researchers are advised to follow in the field of economic evaluation study. On the other hand, some guidelines[28,31] present a "critical appraisal checklist" which generally comprises relevant questions about an economic evaluation to identify and assess the strengths and weaknesses of individual studies. Guidelines developed in Australia[21] and Hungary[25] offered neither a reference case nor a standard checklist but a range of methodological options to be considered for applying in evaluations. This guideline chooses to use a reference case approach similar to that used in both the US and the UK since it intends to provide detail on the design and conduct for economic evaluations.

The scope and major components of Thai HTA guideline were defined as follows. The detailed contents of the guideline were focused on the term "economic evaluation", which refers to a study that considers both the comparative costs associated with the provision of health care interventions, and the comparative clinical effects, measured either in clinical units, health preferences, or monetary benefit[28].

The experts reviewed each of the key components specified by the team, and drafted the guidelines. During the second half of year 2007, a series of consultation meetings were carried out to present the draft to various stakeholders including experts from participating ministries i.e. the Ministry of Public Health, the National Health Security Office, the Social Security Office, the Thai Health Foundation, the Ministry of Finance, academic institutions and health care providers as well as representatives from various pharmaceutical companies. Suggestions from stakeholders were also included before the final publication.

The key elements include the following components:

1.	Defining the scope of the study
2.	Selection of comparator(s)
3.	Defining the type of economic evaluation
4.	Measurement of costs
5.	Measurement of clinical effects
6.	Measurement of utility
7.	Handling time in the economic evaluation studies
8.	Handling uncertainty and sensitivity analysis
9.	Presentation of data and results
10.	Health system and equity perspectives in HTA
11.	Policy making and roles of HTA

The future challenges

Although the guidelines offer some practical guidance to improve the quality of HTA studies in Thailand, it remains to be seen whether HTA will become a useful tool for decision making regarding health care resources. On the one hand, the guidelines address all major methodological issues that might arise when conducting HTA and provide the opportunity to recognize a lack of experience and a lack of information along with other characteristics that are specific to Thai health care settings. On the other hand, other problems include a lack of understanding among potential users and social, political and institutional barriers that might inhibit the use of HTA information are still not overcome. For example, decision makers may lack the confidence to make decisions that are politically indefensible;

therefore it is essential that the public understand and accept the use of HTA information.

In the present situation, HTA in Thailand is at the beginning phase and has not yet been widely applied in policy decisions. The guideline encourages the transparent selection of methods and evidence used in HTA studies. Although Thai HTA guideline cannot guarantee the use of HTA information in decision-making, using HTA evidence in policy will be easier if high quality and locally applicable data are readily available.

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การพัฒนาคู่มือการประเมินเทคโนโลยีด้านสุขภาพสำหรับประเทศไทย

ยศ ตีระวัฒนานนท์, อุษา ฉายเกล็ดแก้ว

การประเมินเทคโนโลยีด้านสุขภาพเป็นการวิจัยเชิงนโยบายอย่างเต็มรูปแบบเพื่อให้ข้อมูลผลลัพธ์ของการประยุกต์ใช้เทคโนโลยีด้านสุขภาพ และนำมาใช้เป็นข้อมูลหลักเพื่อช่วยในการตัดสินใจด้านการจัดสรรปันส่วนทรัพยากรทางสุขภาพ ในประเทศไทยมีการขับเคลื่อนการใช้ข้อมูลการประเมินเทคโนโลยีด้านสุขภาพเพิ่มมากขึ้น โดยนำมาใช้จัดลำดับความสำคัญของมาตรการการดูแลสุขภาพให้มีความโปร่งใสและชัดเจนมากขึ้น การศึกษาที่ผ่านมาพบว่า จำเป็นต้องให้ความสนใจอย่างมากต่อคุณภาพของการรายงานผลลัพธ์และการใช้ข้อมูลสำหรับการวิเคราะห์ ปัญหานี้ลดลงได้โดยการกำหนดแนวทางการประเมินเทคโนโลยีด้านสุขภาพที่เป็นมาตรฐานเพื่อกระตุ้นให้ผลิตข้อมูลที่เป็นมาตรฐาน น่าเชื่อถือ และมีคุณภาพดีสำหรับผู้วางแผนนโยบาย อย่างไรก็ตามประเทศไทยยังไม่เคยมีการกำหนดแนวทางการประเมินเทคโนโลยีด้านสุขภาพซึ่งนำไปสู่การประเมินที่ด้อยคุณภาพ ดังนั้นจุดประสงค์ของบทความนี้คือ เพื่อบรรยายความสำคัญของการพัฒนาแนวทางการประเมินเทคโนโลยีด้านสุขภาพ หลักการที่สนับสนุน กระบวนการในการพัฒนา แหล่งข้อมูล และสิ่งที่ท้าทายในอนาคตสำหรับแนวทางการประเมินเทคโนโลยีด้านสุขภาพ

Special Article

Defining the Scope of Economic Evaluation Study and Selection of Comparators

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One of the most important steps in conducting economic evaluation studies is to have a clearly defined research question and scope of study. The present study describes key components used in defining the scope of economic evaluation study and selecting comparators. All relevant recommendations from international economic evaluation guidelines were reviewed and compared. The author recommends that an economic evaluation study should include a full description of the intervention or program of interest and target populations. The comparator should be the most commonly used alternative or current practice. In some circumstances, the most effective alternative can be a comparator. The most preferable perspective is societal perspective; however, other perspectives are acceptable if justification is provided. Researchers in the field of economic evaluation need to clearly define the scope of study prior to the conduct.

Keywords: *Economic evaluation, Scope, Perspective, Comparator*

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The purpose of health care economic evaluation study is to determine the values of an intervention of interest, compared to the existing medical technology used for a medical condition. One of the most important steps in conducting health care economic evaluation studies is to clearly define research questions and the scope of study. The present study aims to describe components necessary to be defined for the scope of economic evaluation study and the selection of comparators. Relevant recommendations from international economic evaluation guidelines are reviewed and compared. Lastly, recommendations on how to define research questions and the scope of the study and to select the comparators are made for Thai health technology assessment (HTA) guideline.

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Rationale for cost-effectiveness analysis

It is important that the rationale of study should be clearly presented. It should contain description about disease and its epidemiology so that the readers can understand its importance and the burden of disease. If considered relevant, the description should cover etiology, pathology, and prognosis of disease. Authors should describe current clinical practice in the country. Statement of current problems is also very crucial. Authors should describe how this research can be used in the country and the options for treatment or controlling the problem in the country. Before stating the research question, the study should have a rationale for specification of problem. It should provide the readers with reasons why the study is needed. Will they be of interest to policy makers? It needs to tell the readers that policy makers are interested in knowing this as part of their decision making process.

This section provides a concise description of the issue(s) being addressed within the report and

sets the scene for readers. It includes the reasons why the analysis is being carried out, a brief description of the disease and patient groups affected and any funding/cost implications involved, including issues with competitive technologies. It should lay out how a conduct of economic evaluation studies would help policy makers understand the situation and be able to be well-informed with current evidence before making a final decision.

Defining a research question framework

A research question should be well-defined as the first step in conducting economic evaluation studies. Researchers should define the intervention or program, the target population, the comparator(s) being compared, and viewpoint(s) undertaken in the analysis. These components were described as the first question in Drummond's checklist for assessing economic evaluation[1]. All economic evaluation studies need to have a well-defined question posed in an answerable form.

Clear description of intervention or program and target population

A program or intervention of interest must be well described. It should be detailed enough that the reader is able to understand the characteristics of the intervention including "what to do", "how often?", and "for how long?". In addition, it should be clearly stated to whom the program is used for. Therefore, describing the target population is not less important than other components in defining research questions. Target populations may be defined using baseline epidemiologic characteristics describing the type of patient (e.g. age, gender, socio-economic status), with a specific disease, of a certain severity, with or without other co-morbidities or risk factors, their geographic distribution, usual compliance rates, typical patterns of treatment, and so on[2]. Having known the characteristics of population enables readers to identify a particular target population and apply the results of the study appropriately. One example is when an intervention is intended to be used for type 2 diabetic patients who are uncontrolled by an oral hypoglycemic agent and have experienced hypoglycemic episodes while using insulin therapy. This example is used to show the level of specification required for defining population as it would help the users to apply the results to the right population. As an intervention or program may be cost-effective for some subgroups of patients, it is important to clearly identify the populations under the study a priority and, when appropriate, to undertake separate analyses for different groups.

Based on 28 pharmacoeconomic guidelines from 23 countries systematically reviewed by Tarn et al[3], none of the existing guidelines mentioned the importance of a detailed description of intervention. This may be due to the fact that this requirement is so crucial that all researchers should be aware of this already. On the other hand, a clear specification of target population was required in most guidelines (23/28, 82%)[3]. Nine guidelines had specific recommendations for target population; four guidelines stated that population must be clearly specified; two guidelines recommended a need for description of age, sex distribution and co-morbidities of population; one guideline requested a justification of trial population and target population; one guideline specified that population should be determined by a precise indication of the medical technology; another guideline specified that all aspects of a therapy intervention should be described. The remaining guidelines (5/28,18%) did not mention target population.

Selection of comparators

Determining a comparator, to which an intervention is compared, is a very crucial and challenging step in conducting an economic evaluation study. It is so important that Drummond's checklist for assessing economic evaluation has included a question specifically inquiring about the comparator[1]. The question was whether a comprehensive description of the competing alternatives was given. A full description of the comparator is necessary because it enhances the readers' capability in determining applicability of the program, evaluating whether any costs or outcomes have been omitted, and replicating the program as described[4].

In economic evaluation, an intervention should be compared to the comparator (s) which is most likely to be replaced by the intervention in real practice[5]. Such comparator (s) could be current practice, most effective clinical practice, or minimum clinical practice. Typically, current practice or the most prevalent medical treatment is recommended as the comparator because it is consistent with the idea of comparing the intervention with the one to be replaced. Current practice can mean only the most used practice or a combination of all practices, taking into account their share in overall treatment practice. Another potential comparator is the most effective clinical practice. The "current practice" comparator may not

always reflect the appropriate care that is recommended according to evidence-based medicine. The "most effective clinical practice" comparator is therefore considered to be a feasible and relevant option. This comparator can be determined based on recommendations from evidenced-based clinical practice guidelines or current evidence demonstrating its efficacy and safety. The other option is the "minimum clinical practice" which means a practice which has the lowest cost and is more effective than a placebo. In some circumstances, "no treatment" can be an acceptable comparator if it is the only relevant alternative available to patients. This "no treatment" means any treatment without direct medical treatment. It could be symptomatic treatment as well as other types of care. It must be noted that the costs of this "no treatment" must also be calculated. Most guidelines (15/28, 53.6%) stated that the comparator should be the most widely used alternative. Eleven guidelines recommended standard therapy or the most effective option as a comparator. A total of five guidelines (Germany, Poland, Russia, NICE[6] (National Institute of Clinical Excellency) UK and PBAC Australia[7]) suggested that the comparator could be either the commonly used alternative or the most effective alternative. Only four guidelines specified that the comparator should be either "less expensive" or "the least expensive" alternatives.

Several guidelines vaguely described the characteristics of comparators. For example, the comparator should be the closest existing comparator or the most efficient option. American Managed Care Pharmacy (AMCP)[8] has specified that the comparator should be a relevant one but provided little information on the extent of relevance. Three guidelines (Finland, Scotland and Hungary) required the comparator to be the "to be replaced" one. The BMJ guideline[9] recommended that the most cost-effective option should be the comparator. Some guidelines (Norway, Poland, Russia, Spain, Switzerland, Belgium submission and Gold for the US[10]) indicated that a do-nothing alternative could be a viable comparator.

The most important component for the selection of comparators is a justification of the comparator. A full description of rationale for selection of the comparator(s) is crucial for the readers to understand the context of the question and be able to evaluate the appropriateness of the choice of comparator.

Perspective

The perspective of the study should be clearly identified. The most commonly used perspective or viewpoint should be the most comprehensive societal perspective. This perspective incorporates both direct and indirect costs. The societal perspective is the broadest viewpoint since it encompasses all costs and benefits regardless of who incurs the costs or gains the benefits.

Other relevant perspectives include the health care system, major third party payers such as Ministry of Public Health, health care purchasers, hospital and patient perspective. It should be noted that these perspectives are used when the target audience differs. For example, the government might be interested in all costs and benefits incurred only in the governmental sector. For hospital perspective, the hospital directors will be interested in costs and benefits incurred only in patients seeking care at their hospitals. Regardless of the perspective undertaken, it should obviously be consistent regarding both cost and outcome components.

It is recommended that if the societal perspective is undertaken, the data should be transparently disaggregated. This effort should be made to make it possible for the readers to determine the direct medical costs attributed to certain sectors. For example, a separate analysis from the government perspective can be presented apart from the primary societal perspective. A clearly defined perspective helps researchers determine the types of costs that should be included in the analysis. The perspectives taken in the study should be specified to suit decision makers or users of the research findings.

Based on a review of pharmacoeconomic guidelines, the majority of guidelines (9 guidelines) recommended using only societal perspective while most of the remaining guidelines suggested that more than one perspective should be used[3]. For the group of guidelines that recommended the use of only societal perspective, six guidelines (Finland, Germany, the Netherlands, Sweden, and Gold et al guideline[10] for the US, BMJ guideline[9]) merely stated that societal perspective should be chosen. The other three guidelines (Canada, Poland, and Portugal) provided more specifications in addition to using a societal perspective, where the results should be transparently broken down into other relevant viewpoints.

Eight guidelines suggested using either the health care system or health care payer perspective in combination with the societal perspective. Three guidelines (Baltic, Ireland and Australia) specified "health care system", while the other four guidelines (Belgium, Italy, Norway and NICE[6] for the UK) used

various terms. All, however, represented the same meaning of "national health care payer". The remaining guideline (American Managed Care Pharmacy: AMCP[8] for the US) specified "payer" perspective because the guideline was developed as a guideline for private insurance systems. It is important to note that two guidelines (NICE[6] from the UK and AMCP[8] from the US) ranked the importance of perspectives taken. Both guidelines specified the "health care payer perspective" as a reference case and "societal perspective" as a secondary one.

A few guidelines (Russia, Scotland and Switzerland) recommended the use of various perspectives including societal, health care system, patient and employer. The remaining three guidelines (France, Hungary and Spain) suggested that the perspective taken depended on research question, aims of the study, and the audience to whom the analysis is addressed.

Recommendations for Thai HTA guideline

Based on a review of international pharmacoeconomic guidelines, the recommendations for the scope of the study varied because of several potential reasons. First, some guidelines are developed to guide submissions of pharmacoeconomic studies for a national institute, while others are developed for private insurance companies. Second, the guidelines were developed with different time lines ranging from 1995 to 2004. Advances in the field of health care economic evaluation were made during this period. This may explain some of the disagreements in the recommendations.

Several recommendations can be made for Thai HTA guideline. Below is the summary of the recommendations:

1. It is recommended that the target population and the intervention or program of interest should be clearly described. The description should be detailed enough that the readers fully understand how the intervention or program is used and are capable of imitating the same intervention or program.

2. The recommended primary perspective is societal perspective because it takes into account all relevant consequences at a broader scope which provides insight information for the decision makers when the overall effects, outside the health system context, are taken into consideration. If other perspectives are undertaken, justification is needed.

3. The comparator should be the one to be replaced. The characteristics of the alternative should be that of the most commonly used therapy or current practice. Selection of the comparator depends on the research question. If the aim of the study is to replace the most commonly used intervention with the intervention of interest, the comparator should be the most widely used one. On the other hand, if the aim of the study is to replace the standard therapy, the comparator should be the most effective alternative. In some circumstances where do-nothing is the current practice or standard of care, no treatment can be a viable alternative.

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การกำหนดขอบเขตการประเมินทางความคุ้มค่าทางการแพทย์

ณธร ชัยญาคุณาพฤกษ์

ขั้นตอนที่สำคัญที่สุดขั้นตอนหนึ่งในการประเมินความคุ้มค่าทางการแพทย์คือการกำหนดคำถามงานวิจัยและขอบเขตการศึกษาให้ชัดเจน บทความนี้เขียนขึ้นมาเพื่อบรรยายส่วนประกอบสำคัญต่าง ๆ ที่ใช้ในการกำหนดขอบเขตการศึกษา ผู้เขียนได้ทบทวนและเปรียบเทียบข้อเสนอแนะต่าง ๆ ที่ได้จากแนวทางการประเมินความคุ้มค่าทางการแพทย์จากต่างประเทศ และสรุปเป็นข้อเสนอแนะในการกำหนดคำถาม ขอบเขต และการคัดเลือกตัวเปรียบเทียบในการประเมินความคุ้มค่าทางการแพทย์สำหรับประเทศไทย ผู้เขียนเสนอแนะให้มีการอธิบายเกี่ยวกับมาตรการหรือโปรแกรม และประชากรเป้าหมายโดยสมบูรณ์ ตัวเปรียบเทียบควรจะเป็นการรักษา ที่ปฏิบัติกันในปัจจุบัน แต่ในบางกรณีอาจใช้ตัวเปรียบเทียบที่ได้รับการยอมรับว่ามีประสิทธิผลสูงสุดในขณะนี้ มุมมองของการศึกษาควรจะเป็นมุมมองทางสังคม แต่หากจะใช้มุมมองอื่น ควรมีคำอธิบายระบุเหตุผลการเลือกใช้มุมมองนั้น นักวิจัยในสาขาการประเมินความคุ้มค่าทางการแพทย์มีความจำเป็นต้องกำหนดขอบเขตการศึกษาให้ชัดเจนก่อนเริ่มทำการศึกษา

Special Article

Defining Types of Economic Evaluation

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Objective: *Recommend types of economic evaluation for Thai health technology assessment (HTA) guideline.*
Material and method: *Various types of economic evaluation, including their definitions and background theories from research documentations were explored. In addition, the international economic evaluation guidelines were reviewed. Finally, the recommendations for Thai HTA guideline were made.*
Result: *There are generally four types of economic evaluation: Cost-Benefit Analysis (CBA), Cost-Minimization Analysis (CMA), Cost-Effectiveness Analysis (CEA), and Cost-Utility Analysis (CUA). Theories of welfare and extra-welfare economics were used to explain each type of economic evaluation. From the international guidelines, each country's guideline has its own preferred types of economic evaluation. CEA and CUA were more likely to be recommended in those guidelines.*
Conclusion: *For Thai HTA guideline, CUA was recommended to be a method of choice. However, CEA could be used, especially when only intermediate outcomes of compared alternatives are available.*

Keywords: *Type, Economic evaluation, Method*

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Economic evaluation is defined as a comparative analysis of alternatives in terms of both their costs and outcomes. Drummond et al. divided the economic evaluation into six categories[1]. First, if only outcomes of the service or program are examined, the evaluation is called an "outcome description". Similarly, if only costs of the service or program are estimated, it is called a "cost description" In Thailand, the cost description method was the form of primary economic evaluation in the last decade because it is simple and believed to be a foundation for further economic analysis. Both costs and outcomes can also be described in a study and is called a "cost-outcome description". These categories of economic evaluation have no comparison of any alternative.

When two or more alternatives are compared, three categories of economic evaluation are identified. First, if only outcomes are examined and compared between alternatives, the evaluation is called either an "efficacy study" or an "effectiveness study". On the other hand, when costs are compared between alternatives, the evaluation is called a "cost analysis". The last category is called a "full economic evaluation" since it not only compares two or more alternatives, but also examines both costs and outcomes. Therefore, the full economic evaluation provides efficiency information and is appropriate for policy making. The objective of this review is to define the types of full economic evaluation. Their brief theoretical backgrounds are discussed. International economic evaluation guidelines are then reviewed. The adoption of types of economic evaluation is compared across the guidelines. Finally, the recommendations for Thai health technology assessment (HTA) guideline are made.

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Types of full economic evaluation and their definitions

The full economic evaluation has two major components-costs and outcomes of compared alternatives. The cost component is always measured in monetary unit, while the outcome component can be measured in various ways. Based on different outcome measurements, the full economic evaluation is divided into four types of analysis. They are Cost-Benefit Analysis (CBA), Cost-Minimization Analysis (CMA), Cost-Effectiveness Analysis (CEA), and Cost-Utility Analysis (CUA).

CBA measures both costs and outcomes of compared alternatives in monetary units. This means that no matter how outcomes are originally measured, they need to be converted to monetary units for comparison. Theoretically, CBA provides absolute benefit of alternatives. It estimates the value of output, compared to the value of the resource input. It, therefore, can be used in a comparative analysis of alternatives which have different objectives. For instance, CBA is applicable if one compares a new statin drug with a bird flu vaccine. However, very few cost-benefit studies are found in health care because it is counterintuitive to express health outcomes in monetary units.

When the common outcomes of compared alternatives are equivalent or assumed to be equivalent, CMA is the analysis of choice. It identifies the lowest cost alternative. For instance, suppose that a new proton-pump inhibitor is proved to be clinically equivalent to an existing proton-pump inhibitor. CMA determines which one has the cheapest costs. Recently, Drummond et al. did not view CMA as a form of full economic evaluation[1]. Since the estimations of costs and outcomes are uncertain, it is difficult to have equivalent outcomes unless the alternatives are almost identical. Briggs and O'Brien pronounced the death of CMA, since circumstances under which CMA is an appropriate economic method of analysis are rare. It is unlikely that a study is specifically designed to show the equivalence of treatments in terms of costs or effects. Therefore, CMA on the basis of an observed lack of significance in either the effect or cost differences between alternatives should not be used[2].

Generally, very few compared alternatives in health care are clinically equivalent, if they are, or it is difficult to prove. CEA allows the comparative analysis of alternatives with differential degree of success of common outcomes. For instance, two antihypertensive drugs are compared and they have differential degrees of decreasing blood pressure. Basically, CEA by definition requires a single, common natural outcome e.g. cure rate, mmHg, etc. However, it is possible to use CEA to compare any alternatives which do not have legitimate common natural outcomes but share some kinds of common effect e.g. life-years saved, case treated, etc.

Lastly, the outcomes can be measured in utility terms. This type of economic evaluation is CUA. The utility reflects one's preference of the outcomes. Quality of life is an example of adjustment used in CUA. Therefore, CUA provides more complete information because both the quantity and quality of the outcomes are accounted for. Basically, CUA can be viewed as the extended analysis of CEA after or while the outcomes in CEA are being quantified; these outcomes are then adjusted by quality for CUA. For instance, each life-year gained from using a cancer treatment is adjusted by the utility value of health states. Therefore, the outcome is reported as quality-adjusted life-years (QALYs), which is one of the generic outcome measures for CUA.

Each type of economic evaluation has its own characteristics, with different outcome measurements. These measurements have different theoretical supports, which are discussed in the next section. However, CMA is not included in the discussion because it is not considered as a full economic evaluation[1].

Economic evaluation in theory

The theory of economic evaluation has been debated[3]. Traditionally, economic evaluation is based on welfare economics. The welfarist approach focuses on how individuals value the outcomes because they are assumed to know most of their own welfare. While some economists prefer to be strict when dealing with traditional welfare economics, some adopt a more pragmatic decision maker's approach. The decision maker adherents view economic evaluation as maximizing health effects from a given budget. They believe that the health effect should be measured in natural units or health state preference scores. Sometimes their view of willingness-to-pay is biased, however.

Welfare economic approach

In welfare economics, which support the CBA concept, efficiency is referred to as *Pareto efficiency*. *Pareto efficiency* is defined as an allocation of resources, with no alternative allocation, that can make at least one person better off without making anyone else worse off. As long as another alternative allocation exists, and it makes at least one person better off without making anyone else worse off, the allocation is inefficient. A simple decision rule for CBA is that if an alternative has positive benefits, it is possible to make at least one person better off without making anyone else worse off. For instance, a new anticancer treatment is considered for use among three patients. They are asked about their willingness-to-pay (WTP) for the treatment. The first person is willing to pay A baht for the treatment while the second person would like to pay B baht. The third person has a different perspective on the treatment. He has negative willingness-to-pay for the same treatment in the amount of -C baht.

Assuming there is no opportunity cost for the treatment, the summation of the willing-ness-to-pay is calculated to reflect the net benefits. If the treatment is chosen without any other arrangements, the resource allocation to the treatment is not *Pareto efficient* because the third person is worse off from the allocation. However, if the amount of net benefit (A+B-C) is more than zero or positive, it can be adjusted to reach the *Pareto efficiency*. For instance, some benefits of the first and second persons can be transferred to the third person and the arrangement leaves no one worse off. To be more specific, CBA adopts a decision rule based on the Kaldor-Hicks criterion, which states that an alternative should be chosen if and only if those who will gain could fully compensate those who will lose and still be better off. This criterion supports the potential *Pareto efficiency* rule (net benefits criterion) suggesting that only alternatives that have positive net benefits should be adopted. Then, only when compensation occurs, the actual *Pareto efficiency* rule is warranted.

Similarly, the objective of CEA involves *Pareto efficiency*[4]. For instance, a given budget is used to improve either survival probabilities (SP) or mobility status (MS) for a group of individuals. Theoretically, CEA aims to ensure that the improvement of MS is maximized for a fixed improvement in SP. This means there is an attempt to allocate resources in a way that implies technical efficiency because an increase in total benefits from the same amount of resources is found. However, the application of CEA is usually used to make a comparison between an existing alternative and a new alternative which have neither costs nor outcomes constant. The evaluation then considers both incremental benefits and incremental costs. It is noteworthy that when a new alternative costs more than an existing alternative, the decision maker's rule of CEA assumes that the additional resources for the new alternative will be from other alternatives which have a rate of return to the resources at a margin lower than the existing alternative has. In other words, the existing alternative reflects an opportunity cost for the overall resource for the new alternative. Therefore, if the new alternative is evaluated, the benefits from the new alternative should be compared with the benefits from giving up the existing alternative and other alternatives. However, Birch and Gafni conclude that the current applications of CEA often do not comply with welfare economics theory and therefore are not useful for maximizing the total aggregate health benefits at a given budget[4]. If we consider an existing alternative and a new alternative, which have neither costs nor outcomes constant, trading the existing alternative for the new alternative does not obviously show an increase in technical efficiency. Only after value judgments of the benefits and loss are conducted, CEA can show whether the existing alternative or new alternative is preferable.

Garber and Phelps' paper is another recent work that embeds CEA in welfare economics[5]. One of their suggestions is that individual optimality exists when the wage rate is equal to the willingness to pay for an additional unit of time. Brouwer and Koopmanschap clarify this statement as a gap between real-life valuation of effects in society decision making and how the welfare economics has been suggested in CEA[2]. Since it ties productive possibilities with additional life-years, the WTP for persons who are less productive is low. If these persons are people who really need help, such as the handicapped, embedding CEA in welfare economics seems to be unethical from a societal perspective. In other words, societal utility is not explicit in this perspective. Therefore, the value judgment in CEA based on welfare economics becomes an equity concern for health care decision makers when allocating the resources. When the issue of equity plays a role in the decision model, various rules are violated, e.g. classical utilitarianism indicating social welfare equal to the sum of individual utilities, potential Pareto-criterion, etc.

Extra-welfare approach

CEA can identify only technical efficiency because it cannot compare the benefits across alternatives with different objectives. To identify allocative efficiency, utility-based measures of outcomes are required. CUA can offer both technical efficiency and allocative efficiency because it has utility-based measures of outcomes. In other words, CUA, in theory, complies with welfare economics and provides efficiency in production and product mix, reflecting technical efficiency and allocative efficiency, respectively. However, several economists consider the use of QALYs as utility measurements as not being appropriate because the individuals determine their own preferences and the underlying amount of absolute utility does not exist for comparing or aggregating QALYs across the individuals[3]. For instance, Bleichrodt indicates that the possibility of utility aggregation among individuals is questionable[6]. Based on Von Neumann and Morgenstern's theory of expected utility, utility itself can be exchanged and compared. The welfarists view QALYs as utility measures. They are tempted to

extrapolate the possibility of interpersonal comparison of utility to QALYs. However, a monetary notion of utility is needed to facilitate exchanges and comparisons and QALYs do not have this notion. Therefore, QALYs and CUA may not embed well in welfare economic theory.

Extra-welfare economics was proposed to explain both CEA and CUA in theory[3]. Extra-welfarism does not simply include individual utilities in the analysis. It replaces utility with health as the primary outcome for economic evaluation. The objective of extra-welfarism is therefore to maximize health from a given budget, which is consistent with the general objective of health care budget as same as the decision maker approach. Also, health outcomes (or QALYs) are viewed more as capabilities and less as utilities, from having good health. Scientists assign an equal value to the capabilities and then a comparison of values given by different persons at different health states can be made. The health outcomes or health as capabilities are then maximized, which is an ultimate goal of health care or health care budgets. When the focus is on health instead of utility, the question concerning equity among those people who need special health, e.g. the handicapped, is solved. Even though they are not productive, they are still alive, and entitled to minimize their health problems. The extra-welfarist also counts on non-health implications related to health, e.g. age. It therefore corrected the equity consideration in the non-health aspect as well. In doing so, it indirectly maximizes their utilities. In conclusion, the extra-welfarism approach tends to inform the decision makers. It is, however, not likely a prescription for making decisions, e.g. providing rank of alternatives. It not only implicitly notifies the maximization of a social welfare function, which is similar to traditional welfare economics, but also allows possible violations of the Pareto-criterion, e.g. the issue of individual utility comparison.

Comparisons of the international economic evaluation guidelines

Among economic evaluation in health care, several countries focus greatly on the evaluation of pharmaceuticals. Many countries have developed national economic evaluation guidelines which are worth exploring before Thai HTA guideline is recommended.

A total of 28 pharmacoeconomic guidelines across 22 countries were reviewed by Tarn and Smith[7]. A comparison of the key features, such as main policy objectives, preferred analytical techniques, target population, subgroup analysis, time horizon, modeling, sensitivity analysis, and discounting outcomes, etc., of the guidelines is provided. The preferred analytical techniques in the reviewed guidelines are composed of all types of economic evaluation, including CMA, CBA, CEA, and CUA. Among the 22 countries, a total of 12, 19, 20, and 11 countries included CMA, CEA, CUA, and CBA, respectively, in their guidelines. CEA and CUA are the most frequently used in the economic evaluation of pharmaceuticals. One reason could be that most pharmaceutical outcomes, similar to other health outcomes, are ready to be used in CEA and CUA. Another reason, as previously provided, is that CBA requires the analysts to monetize the outcomes, which is counterintuitive from a health care perspective.

From the review, all guidelines can be divided into four major groups: 1) guidelines that allow all four types of analysis with justifications, such as the guidelines of Australia, Belgium, Finland, France, Germany, Ireland, Norway, Portugal, Russia, Scotland, and Switzerland. 2) guidelines that recommend CEA and CUA, from countries such as Italy, Netherlands, Poland, Spain, Sweden, and England & Wales. 3) guideline that recommends CBA and CUA, such as the guideline from Canada. 4) guidelines that recommend only CUA, such as New Zealand. Even though some countries use the same types of analysis, the reasons or logics used in their guidelines may not be exactly the same. However, it would be laborious if every guideline were discussed here. Only the guidelines of Australia, England & Wales, Canada, and New Zealand as examples of groups 1 to 4, respectively, are included here.

The Commonwealth Department of Health and Ageing of Australia published guidelines for the pharmaceutical industry on the preparation of submissions to the pharmaceutical benefits advisory committee in 2002[8]. Since all four types of economic evaluation are allowed in the guideline, it does not provide specific discussions for selection. Only definitions and examples of CMA, CEA, CUA, and CBA are included in the Australian guideline. However, CBA is specifically not encouraged and it is claimed that it is not likely to be helpful for advisory committees in their deliberations.

The National Institute for Health and Clinical Excellence (NICE) recommended CEA and CUA since clinical effectiveness is usually measured in health care[9]. The selection between CEA and CUA depends on the nature of the clinical problem addressed. CUA

can provide a comparison of relative value of health gain from alternatives in different diseases. Even though NICE recognizes an increase in applications of contingent valuation methods in health economic evaluation, CBA is not suggested in the guideline. CMA is also not recommended unless equal effectiveness is demonstrated.

In 1997, the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) launched a guideline for the economic evaluation of pharmaceuticals[10]. The Canadian guideline is unique because CBA and CUA, instead of CEA and CUA, are preferred. A reason provided in the guideline is that CBA is based on the theoretical foundations of welfare economics and the normative principle of a potential *Pareto improvement* and therefore it has the soundest theoretical background. Also, it is the only technique that allows for comparisons across health and other sectors. Additionally, a reason for excluding CEA can be that CUA is generally viewed as a special case of CEA, in which the measure of effectiveness is QALY.

The Pharmaceutical Management Agency (PHARMAC) of New Zealand defines economic evaluation as "Cost Benefit Analysis", which is composed of CMA, CEA, CUA, and CBA[11]. The guideline agrees with the advantage of CUA that can be used in a comparison of different areas of health care, while CEA can compare only one area of health care. Two major drawbacks of CBA are addressed. First, there are significant difficulties in placing a dollar value on health outcomes. No robust technique exists. Further research of developing techniques is required before CBA can be considered more seriously. Second, people implicitly assign different values to different types of health outcomes. For instance, people are willing to pay more for life-saving drugs than other kinds of drugs. It is considered easier in CUA. Finally, PHARMAC provides reasons for choosing CUA in the guideline. One reason is that CUA is achievable and practical, yet still enables comparisons across different health care areas. It helps PHARMAC prioritize competing alternatives and opportunities, without the problems of value judgment of health outcomes. Also, PHARMAC claims that the CUA approach can be used to consider past funding decisions as well as future funding decisions. For instance, it can provide an analytical foundation for decisions to limit access to drugs where the evidence suggests that these drugs are only cost-effective for patients with specific conditions or severity. In doing so, it can free up funds for more worthwhile alternatives currently waiting funding. Another major advantage mentioned in the guideline is when CUA is done properly; it clarifies the assumptions and methods used in coming to a decision. For instance, when calculating a cost per QALY, several things are examined e.g. what costs are included and why? What benefits are included and why? Is a QALY for one person equal to one for another? What time frame is relevant?

In conclusion, each country's guideline has its own preferred types of economic evaluation. Reasons used in the selection vary across the countries. The decision is based on an analytical framework of each type of analyses and also on the perspective of readiness of data information availability in the countries.

Recommendations for Thai HTA Guideline

In the recommendations for Thai economic evaluation guideline, not only do the theoretical foundations of each economic evaluation type need to be considered but also their feasibilities. The availability of data, skilled scientists, and funds are the main factors for any valid analysis. Unfortunately, the available guidelines are of countries with different economic backgrounds from Thailand. Theoretical foundations can be shared with the guidelines from those countries, but feasibilities and other considerations must be taken into account.

Based on Drummond et al.'s recent book, only CEA, CUA, and CBA are methods of full economic evaluation[1]. Most health technologies or drugs do not have equal effectiveness. In the health technology or drug market, new products usually have incremental benefits from existing products. Assuming that an economic analysis is only required when added-value is claimed for the new drug products, CMA is irrelevant in this context. It is also usually not easy to demonstrate that two or more alternatives have equivalent outcomes. Therefore, CMA can be excluded.

CBA may have strong support from the welfare economic theory. However, it requires a robust method to assign values to health outcomes. Extra efforts from scientists are needed. Therefore, CBA is not suggested for Thai HTA guideline. The reason given by NICE of England & Wales and PHARMAC of New Zealand can be borrowed to explain the exclusion of CBA in Thai guideline.

CEA and CUA are recommended to be methods of choice for Thai guideline for two major reasons. First, CEA and CUA are generally used alternatives to CBA since CBA has certain limitations of value judgment and analysts may be unwilling or unable to monetize

health outcomes. It is counterintuitive to place a monetary value on any life saved. On the other hand, clinical effectiveness measured in health care can be directly used in both CEA and CUA. It is intuitive for health care decision makers to present outcomes as clinical effectiveness or quality-adjusted clinical effectiveness. Another reason is that even though CEA and CUA may not embed well in the traditional welfare economic theory, they are supported by extra-welfarism, which is consistent with the general objective of health care budget. CEA can measure technical efficiency, while CUA can measure both technical efficiency and allocative efficiency in the welfare economic approach. The extra-welfarism allows CUA to correct equity problems.

The selection between CEA and CUA depends on the nature of the clinical problems. Both CEA and CUA have advantages and disadvantages. For the advantages of CEA, it can deal with intermediate outcomes, which are usually measured as health outcomes. Also, it basically requires less resource because its outcomes measure only clinical effectiveness, excluding qualitative adjustment. Additionally, the results of CEA are easily interpreted. However, there are at least three major drawbacks of CEA. First, because the measure of primary effectiveness may differ from alternative to alternative, CEA cannot be used to make comparisons across a broad set of alternatives. Second, health care decision makers with a limited budget must not only determine if a new alternative is cost-effective but must also determine which alternative to use to reduce or free up budgets for a new alternative. CEA cannot measure the opportunity costs of funding the new alternative. In other words, CEA cannot measure the allocative efficiency. Third, in any alternative there is usually more than one outcome of interest. In reality, typically there are a large number of relevant outcomes resulting from health care alternatives. Some outcomes are more important than others. A valid justification is needed.

Drummond et al suggests a number of situations where CUA should be used[1]. Certainly, when health-related quality of life is an important outcome, CUA should be conducted. For instance, cancer treatments usually have an impact on patients' daily life and obviously affect their quality of life. CUA should be applied when alternatives affect both morbidity and mortality and a common unit of outcome is required for a combination of both effects. This also leads us to when alternatives compared have a broad range of different types of outcomes and a common unit of outcome is required for comparison, CUA can help in this regard. Similarly, any alternative needs to be compared with an existing alternative that has already been evaluated with CUA, and then CUA should be the method of choice. CUA can deal with a limited budget situation when decision makers need to determine which alternative use to reduce, eliminate, or free up funds for a new alternative. Basically, CUA can measure not only technical efficiency but also allocative efficiency. However, CUA has limitations. It requires extra resources to determine quality-adjusted outcomes. The measurement of QALYs is still controversial and requires further research. Perfect measurement does not exist. Some health care decision makers are still skeptical about the issue of QALYs.

After considering all the advantages and disadvantages of CEA and CUA, CUA is recommended for Thai HTA guideline to be the method of choice when data and resources are available, or when possible, since it provides a more complete picture than the other alternatives. Technically, when CUA is completed, CEA can be examined from the same set of data. However, CEA is more appropriate in case only intermediate outcomes of the compared alternatives are available.

The economic evaluation of health care in Thailand is still in its infancy. In fact, no matter which types of analysis are recommended, there are still some difficulties. The difficulties can be divided into two major categories, which are general difficulties and CEA or CUA technical difficulties. For general difficulties, Thailand lacks information, resources, and experts in this area of research. These difficulties are, in fact, embedded in economics since economics assumes limited resources. To overcome these difficulties, efficient resource allocation is needed. Also, government authorities need to understand and strategically handle the difficulties. For instance, human capacity building seems to be the very first step that should be taken to strengthen the economic evaluation in health care. In this regard, the government authorities need to not only think about training more researchers, but also needs to create demand for the researchers in this area, especially in early phase of capacity building.

For technical difficulties, that are specific to CEA and CUA in Thailand, most health outcomes and health-related quality measurements are from studies in other countries. Translating, converting or applying these analyses to the health care system in Thailand requires extra effort. However, good management, such as working diligently, team work, and strong support will eventually solve the problems. The development

of guidelines of economic evaluation and networking with international communities will also help.

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การกำหนดชนิดของการประเมินความคุ้มค่าทางการแพทย์

สุรฉัตร ง้อสุรเชษฐ์

วัตถุประสงค์ของบทความเพื่อเสนอแนะชนิดของการประเมินความคุ้มค่าทางการแพทย์ในคู่มือการประเมินเทคโนโลยีด้านสุขภาพสำหรับประเทศไทย โดยอาศัยการวิจัยเอกสารที่เกี่ยวข้องกับชนิดการประเมินความคุ้มค่าทางการแพทย์รวมทั้งคำจำกัดความและทฤษฎีพื้นฐาน นอกจากนั้น มีการทบทวนคู่มือการประเมินความคุ้มค่าทางการแพทย์ของชาติต่าง ๆ ท้ายที่สุดข้อมูลที่ได้ทั้งหมดจะถูกนำมาประมวลเพื่อการเสนอแนะในคู่มือการประเมินเทคโนโลยีด้านสุขภาพสำหรับประเทศไทย โดยทั่วไปชนิดของการประเมินความคุ้มค่าทางการแพทย์มีทั้งหมดสี่ชนิด ได้แก่ การวิเคราะห์ต้นทุน-ผลได้ การวิเคราะห์ต้นทุนต่ำสุด การวิเคราะห์ต้นทุน-ประสิทธิผลและการวิเคราะห์ต้นทุน-อรรถประโยชน์ ซึ่งสามารถอธิบายด้วยทฤษฎีเศรษฐศาสตร์สวัสดิการแบบดั้งเดิมและแบบพิเศษ พบว่าจากคู่มือของประเทศต่างๆ มีการเลือกใช้ชนิดของการประเมินความคุ้มค่าทางการแพทย์แตกต่างกัน ส่วนใหญ่แนะนำให้ใช้การวิเคราะห์ต้นทุน-ประสิทธิผลและการวิเคราะห์ต้นทุน-อรรถประโยชน์มากที่สุด สำหรับคู่มือของประเทศไทยเสนอแนะให้ใช้การวิเคราะห์ต้นทุน-อรรถประโยชน์เป็นหลัก อย่างไรก็ตามสามารถใช้การวิเคราะห์ต้นทุน-ประสิทธิผลได้ โดยเฉพาะอย่างยิ่งในกรณีที่มีเพียงการวัดผลลัพธ์คั่นกลางของทางเลือกที่นำมาเปรียบเทียบกัน

Special Article

Measurement of Costs

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Costing plays an important role in health economics, particularly economic evaluation. However, there are some controversial issues: concepts, methods and reference values. Hence, it is pivotal to standardize costing methods and use these as national guidelines to produce comparable studies. This report is divided into 3 parts: theoretical issues, international guidelines comparison, and recommendations for the Thai health technology assessment guidelines. Each section is composed of three general costing steps: identification, measuring and valuation. It is recommended to measure economic or opportunity cost mainly in societal perspective. Cost category is composed of direct medical, direct non-medical and indirect costs. The level of reliability of each kind of costing source data is provided. Valuation of resource use based on national standard cost menu is recommended for national policy making. The recommendations on cost measurement are appropriate for the Thai context and in the current situation.

Keywords: *Cost, Cost measure, Methods, Guidelines, Economic evaluation, Thailand*

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Cost refers to the value of resources used to produce something[1]. It is the core of economics. In terms of health economics or pharmacoeconomics, measuring costs or costing involves identifying, measuring and valuing all resource changes that occur as a certain health care intervention is carried out[2]. Furthermore, cost measuring is employed to estimate economic burden due to illness. It is applied in economics evaluation and outcome research. For health care planning, recent trends and future disease costs are information used for setting priorities and cost containment measures[3,4]. There are several hurdles in conducting the economic analyses including costing[5]. Problems in costing may be categorized as controversial issues in concepts (e.g. including productivity cost)[6], methods (*e.g.* human capital approach versus friction cost method)[7], and reference values (e.g. discount rate)[8]. Hence, it is pivotal to standardize costing methods for further studies. Then the studies can be comparable and used as inputs into national health policy decision making. This article is presented into 3 parts: theoretical issues, international guidelines comparison, and recommendations for Thai health technology assessment (HTA) guidelines. Each section is presented based on three general costing steps: identification, measuring and valuation[2,9].

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1. Theory

1.1 Identification of resource use

Identification of resources covers two topics: types of resource use that are relevant for the disease and the intervention studied, and level of detail that has to be measured and valued[10]. However, for the theory, some other related issues are added.

Economic versus accounting costs

Economics is based on three fundamental concepts[11]: *scarcity* – resources are insufficient to support all demands; *choices* – because of resource scarcity we need to choose between alternative ways of using them; *opportunity cost* – by choosing to use available resources in one way, we forgo other opportunities to use these same resources. So cost or economic cost or opportunity cost of engaging in an activity or producing a product refers to the sum of all

other benefits that can be generated by the same amount of resources taken away for this activity[12]. On the other hand, accountants measure costs by the historical outlay of funds. So, accounting cost is the acquisition price of a product.

Perspective

Perspective is an important issue of a health economic study. Perspective determines the types of costs that should be taken into account. The analysis can be conducted from various viewpoints or perspectives. Defining the objectives of the study allows researchers to select the perspective that is the most appropriate. Perspectives can be classified as patient (first party), provider (second party), purchaser or payer (third party), employer or other sponsor (fourth party), government, and societal perspective[13].

Time horizon

Time horizon is used to define the period of time needed to observe resource use. Ideally, the time horizon should be chosen in such a way that all cost consequences of the intervention under study can be taken into account in the analysis[2].

Types of costs

Drummond *et al*[14] proposed 3 groups of resources used in health care: health care resource use (*e.g.* hospital resources and community care resources), patient and family resource use (*e.g.* transportation, sick absence and care givers), and resource use in other sectors (*e.g.* social welfare).

Cost classification is divided into three category costing types: direct medical, direct non-medical and indirect costs[15]. Direct medical costs refer to those resources whose consumption is wholly attributable to the use of the health care intervention in question[12]. These include costs of diagnosis, treatment, follow-up, rehabilitation, and terminal care, and are both institutional and non institutional. Direct non-medical costs are out-of-pocket expenses for goods and services outside the medical care sector[16]. These include costs of transportation, meals, accommodation, facilities, services, and informal care. Indirect cost refers to lost productivity (paid or unpaid) resulting from morbidity or mortality[12] i.e. cost of productivity loss due to sick leave, permanent disability or premature death.

Cost of informal care

Informal care is care provided by family members, friends, acquaintances or neighbors of patients without financial compensation[2,17]. Providing informal care entails giving up work and leisure time, investing energy and making fewer social contacts. In terms of societal perspective, the loss of time for informal care giving should be assessed in the form of opportunity cost. Regarding categorization, informal care is sometimes considered as indirect cost[15]. Informal care is classified as household activities of daily living (HDL), health care activities (HCA), activities of daily living (ADL), and instrumental activities of daily living (IADL)[18]. HDL includes preparing food and drinks, shopping, doing chores and taking care of children. HCA includes preparing medication, doing rehabilitation, contacting health care providers and organizing home facilities for the patient. ADL includes assistance such as toilet activities, moving around the house, eating and drinking. IADL includes management matters, *e.g.* banking, shopping or traveling.

Indirect cost

As labor is a scarce resource in economic concepts, absence of an individual from work can be quantified in terms of the value of the lost productivity. Productivity cost is a synonym of indirect cost. Another concept is time cost. This concept includes value of both work time and leisure time. Therefore, productivity cost is defined as "the cost associated with lost or impaired ability to work or to engage in leisure activities due to morbidity and lost economic productivity due to death[9]". Work time is divided into paid working time and non-paid working time. Productivity costs refer to loss of production due to illness and mortality. Time loss can be classified as time spent receiving treatment and time spent recovering at home. The patients' time spent receiving treatment is recommended to be classified as direct cost. This classification style can have an effect on the result in case indirect cost is not included[6]. Indirect costs are those costs that are not actually paid. They are defined as productivity lost due to illness. There are two forms of indirect costs: morbidity and mortality costs. Morbidity costs include the value of production losses of those who are sick, absent, unemployed or restricted from working due to an illness. Mortality costs are calculated as the present value of lost production due to premature death caused by illness[15].

Transfer payment

There are some payments, such as sickness compensation, that are a financial cost of a social

security fund or government, and also a financial income of the patients. They are not social costs because this money does not reflect resources consumed due to illness. They will be exchanged with patients' utility which is not related to the illness. This money is called transfer payment, and is not included in the cost of illness. In contrast, cost of payment administration is included because the payment is a consequence of the illness[19].

Future health care cost

Future health care cost or health costs in extended years of life are the costs associated with patients who live longer and consume health care resources as a result of a given intervention. Regarding lifesaving interventions, we have to consider future medical care cost, both related and unrelated to the diseases. Unrelated medical care is care given to treat another disease that is necessitated by the effectiveness of the intervention.

Taxes

It was argued that direct and indirect taxes and social premiums should be excluded from cost analyses since they do not represent costs for society[9]. However, in practice, in most situations it is difficult to exclude, so is included[10].

1.2 Measuring resource use

The measurement of resource use is used to determine the quantities of resources used as part of a given intervention[13].

Increment versus total in resource use

A comparison of alternative interventions, for example cost-effectiveness analysis, reflects the difference in resource use of the intervention and comparator. This increment in resource use can be measured directly by determining the amount of increased (or decreased) resource use. It is the incremental use of resources that is of interest rather than the total cost of an intervention. This means that the same resources used by both intervention and comparator are not necessarily to be measured[9].

Start-up cost

The start-up period is counted from approval of the project to the time when the service or intervention can be provided. The start-up period may take several years consuming labor, time, materials and the use of capital assets. To calculate the total start-up cost, the cost of capital assets has to be annualized. Similarly, if the project period is several years, the start-up cost has to be annualized[19].

Management of missing or censored data

In economic evaluation alongside clinical trials, missing data due to dropouts and censored data (survival times are censored) are common. These data can affect the study results and should not be ignored. It is proposed to classify the analysis of incomplete data into naÔve and principled methods[20,21].

1.3 Valuation of resource use

Cost of medical services

Unit costs used in the valuation process can be from primary or secondary sources. They can be from direct cost measurement, accounting data, standard unit cost, price list, expert opinion and from other studies[13]. In the case of evaluation for country policy making, standard unit costs are preferred. For direct measurement, there are some aspects to be considered in the valuation of resource use. These are adjustment of cost at different time (discounting), valuation of time loss (indirect cost), and prices (market and shadow prices). Regarding decision-modeling techniques, secondary data are employed. Sources of cost data and health effects may be derived from clinical trials, observational studies, administrative databases, case series, expert opinion and/or secondary analysis (such as meta-analysis). Sources are ranked from 1 to 6. Number one refers to the most appropriate[22]. Rank 1 refers to cost calculations based on reliable databases or data sources conducted for specific study – same jurisdiction. Rank 2 refers to recently published cost calculation based on reliable databases or data sources – same jurisdiction. Rank 3 refers to unsourced data from previous economic evaluation – same jurisdiction. Rank 4 refers to recently published cost calculation based on reliable databases or data sources – different jurisdiction. Rank 5 refers to unsourced data from previous economic evaluations – different jurisdiction. Lastly, rank 6 refers to expert opinion.

Cost of informal care

There are two main methods of valuing time spent on informal care: revealed preference methods and stated preference methods[17] Revealed preference methods use real-life decision data to value informal care. This means that preferences of informal caregivers are deduced from informal caregivers' decisions or from decisions in the market for close substitutes of informal

care. Revealed preference methods can be calculated based on opportunity costs or replacement cost. Replacement cost is valued time spent on informal care at (labor) market prices of a closed market substitute (proxy goods). Stated preference methods may be contingent valuation or conjoint analysis. Contingent valuation assesses the minimum amount of money an informal caregiver would need to receive to be willing to provide a certain or an additional amount of informal care. Conjoint analysis is a method for the analysis of respondents' preferences for a set of multi-attribute alternatives.

Indirect cost

To estimate indirect cost, frequently used methods are the human-capital cost approach, willingness to pay, and the friction cost approach[4,7,23-25]. The human capital cost approach is the most often employed. This approach is based on the concept of a potential loss of production as a result of illness. It is assumed that a vacant position will never be filled and that society will continuously lose the production of those patients until retirement. This means that the labor markets are in equilibrium without unemployment. The market wage rates are used for morbidity cost calculation. Per capita GDP is usually used in the calculation of mortality cost. Furthermore, the earnings in the future are discounted at a constant annual rate. There is a comment that the real production loss can be much smaller than the potential loss because the workers who are sick can be replaced for little payment. This is a weak point of the human capital approach. In an attempt to measure "actual" rather than "potential" production loss, an alternative method has been developed called the friction cost method. The basic idea of this approach is that those patients on short-term leave from their work can make up for the loss of production when they return, or can be taken care of by internal labor resources, or that non-urgent work may be canceled or postponed. For long-term work absence, patients can be permanently replaced by someone who is unemployed. The actual productivity loss from the work continues only during the period of time required for worker replacement. This period is called the "friction period". It is assumed that workers who are on sick leave will be replaced after completion of the friction period. This means that if the period of work missed by the patient is shorter than the friction period, all production loss during the absent period is valued as indirect costs. However, if patients are absent from work for longer than the friction period, production loss will be limited to only the friction period. Therefore, the friction period has the role of a cut-off point in determining indirect costs. In practice, more information is needed for this method. Such information is not available in most countries. Thus, it is not popular for estimating indirect costs.

Another alternative method is willingness to pay (WTP) or contingent valuation. This method relies on the view of individuals who are asked hypothetical questions regarding how much they would be prepared to pay to avoid their probability of death or morbidity. WTP could be helpful in indicating how individuals value health and life and in deriving social preferences regarding health policy. Furthermore, WTP might be especially helpful in assessing the burden of pain and suffering which are intangible and not amenable to be evaluated in terms of the monetary value of resources used or forgone. However, this approach is used less frequently because it is difficult to apply and it is affected by income. The lower income earners tend to be willing to pay less than higher income earners.

Market prices and shadow prices

Prices in the health care market do not represent opportunity costs since it is not a free market. Health care is usually regulated by health authorities and government. Market prices may be higher than opportunity costs due to monopolies or tax systems. On the other hand, they may be lower than the opportunity costs due to government subsidies. Ideally, opportunity cost is preferred to market prices. In practice, market prices can be applied in some situations where opportunity costs are not available or feasible. Opportunity costs of goods with distorted market prices or without market prices are called shadow prices[19].

2. Comparisons of the international economic evaluation guidelines

This section is a review based on the report titled "Pharmacoeconomic Guidelines Around the World[26]". The report covers 23 countries and 28 guidelines consisting of 21 pharmacoeconomics guidelines, 6 submission guidelines for formulary listing and 1 for journal publication. Full guidelines are available from the website of the International Society for Pharmacoeconomics and Outcomes Research. The report covers 32 key features and the review presents 8 costing-related features. Some details of 4 outstanding countries in pharmacoeconomic applications: Canada, Australia, the United Kingdom and the Netherlands, are presented.

2.1 Identification of resource use

Although economic cost is needed for economic evaluation, there are some countries that use accounting cost. In the UK, resources are valued using the prices relevant to the National Health Services (NHS)[27]. Most countries employ a societal perspective which includes other perspectives. Some countries, *i.e.* Finland, Sweden, Germany, the Netherlands, and United States of America, use only societal perspective. For time horizon, most countries state that the time horizon of the study needs to be long enough to cover effects of both the health interventions and the consequences of illness. Regarding types of costs, direct medical, direct non-medical and indirect costs are included in most countries. Cost composition is up to the study's perspective. It is recommended that indirect cost be presented separately.

In Canada, buildings and equipment that are used for more than the recommended time have been written off in accounts and no longer incur a depreciation cost. From an economic point of view, they still have opportunity cost. The excluded costs are research related costs (*e.g.* extra test to confirm pathogen), transfer payment (*e.g.* sickness pay), and unemployment insurance and welfare payments. Furthermore, future health care cost (the costs associated with patients who live longer and consume health care resources as a result of a given intervention.) is excluded due to the difficulty of identifying if it is a direct consequence of the program, and availability of data[28]. In England and Wales, value added tax (VAT) is excluded from all economic analysis, although included in budget impact analysis[27].

For the Netherlands, from a social perspective, the costs cover direct cost both within and outside the healthcare system (direct medical cost and direct non-medical cost, respectively). They also cover indirect cost outside the health care system or productivity loss. Indirect cost within the healthcare system or medical cost during life-years saved may be separately included if there is a clear relationship with the intervention. For productivity loss, the friction cost method is recommended[29]. Regarding cost of taxes, although including taxes is controversial, the Dutch manual determines that these taxes should be included because in most situations they are difficult to exclude[10].

2.2 Measuring resource use

In Canada, actual measurement of resource use based on trials is recommended as an appropriate source of resource quantities. For international trials, resource quantities cannot be directly imported into the Canadian system. This is because there are major differences in the way that health care is delivered in many countries. In some practical cases, they may be transportable into Canada but re-validation, explanation and justification are required[28]. Similarly, the Dutch guidelines for pharmacoeconomic research states that "The deployment of people and resources during a treatment must first be described in natural (non-monetary) units, such as hours, tasks, nursing days or daily doses. All cost data obtained from international studies must be validated for use in the Netherlands[29]".

The Danish Institute for Health Technology Assessment published the Health Technology Assessment Handbook[30]. It stated that there are two sources of resource use: patient-specific (stochastic) data and non-patient-specific (deterministic) data.

2.3 Valuation of resource use

Most countries employ a reference/standard list of costs, prices or reimbursement rates. Italy uses micro-costing carried out through studies performed at health care structures. In Canada, a national list of provincial costs for health care is published and used as a source of standard cost[31]. The UK's NHS published a reference cost manual[32,33]. In the Netherlands, the "Dutch manual for costing: methods and standard costs for economic evaluations in health care" is referred to as a sources of standard costs[10]. In Australia, the book titled "Manual of Resources Items and Their Associated Costs" is used as a source for reference costs[34].

3. Recommendations for the Thai health technology assessment guidelines

The guidelines are proposed based on theories, methods, international experience and current feasibility in Thailand. The feasibility is considered based on availability of cost-related data and the skill of Thai researchers. Publications are reviewed as a proxy of researcher's skill.

3.1 Identification of resource use

Economic versus accounting costs

Economic or opportunity cost is the first priority used in economic evaluation[12]. However, in practice, market prices (charge from price list) with appropriate adjustment can be applied as a reasonable proxy of opportunity costs[13].

Study perspective

Major sources of health finance in Thailand come from the government. The government budget allocated to national health insurance comes from the contribution of society in terms of taxes. Therefore, societal perspective needs to be gauged when economic evaluations are undertaken[14]. If we are unable to use a societal perspective, a health sector or health system perspective is used. As a tool of efficiency management for hospital administrators, provider or hospital perspective is used. To study compliance of patients, patient and family perspective is necessary. This is more useful to study illnesses that are not covered or only partly covered by health insurance schemes. In addition, for payers with a capitation payment system (Universal Health Coverage Scheme-UC, and Social Security Scheme-SSS), it is difficult to determine cost from the payer's perspective. For the Civil Servant Medical Benefit Scheme (CSMBS) and some benefit packages of the UC and SSS that employ a fee-for-service payment system, a third party payer perspective can be employed in some situations. In conclusion, Thailand should employ societal, health system, third party payer, provider, and patient perspectives.

Time horizon

For economic evaluation of health interventions, the time horizon must be long enough to capture all effects of the interventions[2]. In the case of a cost of illness study, the study has two alternatives: prevalence-based and incidence-based approaches[15]. For the prevalence-based approach, the study time should be at least one year to avoid seasonal effects on the unit cost analysis of medical services and clinical symptoms. The other approach is an incidence-based cost of illness. This approach measures the economic burden from the start to the end points of illness. It observes only new cases occurring in a given period and monitors them until the end point.

Types of costs

Costs to be included depend on the study perspective. Direct medical, direct non-medical and indirect costs are included in most cases[15]. It is recommended that they be presented separately. Direct medical costs cover treatment cost at the study site(s) and other sites, *e.g.* at private clinics, drug stores, and traditional medicine suppliers. Direct non-medical costs cover personal facilities, travel, food, accommodation, time lost while receiving treatment, informal care and paid personal care. Indirect costs cover morbidity and mortality costs. For cost-effectiveness analysis, if quality-adjusted life years (QALYs) are the measure of effectiveness, indirect or productivity cost are not included. This is to avoid double-counting since QALYs have included morbidity and mortality effects[2]. In some interventions, for example disability prevention, costs incurred in non-health sectors, *e.g.* welfare and education, should be included. Details are in Table 1. Transfer payment and future health care cost are not included[19]. In contrast, since it is difficult to separate taxes, taxes are included[10].

3.2 Measuring resource use

Increment versus total in resource use

A comparison of alternative interventions reflects the difference in resource use of the intervention and comparator. The incremental use of resources is of interest rather than the total cost of an intervention. This means that the same resources used by both the intervention and the comparator do not necessarily need to be measured[9].

Start-up cost

A start-up period may take several years, consuming labor and time, materials and use of capital assets. To calculate the total start-up cost, the cost of capital assets has to be annualized. Similarly, if the project period is several years, the start-up cost has to be annualized[19,35].

Management of missing or censored data

In economic evaluation alongside clinical trials, missing data due to dropouts and censored data should be treated properly. Both the naÔve and the principled methods should be applied[20,21].

3.3 Valuation of resource use

Cost of medical services

There are two alternative sources of cost of medical services used in the valuation: reference unit cost and setting specific unit cost[13]. For reference unit cost, we have "reimbursement rate of public health facilities" used for the Civil Servant Medical Benefit Scheme. The national standard cost menu should be used instead when it is available. For setting specific cost, the unit cost of medical services should be calculated based on the national guidelines when they are available. For country policy planning, studies should employed unit cost of medical services from the national standard cost menu.

Table 1. Description of costs classified by study perspectives

Cost		Source of services/ information	Resource identification	Valuation by perspective				
Category	Subcategory			Patient	Provider/ hospital	Third-party payer	Health system	Societal
Direct medical	Treatment/ health care	Study health setting	medical services	charge	cost	reimburse ment	cost	cost
		Other health facilities	medical services	charge	-	reimburse ment	charge (cost if available)	charge (cost if available)
Direct non medical	Personal facilities	Patient or family	home modification/ special devices/ social services	charge	-	-	-	charge (market price)
	Travel	Public/ owntrans- portation	travel distance, vehicle type	charge or estimated cost	-	-	-	charge (market price) or estimated cost
	Food	Patient or family	extra food	charge	-	-	-	Charge (market price)
	Accom modation	Hotel	days of stay	charge	-	-	-	charge (market price)
	Time loss while receiving treatment[6]	Time loss of patient	hours or days	income loss	-	-	-	produc- tivity cost
	Informal care	Time loss of caregiver	hours or days	income loss	-	-	-	produc- tivity cost
	Personal care/ assistance	Paid helpers	person-day/ month	charge	-	-	-	charge (market price)
Indirect	Morbidity cost	Working time loss	days of illness	income loss	-	-	-	produc- tivity cost
	Mortality cost	Working time loss	work-absence years from death to retired age	income loss	-	-	-	produc- tivity cost
Other sectors	Welfare	Occupation rehabilita- tion	services	fee/travel/ food/ material	-	reimburse- ment	-	cost
	Education	Special education	services	fee/travel/ food/ material	-	reimburse- ment	-	cost

Cost of informal care

Valuation methods for informal care should be conducted using both opportunity cost and replacement cost[17]. Opportunity cost calculation of informal care should correspond to that of the indirect cost of the patient. For replacement cost, wage rates used in this method should be obtained from the national survey of the Ministry of Labor and the National Statistical Office[36,37]. Based on the survey, the category of health and social work should be used in the cost calculations of the health care activities (HCA) and the activities of daily living (ADL). The category of household work should be used in the cost calculations of the household activities of daily living (HDL) and the instrumental activities of daily living (IADL).

Indirect cost

Although it is claimed that the friction cost method is more accurate than the human capital method[6], in Thailand, we do not have the information (the friction period) needed for the friction cost method. Therefore, the human capital approach is recommended. To comply with the concept of equality in health, all kinds of time, *i.e.* paid work, non-paid work and leisure time are covered. In addition, to select reference rates for the calculation, the national average wage should be used to value the time of different workers equally[6]. The national average income from the socioeconomic survey conducted by the National Statistics Office should be applied for the calculation.

Market prices and shadow prices

Ideally, opportunity cost is preferred to market prices. However, in practice, market prices can be applied to some situations where opportunity costs (shadow prices) are not available or feasible.

Final remarks

In conclusion, the measuring cost guidelines are proposed by a review of theories and international related guidelines. The drafted guidelines are commented on by a panel of experts. The guidelines may be different from those of other countries. It is aimed to develop the guidelines that are appropriate for the current Thai situation. The application of these guidelines will improve the quality of health economics evaluation studies. The study results can then be more valuable for health care management at both local and national policy levels. It is important to note that the guidelines still need improvement and should be revised periodically.

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การประเมินต้นทุน

อาทร ริ้วไพบูลย์

การประเมินค่าต้นทุนมีบทบาทที่สำคัญในการศึกษาเศรษฐศาสตร์สาธารณสุขโดยเฉพาะอย่างยิ่งในการประเมินความคุ้มค่าทางการแพทย์ แต่การประเมินค่าต้นทุนนี้มีบางประเด็นที่ยังหาข้อสรุปไม่ได้ แบ่งเป็น 3 กลุ่มได้แก่ แนวคิด วิธีคำนวณ และค่าอ้างอิงที่ใช้ในการคำนวณ ดังนั้นการจัดทำคู่มือมาตรฐานการประเมินต้นทุนแห่งชาติเพื่อให้ผลการประเมินสามารถเปรียบเทียบกันได้ จึงเป็นสิ่งที่สำคัญอย่างยิ่ง บทความนี้มีเนื้อหาประกอบด้วยพื้นฐานทฤษฎีการเปรียบเทียบคู่มือของประเทศต่าง ๆ และข้อเสนอคู่มือของประเทศไทย แต่ละส่วนประกอบด้วยส่วนย่อยของขั้นตอนพื้นฐานในการประเมินต้นทุนได้แก่ การแจกแจงทรัพยากรที่ใช้ การวัดปริมาณทรัพยากรที่ใช้ และการแปลงปริมาณทรัพยากรที่ใช้ให้เป็นมูลค่าของเงิน การวัดต้นทุนทางเศรษฐศาสตร์หรือต้นทุนเสียโอกาสควรวัดในมุมมองของสังคมเป็นหลัก ต้นทุนประกอบด้วยต้นทุนทางตรงด้านการแพทย์ ต้นทุนทางตรงที่ไม่เกี่ยวกับการแพทย์ และต้นทุนทางอ้อม มีการเสนอแนะระดับความน่าเชื่อถือของแหล่งที่มาของข้อมูลต้นทุนเอาไว้เป็นแนวทาง ในการแปลงปริมาณทรัพยากรที่ใช้เป็นมูลค่าในรูปแบบตัวเงิน แนะนำให้ใช้รายการต้นทุนต่อหน่วยมาตรฐานของประเทศสำหรับการวิเคราะห์เพื่อความเหมาะสมสำหรับใช้เป็นข้อมูลการตัดสินใจเชิงนโยบายของประเทศ ข้อเสนอแนะสำหรับการประเมินต้นทุนนี้เหมาะสมในบริบทของประเทศไทยในสถานการณ์ปัจจุบัน

Special Article

Measurement of Clinical Effects

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The measurement and valuation of clinical effects is a significant component of economic evaluation. Decision makers are commonly interested in how a particular health intervention works in everyday practice; therefore, the resulting outcome under this circumstance is called the effectiveness. Clinical effects usually measure final intended effects of a proposed health technology in terms of the ultimate change in health state brought about by the technology. The systematic review and meta-analysis of high quality RCTs is the most favorable method to synthesize evidence because they are disciplined and transparent methods. The present chapter focuses on how to make a valid measure of clinical effects for use in cost-effectiveness analysis and how clinical effect is to be appropriately defined and measured.

Keywords: *Clinical effects, Clinical evidence, Measure, Effectiveness*

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The measurement and valuation of clinical effects is a significant component of economic evaluation because economic evaluation seeks to inform decision makers about the net change in costs and clinical benefits arising from alternative approaches to providing a particular sort of care. However, it is always difficult to identify all the benefits and disadvantages of an intervention. Traditionally, health benefit has been measured using mortality parameters such as 'number of deaths averted' or 'life-years saved'. Since health is more than just being alive, its effects on morbidity are increasingly being taken into consideration[1].

When the benefits of alternative interventions are identical, or at least very similar, the cost-effectiveness analysis is equivalent to the cost-minimization approach. Under these circumstances, there is no need to measure the clinical benefits as the intervention with the least cost is the most cost-effective. Unfortunately, this situation seldom arises, in part because of the uncertainty that usually exists around the estimates of benefits that require a full investigation of the uncertainty[2].

Where the benefit of competing interventions can be measured along a single dimension, cost-effectiveness analysis can be used to rank interventions in terms of their ratios of cost per unit of effect. Some economic evaluation studies include 'surrogate measures', for example, a reduction in left ventricular size, a reduction in mmHg of blood pressure or improvements in bone mineral density, however, these surrogate measures should be avoided. The use of surrogate measures could limit the full application of economic evaluation studies, since these studies aim to inform decision makers about the trade-off between health investment and its outputs that contributes to overall welfare (welfarists) or health itself (extra-welfarist), not on said surrogate indicators. As a result, the clinical effects used in economic evaluation studies are usually measured in terms of 'life-years saved' for treatments, or 'number of cases detected' for screening programs[3].

The advantages of cost-effectiveness analysis are that the benefits or outcomes of health care programs are explicitly measured and the units of measurement are easy to understand and readily

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accepted by both the public and medical professionals. However, one of its disadvantages is that a single physical measure (such as life-years saved) is unlikely to capture all the dimensions of the benefits of interventions. Some interventions may not save many lives but may reduce pain or otherwise increase the quality of life. Another problem arises because units of measurement vary from program to program; it is difficult to compare the relative effectiveness of programs with different outcomes. As a consequence, there now exists a number of approaches which combine morbidity and mortality dimensions into a composite measure, namely Quality Adjusted Life Year (QALY) or Disability Adjusted Life Year (DALY). This in turn leads to the development of cost-utility analysis.

The present article focuses on how to make a valid measure of clinical effects for use in cost-effectiveness analysis while another article examines the more specific issues of valuing health consequences, health state preference scores and utility weights. Specifically, this chapter addresses a number of important questions; namely, how clinical effects are to be defined and measured.

Efficacy vs. effectiveness

The British pioneer clinical epidemiologist Archie Cochrane defined "efficacy" as the extent to which an intervention does more good than harm under ideal circumstances ("Can it work?"), and "effectiveness" as the extent to which an intervention does more good than harm when provided under the usual circumstances of healthcare practice ("Does it work in practice?")[4]. For instance, in randomized controlled clinical studies, researchers seek to test the effects of health technology under standardized conditions by reducing the systematic effects of other factors which can influence the outcome of the technology. These effects are usually gauged as efficacy. In clinical practice, however, there will often be a number of factors which contribute to an outcome which differs from that from testing done in random clinical studies. The resulting outcome under this circumstance is called effectiveness.

Decision makers are commonly interested in how a particular intervention works in everyday practice. Economic evaluation should, therefore, measure the effectiveness found in a clinical everyday setting rather than the efficacy achieved in a well-controlled experimental setting[5-8].

During the past ten years, one of the growing trends in this evaluation has been the incorporation of economic evaluations alongside randomized controlled trials of healthcare interventions. Frequently, these assessments are incorporated into the drug development process; phase III, during which a drug's efficacy is evaluated prior to regulatory approval, and phase IV, which occurs after the drug is marketed[9]. This poses big challenges to researchers, for example, whether any adjustments should be made on clinical effects and costs to increase the relevance of economic evaluation studies that are comparable to real-life clinical practices. Some researchers suggested the use of modeling approaches such as decision trees or Markov models to estimate the consequences and costs of the health technology as they would appear in general practice. If this is the case, the conditions, assumptions and data used to create the basis for the models must be clearly presented in such a manner as to make them relevant, understandable and re-examinable. The data basis used must be as relevant as possible with regard to the indication and treatment context of the drug in clinical practice.

Intermediate vs. final outcomes

Although there are no limits to the types of measures of clinical effects included in economic evaluation studies, the surrogate outcome indicators[1], such as a reduction in left ventricular size or a reduction in blood pressure, may themselves sometimes have some value or clinical meaning. It is widely accepted that economic evaluation should use a final outcome as its effectiveness measure[10,11]. Researchers should consider the final intended effects of the proposed health technology in terms of the ultimate change in health state brought about by the technology because this information will provide meaningful guidance to policy makers in making broad resource allocation decisions. For instance, the ultimate aim of lowering moderately elevated blood pressure is to prevent death and impaired quality of life from a stroke or possibly a myocardial infarction. The ultimate aim of treating a patient with severe asthma is to prevent death, to prevent hospitalization and to return the patient to a normal level of functioning.

However, results on health improvement are obtained from experimental studies that usually report short-term or surrogate clinical outcomes since only a few clinical trials are large enough to measure changes in final outcomes. In this case, if relationships have been established, or have been proposed, between surrogate and final outcome indicators, the use of decision modeling may be necessary for the extrapolation

of short-term or surrogate clinical outcomes to long-term or final health benefits. The form of the relationships, which have been established between the surrogate and final outcomes may vary according to whether the data was derived from longitudinal studies or randomized trials. Examples include blood pressure and blood cholesterol and incidence of acute coronary syndrome; level of prostate-specific antigen and survival from prostate cancer; and serological liver function tests and the cure of viral hepatitis.

Quality of evidence

The process of obtaining efficacy or effectiveness data can present its challenges. In practice, the preferred source of data is dependent on the complexity of the question being investigated. Researchers must think carefully about the economic question at hand and the most appropriate sources of data for that question. Generally, there are different ways of gathering the effectiveness of a health intervention in economic evaluation[5]. These include:

- incorporating economic evaluation within a randomized controlled trial (RCT);
- using information from RCT, observational cohort or case-control studies;
- combining or modeling data from a variety of studies

As there are a growing number of RCT-based economic studies, the International Society for Pharmacoeconomics and Outcome Research (ISPOR) has recently developed a guidance document for the design, conduct, and reporting of cost-effectiveness analyses conducted as a part of clinical trials[12]. An advantage of incorporating economic evaluation within RCT is that the method allows for the prospective collection of cost and effectiveness data from a single source.

If well-designed and properly executed, RCTs are believed to provide the best evidence on the outcome of health care interventions. However, results from an RCT usually represent the efficacy of an intervention but not necessarily its effectiveness[6]. There are some exceptions where effectiveness studies use pragmatic designs in normal health care settings. In addition, the patient inclusion and exclusion criteria of the trial may limit the generalizability of the results; fully correcting these biases in economic evaluation is problematic[5]. However, RCTs have drawbacks too. Besides the issues of external validity, another limitation is that an RCT cannot be used in some instances such as intentional exposure to harmful substances[13]. In addition, an RCT conducted for social intervention or policy intervention is quite limited, when compared to medical intervention, in terms of the number of studies that can be conducted. In contrast to RCTs, data from observational studies is more prone to being confounded[5].

Synthesis methods are generally recommended as an alternative where there is insufficient data from any one source[5,6,8,14]. Combining data from a variety of studies can also increase the power to detect true effects, improve the precision of the estimate of effect size and also increase generalizability for applying results across settings[6]. Meta-analysis is a process of combining study results in such a way as to be able to draw conclusions about the efficacy/effectiveness of health technology. It can also highlight advantages and disadvantages of the proposed health technology and its comparators which are too small to be detected accurately in individual trials. However, it has been argued that there is potential for bias if the study is not based on the best available effectiveness data.

Table 1. Levels of clinical evidence

1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.
2++	High-quality systematic reviews of case control or cohort studies. High-quality case control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal.
2+	Well-conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal.
2-	Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal.
3	Non-analytic studies: for example, case reports, case series.
4	Expert opinion.

Source: Based on Sackett and others (Canadian Task Force on the Periodic Health Examination)[17]

Even though several measures, namely Relative Risk (RR), Odd ratio (OR) and Absolute risk reduction (ARR) have been widely used to measure clinical outcomes for economic evaluation, the use of Number-Needed-To-Treat (NNT) is not recommended[15]. NNT, the reciprocal of the ARR, expresses the number of patients that need to be treated for a period of time for one less adverse event to be observed at a specific point in time. Although the economic evaluation based on NNT can be conducted so as to calculate the cost per avoided treatment by multiplying the treatment cost per patient by NNT, the results of this analysis may yield biased, misleading information, and are better avoided[15]. The major limitation of using NNT in economic evaluation stems from that fact that an effect measure with one dimension (survival probability) cannot capture an effect with two dimensions such as time and survival probability. These limitations, therefore, affect the chance of correctly accounting for all costs and benefits and their timing, and hence reduce the ability for such evaluations to serve as a useful tool in the decision making processes[15].

Recommendations for Thai Health Technology Assessment (HTA) Guidelines

This guideline recommends that clinical effectiveness should be used in economic evaluation studies rather than clinical efficacy, derived under highly controlled circumstances. Outcome measures should include the final intended effects of the proposed health technology in terms of the ultimate change in health state brought about by the technology while the use of surrogate indicators and NNT should be avoided.

The efficacy or effectiveness data should be obtained in a systematic and transparent way. Researchers must make the presentation of the data transparent and explain the rationale for the source of the data used in the study. The inclusion of grey literature, such as research reports, master dissertations or Ph.D. theses is also considered to be very important in the Thai context.

The systematic review and meta-analysis of high quality RCTs is the most favorable method to synthesize evidence. The advantages of using systematic reviews of clinical effects are twofold[16]. First, a more precise estimate can be attained from combining the outcome data from a number of studies. Second, by using the results from studies carried out in a range of settings, assuming that these studies are sufficiently homogenous to be comparable, the estimate can then be applied to a more general patient population with different baseline risks, rather than specifically for a population group selected for an individual trial.

Where the meta-analysis of RCT is impossible for particular reasons, then evidence available in a higher hierarchy should be selected, based on the Table 1, which presents the broad agreement on the level of clinical evidence.

Moreover, the use of modeling in economic evaluation is acceptable. As recommended in various guidelines, the use of modeling methods should be considered where: (i) trial samples are not consistent with the typical patients likely to use the intervention within the context of the economic evaluation; (ii) the extrapolation of a short term clinical trial to ultimate health effects is needed; and (iii) relevant comparators have not been used or the trial did not include evidence on the relevant subgroups[5,14,18,19]. It is noteworthy that the model should be used in a transparent way but not as a replacement for scientific evidence. Transparency of selection and a clear statement describing the choice of input parameters in a model is very important. The conditions, assumptions and data creating the basis for the economic models must be clearly presented in such a manner as to make them relevant, understandable and re-examinable.

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การวัดผลได้ทางคลินิก

ยศ ตีระวัฒนานนท์, มนทรัตม์ ถาวรเจริญทรัพย์, อดุลย์ โมฮารา

การวัดและการประเมินผลได้ทางคลินิก เป็นส่วนประกอบสำคัญของการประเมินความคุ้มค่าทางการแพทย์ โดยทั่วไปผู้ตัดสินใจมักสนใจว่ามาตรการทางสุขภาพนั้นๆ สามารถนำมาใช้ในเวชปฏิบัติประจำวันได้อย่างไร ดังนั้น ผลลัพธ์ที่เกิดขึ้นภายใต้สภาวการณ์เช่นนี้ จึงเรียกว่าการวัดประสิทธิผลทางคลินิก ผลลัพธ์ทางคลินิกควรวัดผลลัพธ์สุดท้ายที่เกิดจากการใช้เทคโนโลยีด้านสุขภาพนั้น ๆ โดยวัดจากผลการเปลี่ยนแปลงสุดท้ายของสภาวะทางสุขภาพอันเนื่องมาจากเทคโนโลยีด้านสุขภาพ การทบทวนวรรณกรรมอย่างเป็นระบบ (systematic review) และการวิเคราะห์อภิมาน (meta-analysis) ของการศึกษาแบบสุ่มทางคลินิก (RCT) ที่มีคุณภาพ เป็นวิธีการที่ดีที่สุดในการสังเคราะห์หลักฐานทางคลินิก เนื่องจากเป็นวิธีการที่มีระเบียบแบบแผนและมีความโปร่งใส บทความนี้จะกล่าวถึงผลลัพธ์ทางคลินิกที่มีความน่าเชื่อถือสำหรับวิเคราะห์ต้นทุนประสิทธิผลรวมถึงการระบุและวัดผลลัพธ์ทางคลินิกอย่างเหมาะสม

Special Article

Measurement of Clinical-Effect: Utility

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The utility approach to assessing health-related quality of life is the most widely used technique for assessing preferences for health outcomes in the economic evaluation of health care. The scale for utility scores assigns a value of 1.0 to perfect health and 0.0 to death. The utility scores are employed to weigh time spent in each health state to estimate quality-adjusted life years (QALYs) gained, which is used as the denominator in cost-utility analysis and cost-effectiveness analysis. Utility scores are obtained through direct assessments using techniques such as standard gamble (SG), time-trade off (TTO), and visual analog scale (VAS), or by using multi-attribute systems such as the Health Utilities Index (HUI) or EuroQol (EQ-5D). According to international HE guidelines, the most preferred utility methods are SG and TTO, followed by EQ-5D, VAS and HUI, respectively. In Thailand, the EQ-5D is the most recommended utility method because it has acceptable feasibility and validity.

Keywords: *Utility, Preference, Health-related quality of life, Quality of life weights, Quality-adjusted life years, QALYs*

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Many diseases have a negative impact not only on patients' survival, but also on their health-related quality of life (HRQoL), which is not captured by conventional or biological clinical measures. HRQoL assessment has been extremely important for understanding the impact of diseases and treatments on patients' lives. It is a multidimensional construct including many health concepts, *e.g.* physical functioning, social and role functioning, mental health, and general health perceptions[1]. A common approach to measuring HRQoL is to employ generic and disease specific health status instruments[2,3]. The generic instruments can result in a single outcome score (health index) or a profile of scores (health profile). The index and the profile represent the two approaches to HRQoL assessment: the utility approach and the psychometric approach. Generic health profiles allow a determination of the effects of the treatment on different aspects of quality of life without necessarily using multiple instruments[4]. In addition, health profiles can be applied to a wide variety of conditions, so they allow comparisons of the effects on quality of life of different treatments in different diseases. However, generic health profiles have limitations. They may not be responsive to changes in specific conditions. For example, the items of the EuroQoL (EQ-5D) or SF-36 may not relate to symptoms that improve when antiretroviral drugs are used: fever, diarrhea, and weight loss. Another limitation of health profiles is that they do not produce a single preference score or value to calculate quality-adjusted life years (QALYs), so they cannot be used in cost-utility analysis (CUA). Utility measures of quality of life, such as standard gamble and EQ-5D, are another type of generic instrument. These measures are reported as a single index score. A major advantage of utility measurement is its application to CUA, which will be described in more details later.

The second approach to quality of life measurement focuses on aspects of health status that are specific to the area of primary interest such as disease-specific measures[4]. Specific measures therefore may be clinically sensible to the physician. The disadvantages of specific instruments are that they are not comprehensive and cannot be used to compare across conditions.

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Rationale of utility measurement and its theory

Utility is the value or worth placed on a level of health status, or improvement in health status, as measured by the preferences of individuals or society[5]. The utility measurement is necessary for the calculation of QALYs gained to ascertain the most commonly used health outcome measures in CUA and in cost-effectiveness analysis (CEA)[5,6]. Gold *et al* treat CUA as a specific type of CEA[6]. The QALY is a measure of life expectancy weighted by a utility score which is measured on a cardinal scale between 0 (death) and 1 (full health). It should be noted that the QALY also permits negative HRQoL values to represent health states worse than death[7]. In addition to application in CUA, a utility can be used for a clinical population to provide a single summary measure of HRQoL. This is because the utility score reflects both the health status and the value of that health status to the patient. Utilities can also be used as quality weights for calculating quality adjusted life expectancy as measures of population health[8]. There is no consensus regarding the most appropriate utility measurement approach. The recommendation of utility measurement in Thailand will be discussed in detail later.

The utility theory and its applications to health outcome measurement has its roots in the work of von Neumann and Morgenstern[9]. In 1944, John von Neumann, a mathematician, and Oscar Morgenstern, an economist, published their theory of rational decision-making under uncertainty, now called expected utility theory or von Neumann-Morgenstern utility theory. This decision theory described how a rational individual should make decisions when faced with uncertain outcomes. The utility approach that is based on this utility theory is called standard gamble (SG).

Sometimes the terms "utility", "value", and "preference" are interchangeably used; however, they differ. Preference is the overall concept and has two different types: utility and value. There are two important aspects of the measurement process. One is the way in which the question is framed, and if the outcomes are certain or uncertain. The other is the way in which a subject is asked to respond: scaling or making a choice. The methods of measuring utilities are shown in Table 1[5]. The first dimension of the measurement process is question framing. A question framed under certainty asks the subject to compare two or more outcomes and to choose between them or to scale them. The outcome is certain and has no probabilities. A question framed under uncertainty asks the subject to compare two alternatives where at least one of the alternatives is uncertain. This outcome contains probabilities. The difference between the two methods of questioning is that whereas the certainty method does not capture the subject's risk attitude, the uncertainty method does. In the real world future health outcomes are uncertain, so the utility method is a more appropriate measurement method than the value method.

The second aspect of the measurement process is the response method. A subject can be asked to determine their strength of preference by giving a number on a numerical scale. Alternatively, a subject can be asked to choose between two alternatives. The first approach is rooted in psychology or psychometric scaling, while the second method comes from economics and decision sciences. Many analysts prefer the choice-based method.

In summary, the methods in cells 1 and 3 measure values, while those in cell 4 measure utilities (Table 1). The difference between cells 3 and 4 is risk attitude. The difference between cells 1 and 3 is the difference between choosing and scaling. The details of each method are described in the next topic.

Utility Methods

Directly measured utility methods

There are three well-known methods of directly measuring utilities namely Visual Analog Scale (VAS), SG, and Time trade-off (TTO).

Visual analogue scale

The VAS is a common rating scale approach which is based on the information integration theory, which explains the cognitive process of judgment[10]. This theory includes two constructs: integration and valuation. Other rating scales include the rating scale (RS) and the category scale (CS). The RS refers to a

Table 1. Methods of measuring utilities

Response method	Question framing	
	Certainty (values)	Uncertainty (utilities)
Scaling	1 Rating scale Category scaling Visual analogue scale	2
Choice	3 Time trade-off	4 Standard gamble

scale of numbers, often 0-100. The CS contains a number of categories, often 0-10. The VAS shows a respondent a line, often 10 cm in length, with defined endpoints such as "death" at the lower bound and "perfect health" at the upper bound. The respondents are asked to mark the point on the scale to indicate their value of health. The line can vary in length, and be vertical (mostly) or horizontal. The VAS approach is the least difficult direct method of assessing utility, and takes less respondent time.

Standard gamble

The SG method is based on the utility theory of decision making under uncertainty proposed by von Neumann and Morgenstern[9], and is the original method of measuring utility[11]. Using the SG, utility is determined by the choices respondents make as the probabilities of immediate death or full health are varied. For example, respondents are offered two alternatives between 1) living in a health state with HIV/AIDS for the rest of their life and 2) taking a risky treatment. If the treatment were successful, the patients would live in perfect health. However, if the treatment failed, they would die immediately, with no pain. The probability of treatment success (p) is varied until the respondent is indifferent towards the two alternatives. The utility of the respondents is the probability (p) they chose. The SG approach is graphically presented in Fig. 1.

Time trade-off

The TTO is theoretically appealing because it is conceptually equivalent to a QALY. It was developed as an alternative to SG and was designed to overcome the problem of explaining probabilities to respondents[12]. In a TTO, subjects are asked about the number of years in a health state (t) they would be willing to tradeoff for a shorter life span in full health (x). The utility is x/t. For example, the respondents are given a choice between living with HIV for 10 years or living for a lesser number of years in perfect health. The utility is calculated by dividing the lesser number of years by 10 years.

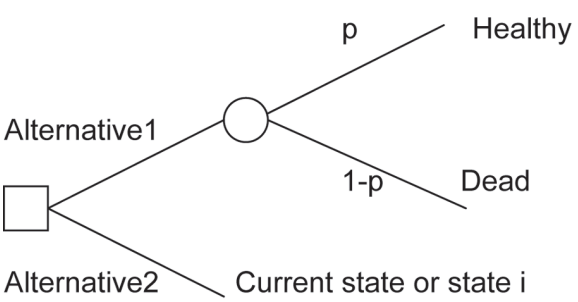

Fig. 1 Standard Gamble for a health state preferred to death

Indirectly measured utility methods

An alternative method commonly used indirectly derives utility via a multi-attribute health status classification system. This method involves a two-step procedure and makes use of health status instruments such as quality of well-being (QWB), EQ-5D, and the health utilities index (HUI). Respondents are asked to rate their level of a particular health state with several attributes e.g. mobility and pain. These attribute levels are then mapped to a 0-to-1 quality of life scale using weights that were previously elicited from the community by the instrument developers. Using these methods, respondents indirectly assign their health states to a quality of life weight or utility. Hence, these are called indirect methods of utility measurement.

Quality of well-being

The QWB scale includes 4 attributes: mobility, physical activity, social activity, and the symptom-problem complex[13]. There are 3 categories on the mobility and physical activity scales and 5 on the social activity scale. The symptom-problem complex has 27 symptoms. The scoring function is based on CS measurements from a random sample of the general public. The resulting scoring function is between 0.00-1.00. The QWB scale is time consuming to use and code. Its estimated time to complete is 15-18 minutes, but a shorter version is available.

EuroQoL

The EQ-5D includes 5 attributes: mobility, self care, usual activity, pain/discomfort, and anxiety/depression[14]. Each attribute has 3 levels: no problem, some problems, and major problem. The scoring function was measured using the TTO method on a random sample of approximately 3,000 adults in the United Kingdom[15,16]. The resulting score was between -0.59-1.00. The estimated time of completion was about 1 minute. The EQ-5D has been translated into many languages including Thai (see Appendix).

Health utilities index

The most common HUI methods are HUI2 and HUI3[17,18]. The HUI2 method was initially applied to childhood cancer. Subsequently, the HUI2 method has

been modified for adult applications. The HUI2 consists of 7 attributes: sensation, mobility, emotion, cognition, self-care, pain, and fertility. Each attribute has 4-5 levels, varying from highly impaired to normal. In addition, the fertility attribute can be easily dropped from both the classification system and the scoring formula if not needed. The HUI2 scoring function was measured on a random sample of parents of schoolchildren in Hamilton, Canada using both VAS and SG methods. The resulting score was between -0.03-1.00.

The HUI3 method was based closely on the HUI2 method. The fertility attribute, however, was dropped, and the sensory attribute was expanded into three attributes: vision, hearing, and speech. The HUI3 consists of 8 attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain with 5 or 6 levels per attribute. The HUI3 scoring function was measured on a random sample of general adult population in Hamilton, Canada using both VAS and SG methods. The final version of HUI3 employed the SG method[19]. The resulting score was between -0.36-1.00. The questionnaire takes about 10 minutes for self-administration and 2-3 minutes for interviewer administration.

SF-6D

The SF-36 was reconstructed into a six dimensional measure called the SF-6D[20]. A sample of 249 SF-6D health states were valued by 611 subjects, considered to be representative of the UK population, using the SG method. Models were developed to predict health state evaluations for all possible health states defined by the SF-6D. Brazier et al devised an algorithm for estimating utilities from existing SF-36 data via their SF-6D classification. The SF-6D was able to explain about 58% of the variance in the SG scores. The resulting score was between 0.46 - 1.00.

Other methods for deriving utilities

In addition to directly and indirectly measuring utilities methods, other approaches that can be used to derive utilities are as follows:

Expert opinion

Expert opinion can be employed to estimate utilities. It should, however, only be used when no other data sources exist or when the parameters are of secondary importance in the analysis. In addition, it should be elicited in a structured manner, such as the Delphi method[21].

Mapping VAS to SG or TTO

Since VAS is easier to administer, cheaper and less time consuming than SG and TTO, there is an attempt to map VAS to SG or TTO. However, there is a lack of evidence of a stable relationship, so SG or TTO scores should be obtained directly rather than estimating the scores from VAS.

Willingness to pay

Willingness to pay (WTP) is a technique for assessing preference for health outcomes of public health and healthcare interventions. WTP estimates are used to assess the value of heath gain in monetary values. In the WTP method, patients are asked how much they are willing to pay to be free of the disease, where a higher WTP indicates a worse quality of life. The method used to measure WTP is known as the contingent valuation method[22].

Comparisons of the international economic evaluation guidelines

Twenty-nine guidelines from 24 countries are included in the International Society of Pharmacoeconomics and Outcome Research (ISPOR) health economic (HE) guidelines including 22 HE guidelines, 6 submission guidelines for formulary listing and one for journal publication[23]. The countries that provide HE guidelines are as follows: Austria, Australia, the Baltic region (Latvia, Lithuania, Estonia), Belgium, Canada, China, France, Germany, Hungary, Ireland, Israel, Italy, Netherlands, New Zealand, Norway, Poland, Portugal, the Russian Federation, Scotland, Spain, Sweden, Switzerland, England & Wales, and the United States of America (USA).

The utility approaches that many countries (9 countries) prefer to use for economic evaluation are SG and TTO methods. These countries include Poland, Belgium, France, Switzerland, Sweden, England & Wales, Italy, Portugal and China. EQ-5D ranks as the third preferred utility method. There are countries which employ the EQ-5D: Hungary, Poland, Sweden, Portugal, New Zealand and the Baltic Region. There are 4 countries that allow the use of the VAS or the rating scale. These countries are Poland, France, Switzerland, and China. Poland and the Baltic region are the only 2 countries that recommend the use of HUI. In addition, France permits the use of a WTP approach, but it must be justified. None of the countries recommend using expert's opinions. Most of the countries do not give the reasons for selecting their preferred utility methods, but a number of countries have described that the SG

and the TTO have been chosen because they are choice-based methods or based on the utility theory, which is the sacrifice of length of life for better health, while the VAS is not appropriate because it measures value rather than utility.

Nevertheless, many countries (10 countries) do not state specifically which utility methods should be applied for HE evaluations. These countries are: the Russian Federation, Germany, the Netherlands, Austria, Ireland, Scotland, Spain, Canada, Norway, and the U.S.A. The guidelines of Canada and Austria state that the selection should be justified and those of Scotland and Ireland state that the utility methods need to be outlined and qualified. Spain and the USA have just said that generic measures should be used without specifying the preferred methods. Similarly, the Netherlands has said that direct and indirect methods should be utilized but it did not specify which methods. Germany has said that the index and profile approaches should be employed. The Russian Federation has not stated anything about the preferred utility methods.

Specifically, Norway has proposed transforming utility to value (not the same as value, which is another type of preference) and supplementing this with cost-value analysis. Nord, a well-known Norwegian health economist, has reported that valuing health programs in terms of QALYs disregards societal concerns for fairness in resource allocation[24]. Thus, obtaining estimates of value incorporating concerns of fairness, based on the degree of severity of the illness, allows a more comprehensive and valid cost-value analysis of health care.

The submission guidelines of Belgium, Israel, and the USA do not state the preferred method to derive utility, while those of the British Medical Journal, Australia, and England & Wales say that the details of the methods used need to be given. Only Canada's submission guidelines originating from the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) state a preference for the use of indirect approaches including HUI, EQ-5D, and QWB. Most guidelines suggest contemporary use of valid and reliable generic and disease specific instruments for assessing HRQoL.

Recommendations for Thai Health Technology Assessment (HTA) Guidelines

Based on international HE guidelines, the most preferred utility methods are SG and TTO, followed by EQ-5D, VAS or RS, HUI, and QWB, respectively. Which utility method should be recommended in Thailand? The following criteria for determining performance of a utility method can be used[25].

1. Practicality: Its acceptability to respondents. Such acceptability can be a function of length of time, complexity and respondents' interest in the task.

2. Reliability: The ability of a measure to reproduce the same values on separate administrations when there has been no change in the health state being valued.

3. Validity: The extent to which an instrument measures what it is intended to measure.

4. Responsiveness: Its ability to measure changes in health.

According to the psychometric criteria above, for Thai people I would recommend EQ-5D as the most preferred utility method. The reasons for choosing the EQ-5D are as follows:

In terms of practicality, compared to other direct methods (SG, TTO) and indirect methods (HUI, QWB, SF-6D), EQ-5D is shorter and easier to administer and to understand. The SG and TTO techniques are quite difficult and need well-trained interviewers. As for the HUI, QWB, and SF-6D, they are also time-consuming to administer, and thus causing respondent burden. As for VAS, it is viewed as the least difficult direct method. My study ($n = 120$) compared the performance of EQ-5D, VAS, and SG. It was found that EQ-5D was slightly easier than VAS but the difficulty rating scores were not significantly different ($p > 0.05$)[26]. One reason why the EQ-5D method was easier than the VAS method was that it provided interviewees with the dimensions of health, so they did not need to integrate them like using the VAS method.

Regarding validity, SG is undoubtedly the most theoretically appealing of the utility techniques because it has foundations in the expected utility theory which is the dominant theory of decision-making under uncertainty[9]. However, there is evidence that respondents violate the axioms of the utility theory (such as risk attitude)[27]. There is also evidence showing that SG values can be influenced by the frame of the gamble and the manner in which the task is presented[28]. The specific probabilities that are used may influence the SG scores as well[29].

An alternative method to the SG method is the TTO method. There is evidence to suggest that duration effects (a period of time of a health state) and time preference effects (the rate at which a decision maker is willing to trade a present for a future outcome) can have an impact on the elicitation of TTO values[30]. Elderly people under severe conditions often refuse to

trade off length of life because they place a greater value on survival than on their quality of life[31,32]. Some reasons for refusing to trade life time in exchange for health improvements are expressed in the following words: "I choose to live day by day", "time with my family is too precious", "the question is too hypothetical so older patients failed to grasp what was asked." In addition, both SG and TTO may be influenced by indifferent point searching procedures[33].

Even though VAS is not a choice-based technique like the SG and the TTO methods, it does not consider attitude toward risk or incorporate time horizons. The rating task can be also influenced by upper and lower bounds[34]. Subjects also tend to shy away from using the ends of the scale[35]. A rating task depends on a subject's numeric or quantitative reasoning skills[36]. If respondents have little experience with rating their health in relation to numbers, they may perform rating tasks like VAS poorly. In addition, cognitive abilities and emotions can also be a threat to the validity of the elicitation of SG, TTO, and VAS[37].

Because of the problems described above of the direct methods of deriving utilities, there is an alternative approach: discrete-state health index models or the multi-attribute health status classification system. As described before, this system works by attaching fixed utility weights to observable health states. Respondents are not required to make judgments or decisions about their utilities. Commonly used methods include EQ-5D, HUI, and QWB. Most international guidelines prefer EQ-5D to HUI or QWB. Also, the most frequently used instrument for calculating QALYs based on actual measurements of patients' HRQoL is EQ-5D[38].

Moreover, the EQ-5D method has acceptable reliability, validity, and responsiveness[39-41], even though some studies reported that the EQ-5D method had poor responsiveness[42]. It also has the problem of high ceiling effects[43,44]. The high ceiling effects and lack of sensitivity to change problems may be caused by having only three degrees of severity in the EQ-5D's dimensions. I have been told that the EuroQoL group is developing a new version of EQ-5D with five levels of severity. For now, one approach to coping with these problems is to develop a disease-specific utility instrument. This method can estimate the EQ-5D scores from disease-specific measures or map clinical data to the utility values. However, the disease-specific utility instrument does not allow for comparison across diseases, only among different strategies within the same disease.

A summary of the recommendations of utility methods in Thailand is as follows:

1. If a researcher collects a primary data of utility, EQ-5D is the most recommended utility method (the Thai algorithm version is preferred when available). Other algorithms that we can use include the UK[15], US[45], and Japanese[46] versions. Other direct and indirect utility methods such as VAS, SG, TTO, HUI, QWB, SF-6D, WTP can also be used but should be justified. The utility method selected should have data supporting the practicality, reliability, validity, and responsiveness among Thai people.

2. For a secondary data of utility, if there are Thai utilities available, the Thai utilities should be used. But if Thai data are not available, utilities from other population groups, whose characteristics are similar to those of the Thai people, should be applied. Alternatively, a systemic approach including meta-analysis should be employed to combine utilities taken from different studies. It is also recommended that they subject the results to sensitivity analyses to utilities.

3. Expert opinion, mapping VAS to TTO and SG are not recommended.

4. Disease-specific measures should be used contemporarily with utility measures.

5. A perspective of utility measurement depends on the objectives of the study. Use a patient's perspective when making treatment decisions for the individual patient; use a societal perspective (general public) when making program funding or policy decisions and generating Thai population-based utility weights for indirectly measured utility methods. A proxy can also be used when the subjects such as children, the elderly, and disabled cannot answer. A proxy can be parents, family members, or care givers. Whichever perspective or subject is applied, we must be sure that the subjects are well-informed and unbiased.

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Appendix

แบบสอบถามคุณภาพชีวิต EuroQoL (Thai version)

โปรดกาเครื่องหมาย √ ลงในกล่อง ☐ ที่แสดงถึงภาวะทางสุขภาพของข้าพเจ้าในวันนี้ได้มากที่สุด

1. *ความสามารถในการเคลื่อนไหว*
   - ☐ *ข้าพเจ้าไม่มีปัญหาเกี่ยวกับการเดิน*
   - ☐ *ข้าพเจ้ามีปัญหาเกี่ยวกับการเดินบ้าง*
   - ☐ *ข้าพเจ้าไม่สามารถเดินได้ จำเป็นต้องนอนอยู่บนเตียง*

2. *การดูแลตนเอง*
   - ☐ *ข้าพเจ้าไม่มีปัญหาในการดูแลร่างกายด้วยตนเอง*
   - ☐ *ข้าพเจ้ามีปัญหาบ้างในการใส่เสื้อผ้าหรืออาบน้ำด้วยตนเอง*
   - ☐ *ข้าพเจ้าไม่สามารถใส่เสื้อผ้าหรืออาบน้ำด้วยตนเอง*

3. *การทำกิจวัตรประจำวัน (เช่น การทำงานหาเลี้ยงชีพ, การเรียน, การทำงานบ้าน, การทำกิจกรรมกับครอบครัว, หรือการทำงานอดิเรก)*
   - ☐ *สุขภาพของข้าพเจ้าไม่มีผลต่อการทำกิจวัตรประจำวันดังกล่าวข้างต้น*
   - ☐ *สุขภาพของข้าพเจ้ามีผลบ้างต่อการทำกิจวัตรประจำวันดังกล่าวข้างต้น*
   - ☐ *สุขภาพของข้าพเจ้ามีผลทำให้ข้าพเจ้าไม่สามารถทำกิจวัตรประจำวันดังกล่าวข้างต้น*

4. *ความเจ็บปวด/ความไม่สบาย*
   - ☐ *ข้าพเจ้าไม่มีอาการปวดหรือรู้สึกไม่สบาย*
   - ☐ *ข้าพเจ้ามีอาการปวดหรือรู้สึกไม่สบายปานกลาง*
   - ☐ *ข้าพเจ้ามีอาการปวดหรือรู้สึกไม่สบายอย่างมาก*

5. *ความวิตกกังวล/ความซึมเศร้า*
   - ☐ *ข้าพเจ้าไม่มีความวิตกกังวลหรือความซึมเศร้า*
   - ☐ *ข้าพเจ้ามีความวิตกกังวลหรือความซึมเศร้าปานกลาง*
   - ☐ *ข้าพเจ้ามีความวิตกกังวลหรือความซึมเศร้าอย่างมาก*

การวัดอรรถประโยชน์

พรรณทิพา ศักดิ์ทอง

วิธีการวัดอรรถประโยชน์ (utility) เพื่อใช้ประเมินคุณภาพชีวิตที่เกี่ยวกับสุขภาพเป็นวิธีการที่ใช้กันอย่างแพร่หลายมากที่สุดเพื่อหาความพึงพอใจ (preferences) ของผลลัพธ์ทางด้านสุขภาพในการประเมินความคุ้มค่าทางการแพทย์ของการดูแลทางด้านสุขภาพ คะแนนอรรถประโยชน์จะมีค่าอยู่ระหว่าง 0-1 โดยที่ 1 เท่ากับภาวะสุขภาพที่สมบูรณ์และ 0 เท่ากับการเสียชีวิต คะแนนอรรถประโยชน์จะนำมาใช้ในการคูณกับช่วงเวลาที่ใช้ในแต่ละสภาวะทางสุขภาพเพื่อใช้สำหรับการคำนวณหาปีสุขภาวะที่เพิ่มขึ้น (quality-adjusted life years gained) ซึ่งเป็นตัวหารในการวิเคราะห์ต้นทุนอรรถประโยชน์และการวิเคราะห์ต้นทุนประสิทธิผล คะแนนอรรถประโยชน์สามารถหาได้โดยวิธีการประเมินทางตรงเช่น วิธี standard gamble (SG), time-trade off (TTO) และ visual analog scale (VAS) และโดยวิธีทางอ้อม เช่นการใช้แบบสอบถาม Health Utilities Index (HUI) และ EuroQol (EQ-5D) ตามคู่มือการประเมินเทคโนโลยีด้านสุขภาพของประเทศต่างๆ พบว่าวิธีการวัดอรรถประโยชน์ที่ได้รับความนิยมมากที่สุดคือวิธี SG และ TTO ตามมาด้วยวิธี EQ-5D, VAS, HUI ตามลำดับ สำหรับประเทศไทยวิธีของการใช้แบบสอบถาม EQ-5D น่าจะเป็นวิธีที่เหมาะสมมากที่สุดเนื่องจากวิธีการนี้มีความเป็นไปได้และมีความเที่ยงตรงที่สามารถยอมรับได้

Special Article

Handling Time in Economic Evaluation Studies

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Background: *Time horizon and discounting are important issues in economic evaluation studies and have an impact on the priority of different programs.*
Objective: *Provides supporting rational and theories to propose the appropriate discount rate for both cost and effect and time horizon for conducting economic evaluation studies in Thailand.*
Material and Method: *Describe the theories that explain time horizon for both the cost of a study and its effect.*
Conclusion: *The recommended uniform discount rate for both costs and effects at the base case is 3% with a variance in range from 0-6% by sensitivity analysis. The time horizon should be long enough to capture the full costs and effects of the programs.*

Keywords: *Time horizon, Discounting, Economic evaluation guideline, Thailand*

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Time horizon refers to the time period over which cost and outcome data should be measured. The time horizon may be short or long depending on several factors such as the nature of disease, budget and so on. An analyst must specify the time period to be long enough to capture both relevant cost and outcome data in order to adequately interpret results[1]. The period of time that an intervention should be evaluated is still a vexing question[2-5]. An unresolved issue related to the time horizon is how to incorporate the effect of interventions on diseases such as the effect of cardiovascular therapy on diabetes. It is known that interventions that extend life will result in future unrelated costs and benefits to the specific disease being examined and have to do only with the aging process itself[6]. The US Public Health Service Panel on Cost-Effectiveness in Health and Medicine[3] recommended that individual researchers use their own judgment when deciding whether to include or exclude these costs and benefits. If these costs are small relative to the magnitude of the cost-effectiveness ratio, they can be excluded. On the other hand, if these costs are quite large, they recommend using a sensitivity analysis to assess the effect of these costs and benefits.

Based on WHO recommendations[7], Cost Effectiveness Analysis (CEA) should evaluate all interventions over a period of 10 years at full implementation. This time horizon might not be appropriate in some situations, especially for chronic diseases or vaccination. In this case, the time horizon for the analysis obviously needs to be longer. Analyses must include all health effects of the intervention that occur during the 10 years or subsequently. The general rule is that the time horizon should be long enough to capture the full effects of the intervention[6,8]. This rule is supported by a study review comparing different guidelines from various countries[9].

The theory behind discounting

Why do we need to discount?[2,3,10,11]

For projects that continue longer than a one year period or with costs and effects that were incurred in different time periods, it is inappropriate to compare costs and effects. This is because their values are different in different time periods. In order to make them compatible, all values need to be adjusted to present values (present worth). Future values will be adjusted by a fixed rate called the "discount rate". Two well

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known economic concepts related to discount rates will be mentioned here: time preference and opportunity cost of capital.

1. Time preference[12]

This idea shows that people have different utilities in different time periods. They prefer to have goods and services in the present rather than in the future. If society wishes people to postpone their consumption to the future, it has to compensate or pay a premium rate to people for waiting. The premium rate is called the social rate of time preference (SRTP).

The reasons why people prefer present consumption are pure time preference and wealth effect. The pure time preference is purely psychological. Individuals may have a pure preference for the present, for example, they are impatient. The wealth effect is that the quantity of availability of consumption goods will increase over time. In other words, people expect to have higher incomes in the future. Given a decreasing marginal utility of consumption, an investment which gives one unit of the consumption good in the future in exchange with one unit of the consumption good in the present is not acceptable. Investing in the future in a growing economy will increase consumption inequality over time. Since individuals have preferences for a uniform consumption over time, a delay in consumption or investment should be implemented only if its rate of return is large enough to compensate for this negative impact on welfare. By using the two reasons mentioned above, the social rate of time preferences can be calculated from the following equation.

$$s = p + (u)(g) \qquad (1)$$

s = Social rate of time preference
p = Pure rate of time preference
u = Rate of diminishing marginal utility or the elasticity of marginal utility
g = Expected growth in consumption per head

According to Sussman F and Scheraga DJ[13], it is difficult to determine the magnitude of the first term (p) because 1) while a positive (and larger) discount rate may reflect the way in which private individuals actually behave when planning lifetime consumption and saving decisions, it may not represent the way in which, as citizens, they would ask policy makers to behave on their behalf, 2) when an environmental problem such as climate change is concerned, it is difficult to justify a rate of time preference much above zero, and 3) using too low a discount rate in project evaluation could lead current generations to sacrifice their consumption in return for small increments in future generation consumption. However, a number of economists agree that a pure time preference (p) is nonzero since it places a lower weight on damages or benefits to future generations.

The second term (ug) relates to the rate of diminishing marginal utility and growth in consumption over time. For developing nations, which may be experiencing high growth in income, (and hence consumption) at approximately 5 % to 8 % annually, discount rates as high as 10% to 16% may be reasonable[13]. Gollier C[14] stated that the larger the growth rate, the larger the socially efficient discount rate. A problem arises, however, when the growth rate is not known with absolute certainty. He also suggests a negative growth rate due to the scarcity of environment and resources.

Due to the complexity of the calculation of the social rate of time preference, other alternatives, such as saving rates, may be used as a proxy for the social rate of time preference. The average saving rate can be the social rate of time preference because the saving rate means that people save more money and consume less. Nevertheless, the weakness of saving rates is that people have different rates of time preference.

Generally, the rate of time preference is considered by many economists to be implicitly revealed in the market by interest rates on low-risk, long-term investments such as government bonds or approximately 2% to 5% in real (inflation-adjusted) terms[15]. In Thailand, most research in economics uses the social rate of time preference as a substitute for a discount rate because investment is a resource allocation for both present and future consumption. Tubpun Y[16] introduces the use of the return of government bonds for social rate of time preference because they have the lowest rate for long-term saving. Although the return is quite low, they represent the minimum value of social rate of time preference.

2. Opportunity cost of capital

Resources are scarce and there are many potential uses for any given pool of resources. Therefore, the true cost of using resources for any purpose, consumption, or investment can be described by the benefits forgone in their next best use. Resources used for a health program could be invested elsewhere such as in another health program, in the manufacturing sector, or in other public sector activities like education and high yield real returns. Thus, the opportunity

cost of the health care program is the foregone returns from investment in another health program, manufacturing, or education[17].

This idea shows that discount rate is a social opportunity cost. Basic economic theory expresses that a society or a country has limited resources which can not satisfy all the people in both the government and private sectors. When resources are used from society, there will be less available resources for other sectors. Therefore, a discount rate reflects forgone options of social capital.

The social opportunity cost of capital can be obtained from the real long term rate of return on equity capital. However, this rate may be too high for public project appraisals because public projects are less risky than private projects. Sometimes, the social opportunity cost of capital can be derived from the long term government bond rate.

The social rate of time preference and the social opportunity cost of capital can be the same rate only if a capital market is perfect competition. In practice the possibility that these two rates are equal is very unlikely. An analyst may find it difficult to determine the discount rate for a project. One way to solve this problem is to introduce a weighted discount rate. A new discount rate can be formed by using the social rate of time preference and the social opportunity cost of capital[12].

$$w = (h_1)(q) + (h_2)(s) \qquad (2)$$

w = Social weight discount rate
h_1 = The share of investment in national income
h_2 = The share of consumption in national income
s = Social rate of time preference
q = Average real rate of return on private capital

Should discount rates be equal for both costs and effects?

Discounting is performed to adjust future costs and effects for their differential timing. Discounting future costs and benefits in Cost-Benefit Analysis (CBA) is not controversial. However, discounting health effects such as life years saved (LYS), Quality Adjusted Life Years (QALYs) in CEA and Cost-Utility Analysis (CUA) respectively, has become controversial. The main argument against discounting health effects is that health, unlike wealth, cannot be invested to produce future gains[18]. Therefore, some advice from various authors suggests that health effects should not be discounted or if discounted, the rate should be very low, at 1.5%-2%[18,19].

There are several arguments in favor of both uniform and differential discount rates as described below.

1. Arguments in favor of a uniform discount rate

1.1 The consistency thesis

The US Public Health Service Panel on Cost-Effectiveness in Health and Medicine[3] points to the consistency argument of Weinstein and Stason as an important foundation when recommending the use of similar discount rates for both costs and health effects. They illustrated the consistency argument by comparing several hypothetical programs with varying timing of costs and health effects. The crucial assumption underlying their reasoning is that life years are valued the same in relation to dollars in the present as in the future. Thus, a constant steady-state relation between dollars and health benefits is assumed and opportunities for purchasing health benefits with dollars do not change over time. This implies that programs with the same cost and benefits at different points in time should receive equal priority. The only way to achieve this result is to use a uniform discount rate for both costs and health effects[3,20-22].

1.2 The paralyzing paradox

Another argument, the paralyzing paradox, purposed by Keeler and Cretin (1983) presents that under certain conditions, if program costs and effects are discounted at different rates, but rather a lower discount rate for effects when compared to that for costs, the infinite postponement of the programs would be the preferred option. This is because the cost-effectiveness (CE) ratio of any program is better if we delay program implementation. This can be illustrated by a simple example. Assume that a program costs $10,000. Costs will be discounted by 10% and effects will not be discounted. The CE ratio for this year will be $10,000 per QALY. After 1 year, the CE ratio will be $9,090 per QALY ($10,000/1.10). If the value of effects (QALY) is not discounted, then the CE ratio of the program is improved for every year it is delayed. This still persists if QALY are discounted at any rate below 10%. Therefore, without further restrictions, the program would be postponed indefinitely[3,21,22].

However, the relevance of these arguments have been challenged by a number of authors who have shown that these arguments largely rely on assumptions made about the nature of decision making and the relationship between health and money.

2 Arguments in favor of differential discount rates

2.1 Criticisms of the consistency thesis

The requirement of the consistency thesis is that health and money can be exchanged at a rate that remains constant over time. Some authors argue that health cannot be exchanged with money. Health can be exchanged for health only, in the sense that money spent today in order to save lives tomorrow could have been invested in research to save even more lives. This implies that lives are "produced" by monetary payments and not "exchangeable" for money. This is implicitly an argument for a lower discount rate for health benefits[22]. Also, health benefits can change over time due to two situations: 1) the improvement of technology in the future, which leads to a cheaper payment to save lives and 2) it becomes more costly to save lives due to environmental or other factors. This is an argument for different discount rates for costs and health effects[22]. Van Hout[5] argues that the discount rates for costs and effects should be based on the separate and probably different growth rates of wealth and health and the diminishing marginal utilities related to this growth. Therefore, the assumption of similar growth rates is debatable.

2.2 Criticisms of the paralyzing paradox

The assumption behind the paralyzing paradox is that both the benefits produced by certain costs and the population remain stable, and thus it is possible to obtain additional benefits by incurring higher costs. The theoretical foundation of Keeler and Cretin may be correct, but the following arguments can be made. First, the option of infinitely postponing health programs is not relevant for policy making because the budgets have to be spent. Also, the question that policy makers are confronted with is not whether to implement a program now or delay it, but rather which program to implement now[21,23]. Secondly, the political character of public decisions regarding the allocation of resources cannot be ignored[22]. Therefore, this paradox has no relevance in the real world, and it would appear to be difficult to maintain its validity[22].

Comparisons of the international economic evaluation guidelines

Smith DH and Gravelle H[24] conducted a thorough search for primary literature, textbooks, official and semi-official sources, and government bodies on recommendations for discounting. Sixteen different sources were identified. Of those, one indicated the discount rate for Disability Adjusted Life Years (DALYs). The remaining 15 identified sources recommended discounting for both costs and effects. Most (13 of 15) recommended a specific rate or range of discount rates. Ten resources recommended equal discount rates for both costs and effects. Only one source from the UK recommended a lower but still non-zero discount rate for health effects, but this has been changed recently[23]. Eight sources recommended that the analysis should include a 0% discount rate. The range of discount rates is between 1% and 8%. The specific rates most frequently recommended are 3% and 5%. None of the sources recommended that the rate should depend on the length of the time horizon.

Additionally, 28 health economic evaluation guidelines showed that 24 countries specify a uniform discount rate for both costs and health effects except for France, which recommends a 2.5%-5% discount rate for costs and effects, the Russian Federation, which recommends a 5% discount rate for cost and does not mention effects, Scotland, which states 6% and 1.5% discount rates for costs and effects respectively, and the British Medical Journal, which recommends a 3%-6% discount rate for costs and 0% or one lower than that used for costs as a discount rate for effects[25].

Recommendations for Thai Health Technology Assessment (HTA) Guidelines

Based on rational, theories, and information from the other international guidelines provided above, the authors purpose recommendation regarding time horizon and discounting for conducting health economic evaluation in Thailand as follows:

1. The time horizon should be long enough to capture the full costs and effects of the intervention. No other well-known international guidelines specify the appropriate time horizon that is needed for conducting health economic evaluations except for WHO, which recommends that CEA should evaluate all interventions over a period of 10 years at full implementation. From a practical perspective, a 10 year period might not be able to capture the overall costs and effects of some diseases or preventive programs. Therefore, the time horizon of the Thai health economic evaluation should be long enough to capture the full costs and effects of the intervention. In doing this, the study may use modeling techniques and/or epidemiologic data to estimate future costs and effectiveness with appropriate discounting rate to subsidize the budget needed.

2. Cost and outcome should be discounted because of economic concepts related to discount rate.

These concepts are time preference and opportunity cost of capital. The time preference implies that people have different utilities at different times. They prefer goods and services in the present rather than those in the future. Society has to compensate or pay a premium rate to people for waiting. The opportunity cost concept shows that the discount rate is the social opportunity cost. Basic economic theory expresses that a society or a country has limited resources that can not satisfy all the people. When resources are used from society, there will be less available resources for other sectors.

3. Discounting costs and outcomes should be done using the same rate. Two arguments that imply a uniform discount rate for both costs and effects are the consistency thesis and the paralyzing paradox. Although both arguments have received criticism from various authors, the current practice of discounting in health economic evaluation still seems to be based on these two arguments. Additionally, as shown in the most well-known accepted international guidelines, a uniform discount rate for both costs and effects is implicitly recommended. Furthermore, the National Institute for Health and Clinical Excellence (NICE), which once used differential discount rates for costs (6%) and effects (1.5%), has recently changed their recommendation of their discount rate to 3.5% for both costs and effects. Therefore, the application of the same rate for discounting costs and effects in Thai health HTA guidelines is recommended.

4. The appropriate discount rate for cost and outcome at the base case is 3% and an analyst should perform sensitivity analysis using a uniform discount rate ranging from 0-6%.

5. Calculations for discounting are straightforward as shown in the formula below.

$$PV = FV * (1/(1+r)^t)$$

PV = present value; FV = future value

r = the discount rate; t = the duration or time at year t

$(1/(1+r)^t)$ is called discounting factor.

Conclusion

The recommended discount rate for costs and effects at the base case is 3%. A sensitivity analysis should be conducted by varying its range from 0-6%. The time horizon should be long enough to capture the full costs and effects of the intervention of the implemented programs.

Acknowledgements

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การจัดการกับเวลาในการประเมินความคุ้มค่าทางการแพทย์

อัญชลี เพิ่มสุวรรณ, กันต์สินี กันทะวงศ์วาร, ปิยะลักษณ์ พุทธวงศ์

กรอบเวลาและการปรับลดเป็นประเด็นสำคัญในการประเมินทางความคุ้มค่าทางการแพทย์ ซึ่งมีผลกระทบต่อการจัดลำดับความสำคัญของโครงการต่าง ๆ ที่เปรียบเทียบกัน บทความนี้ได้นำเสนอเหตุผลและทฤษฎีสนับสนุนสำหรับอัตราลดของต้นทุนและผลลัพธ์ และกรอบเวลาในการประเมินความคุ้มค่าทางการแพทย์ในประเทศไทย อัตราลดของต้นทุนและผลลัพธ์ที่แนะนำในกรณีพื้นฐานทั่วไปคือ ร้อยละ 3 และเปลี่ยนช่วงอัตราลด ร้อยละ 0-6 โดยใช้การวิเคราะห์ความไว กรอบเวลาควรมีระยะเวลายาวนานเพียงพอให้ครอบคลุมต้นทุน และผลลัพธ์ของโครงการ

Special Article

Handling Uncertainty of the Economic Evaluation Result: Sensitivity Analysis

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An economic evaluation of health technology and interventions often comes with uncertainty in the parameters that were used in the model. To determine sensitivity of the result obtained from a reference case analysis, researchers can employ deterministic and probabilistic approaches. This methodological guideline summarizes the principles underlying the sensitivity analysis and recommends that the probabilistic sensitivity analysis is the best method to handle the parameter uncertainty.

Keywords: *Acceptability curve, Monte Carlo simulation, Sensitivity analysis, Tornado diagram*

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The result obtained from an economic evaluation of health technology and interventions can vary upon and be very sensitive to the assumptions and certain parameters specified in a reference (or base) case analysis. In addition, transferring the analysis result from one setting to another may introduce additional uncertainty due to differences in economic and health care contexts. A methodological approach to the parameter uncertainty is called sensitivity analysis (SA) and will be the focus of the present article.

Types of sensitivity analysis

Briggs classified methods of handling uncertainty due to parameters in the economic evaluation model into three types[1]. The first approach is called a deterministic sensitivity analysis (DSA). This DSA is conducted by varying the value of each parameter, given that the remaining parameters are constant. The second approach is an extreme scenario analysis, in which several important parameters are set under two extreme scenarios (the best-case vs. the worst-case) for the intervention of interest. The last approach is a probabilistic sensitivity analysis (PSA) which assumes that a variation in each of the parameters follows a defined pattern of data distribution. The next subsection sheds light on a detailed analysis approach for common SA.

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Deterministic sensitivity analysis

The most common type of DSA is the oneway sensitivity analysis, which is found in more than 70% of publications[2]. In this simplest SA, one parameter is set to vary over a reasonable range (for example, minimum-maximum, standard deviation, 95% confidence interval), one at a time. Then, the resulting cost, effectiveness, and cost-effectiveness ratio (CER) are determined accordingly. The sensitivity of the results can be easily detected through a line graph depicting the relationship between the varying cost- or effectiveness-related parameters and the cost and effectiveness outcomes (Fig. 1 and 2).

The above one-way SA shows a variation in the CER of tissue plasminogen activator (t-PA) when compared with streptokinase due to varying clinical efficacy (in terms of an increase in patient survival) and treatment cost of t-PA[3]. Noticeably, a reduction in CER of t-PA, due to an increase in t-PA efficacy, is not linear and is very sensitive to the first 2-5 years of increased survival (Fig. 1), whereas the result is proportional to the whole range of treatment cost increment (Fig. 2).

Tornado diagram

An alternative presentation of one-way SA is

a tornado diagram. In the diagram, sensitivity of the study result is reflected through the length (maximum-minimum values) of a horizontal bar that represents variation in the cost and effectiveness outcomes for each parameter. The very influential parameters appear at the cloud level or at the top of the tornado, whereas the less influential parameters are at the base of the tornado. The reference case result is a vertical straight line stretching through the tornado touchdown point.

Fig. 3 illustrates a tornado diagram of the referent CER for paclitaxel used additionally to anthracyclines as an adjuvant in early stage breast cancer[4]. The relative efficacy (in terms of hazard ratio, HR) of paclitaxel can affect the study result a lot more than variations in adverse drug events, treatment of recurrence, and terminal care cost.

A major limitation of one-way SA is that it cannot accommodate all parameter uncertainties, whereas the extreme scenario analysis tends to exaggerate true uncertainty. Manning et al. argued that probabilistic sensitivity analysis (PSA) would capture the uncertainty to within a fraction of the actual uncertainty[5]. This will be elaborated in the next subsection.

Probabilistic sensitivity analysis

Recent papers have proposed innovative

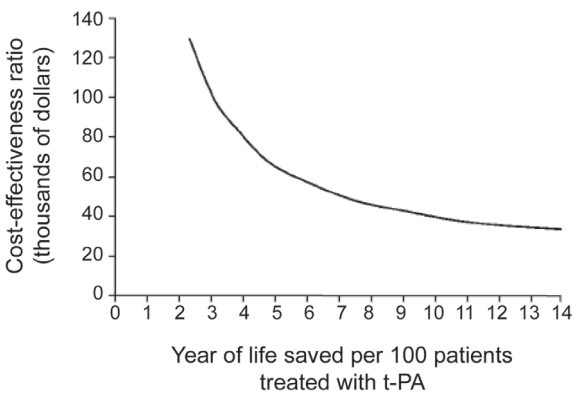
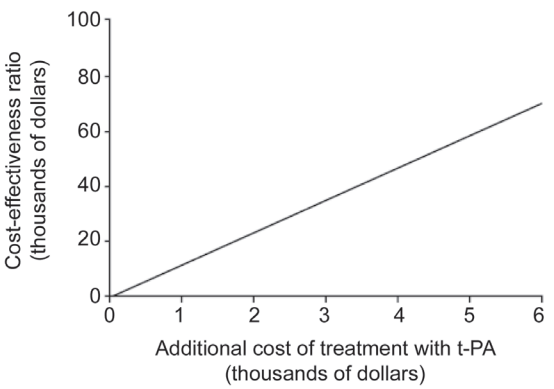
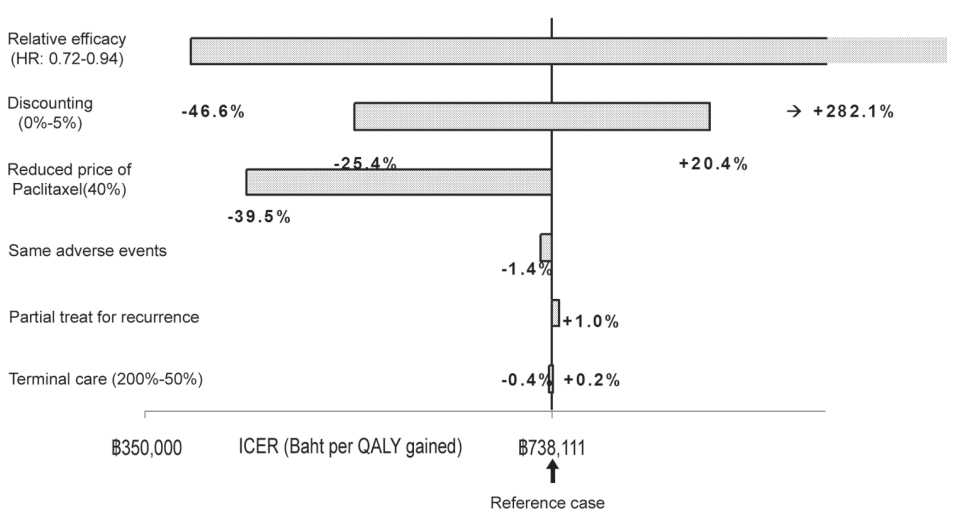


Fig. 1 One-way SA due to a change in patient survival from t-PA as compared with streptokinase



Source: Mark et al (1995)

Fig. 2 One-way SA due to the treatment cost difference between t-PA and streptokinase



Source: Limwattananon et al (2006)

Fig. 3 Sensitivity of CER for paclitaxel due to various model parameters

methods in handling the uncertainty due to parameters derived from the secondary data and individual-level information[6-8]. Probabilistic sensitivity analysis (PSA) is a more powerful approach in dealing with the uncertainty stemming from several parameters. Performing PSA is facilitated by a computer-based Monte Carlo simulation. This is done through feeding a randomly selected set of parameters into the analysis model repeatedly several hundred or even several thousand times. How the values of each parameter will be selected depends upon the defined data distribution. Table 1 presents data distribution patterns commonly used for cost- and effectiveness-related parameters.

It should be noted that a normal distribution as assumed for conventional parametric statistics plays a limited role in PSA since most real-world economic and health data do not behave well. In Table 1, the parameters on probability and utility follow a beta distribution, in which the minimum and maximum values are restricted to zero and one. The relative efficacy (or relative risk) of an intervention tends to be distributed normally after the parameters are transformed by a logarithmic function. For the cost parameter, several economists have stated that its variance is not constant and can be approximated as a square of the mean and this fits a gamma distribution[9-12].

Fig. 4 illustrates the PSA of an economic evaluation of anastrozole as an adjuvant for early-stage breast cancer, using a cost-effectiveness (CE) plane[13]. The horizontal axis represents the incremental effectiveness of the drug of interest as compared with the standard tamoxifen therapy in terms of quality-adjusted life years (QALYs). The vertical axis captures the cost difference in Baht between the two interventions. Uncertainty in the effectiveness and cost is reflected by the distribution of 1,000 dots generated by running the Monte Carlo simulation 1,000 times for the important cost and effectiveness-related parameters and assuming various data distributions as shown in Table 1.

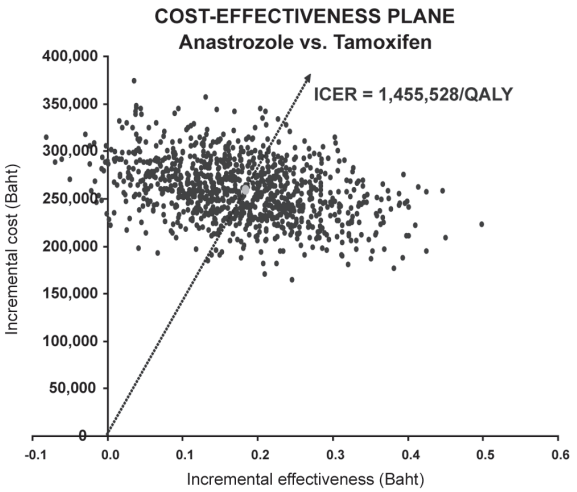
The result from the reference case analysis is the dot located in the middle of the 1,000 uncertainty dots. The incremental cost-effectiveness ratio (ICER) of anastrozole (as compared with tamoxifen) is equal to the slope of the straight line drawn from the origin to the reference case dot. This is equal to 1,455,528 Baht/QALY. Notably, the reference case ICER divides the cost-effectiveness uncertainty cluster into two groups. Approximately half of the uncertainty dots are located in the left-hand side of the reference ICER and have the ICERs greater than 1,455,528 Baht/QALY whereas the second half, to the right, encompasses a relatively lower ICER when compared with the reference case. This means that if one set the cost-effectiveness threshold at 1,455,528 Baht/QALY, anastrozole would have an approximately 50% chance (or probability = 0.5) of becoming cost-effective. Hence, the probability that an intervention will become cost-effective can be derived from the proportion of the uncertainty dots lying below the ICER line. The PSA depicted by this uncertainty plot on the CE plane can be used to determine how likely it is that an intervention of interest will be accepted as a cost-effective intervention with respect to varying ICER thresholds. This will be explained through the decision criteria in the next subsection.

Net benefit approach

Probabilistic sensitivity analysis is helpful in overcoming the limitation due to the use of a single CER threshold as the decision rule for cost-effective interventions. The fact that both the cost numerator and the effectiveness denominator are unavoidably uncertain in some degrees will make the derived ratio (i.e., ICER) even more complicated in its uncertainty. In addition, if the point estimate of the ICER result was negative, the authors would not know exactly if the numerator or denominator is negative (in other words, the intervention of interest was either less expensive or less effective than the comparator). An alternative approach is to vary the predetermined ICER threshold, then see how likely the intervention of interest will produce its ICER below such a threshold. This decision criterion is called a 'net benefit approach (NBA)'.

Table 1. Data distribution for cost and effectiveness parameters

Parameter	Family of distribution	Nature of data	Possible range
Probability	Beta distribution	Proportion	0-1
Utility	Beta distribution	Integer	0-1 (0 = death, 1 = full health)
Relative efficacy or relative risk	Log-normal distribution	Ratio	0-11 – Positive numbers
Cost	Gamma distribution	Very skew	Positive numbers



Source: Limwattananon et al (2005a)

Fig. 4 Uncertainty of the incremental cost and effectiveness of anastrozole

The principle of NBA can be explained through the following formulations:

Given that:

C_A is the total cost incurred by an intervention of interest 'A'

C_B is the total cost incurred by an appropriate comparator 'B'

E_A is the effectiveness outcome of 'A'

E_B is the effectiveness outcome of 'B'

IC is the incremental cost of 'A' when compared with 'B'

IB is the incremental effectiveness of 'A' when compared with 'B'

$ICER_{A\ vs.\ B}$ is the incremental cost-effectiveness ratio of 'A' when compared with 'B' and is equal to the ratio between IC and IE

$$ICER_{A\ vs.\ B} = IC/IE = (C_A - C_B) / (E_A - E_B)$$

Willingness to pay (WTP) is a monetary threshold (or ceiling ratio) to be traded off for an effectiveness unit of A relative to that of B. Hence, the intervention A is deemed 'cost-effective' as long as the $ICER_{A\ vs.\ B}$ is less than the set WTP threshold.

Based on the Monte Carlo simulation, which results in a cluster of the ICER uncertainty dots, an initiation of NBA is used to define a monetary threshold (i.e., economic cost) that societies, payers, or patients (depending on whose perspective) are willing to pay for a unit of effectiveness (e.g., year of life, QALY) gained by the intervention of interest relative to a comparator. In the CE plane, the number of uncertainty dots below such a threshold proportional to all dots was counted as the % acceptance of cost-effectiveness.

Fig. 5 illustrates the PSA of the addition of trastuzumab to a conventional chemotherapy (paclitaxel) for treating metastatic breast cancer[14].

The authors can see that trastuzumab is unlikely to be cost-effective if the society's WTP is not beyond 1 million Baht per QALY gained. Even though the society is willing to pay as much as 2 million Baht per QALY for the effectiveness of trastuzumab, the chance that the drug will be accepted as a cost-effective intervention is less than 20%.

The NBA for a cost-effectiveness decision can be operationalized through the measures of net health benefit –NHB[15] and net monetary benefit –NMB[7,16].

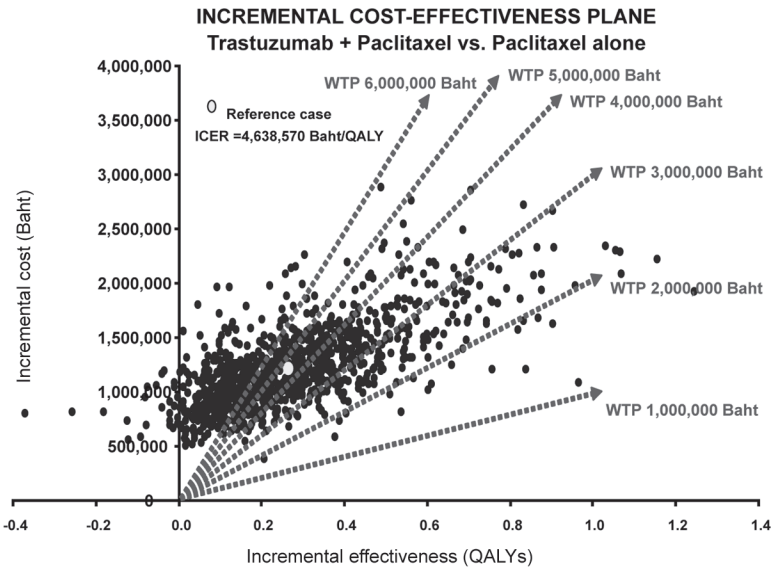
The NHB is a measure in an effectiveness scale which is a magnitude of the difference between the incremental effectiveness (IE) and the ratio of the incremental cost (IC) divided by the WTP threshold. Similarly, the NMB is a measure in a cost scale which is equal to the difference between the product of IE multiplied by WTP and minus the IC.

$$NHB = (E_A - E_B) - [(C_A - C_B) / WTP]$$
$$NMB = [(E_A - E_B)WTP] - (C_A - C_B)$$

Acceptability curve

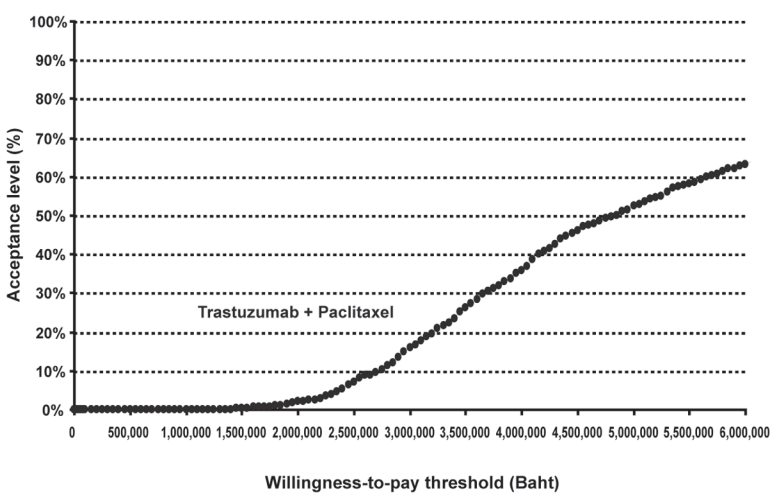
If the NHB or NMB is positive (or greater than zero), the intervention 'A' is considered a cost-effective intervention. This means that intervention 'A' yields, in the NHB sense, an increase in effectiveness at a greater extent than the effectiveness that could be expected from the set WTP threshold or, in the NMB sense, an increase in cost at a lower extent than the cost expected from the set threshold. When the WTP threshold is raised, the likelihood that intervention 'A' becomes cost-effective will increase accordingly. This process will be performed repeatedly with respect to an increasing WTP until the cost-effectiveness acceptance for intervention 'A' approaches 100%. The relationship between varying WTP thresholds and the likelihood (%) of cost-effectiveness can be depicted by an acceptability curve[8,17] (Fig. 6).

The acceptability curve for trastuzumab (Fig. 6) crosses the horizontal axis at approximately 1.1 million Baht of the WTP threshold[14]. This means that if the society is willing to pay for a one-year increase in the patient's life at the amount of 1 million Baht, trastuzumab will not be cost-effective at all. The drug will, however, have more than a 50% chance of becoming



Source: Limwattananon et al (2005b)

Fig. 5 Uncertainty of the incremental cost-effectiveness of trastuzumab



Source: Limwattananon et al (2005b)

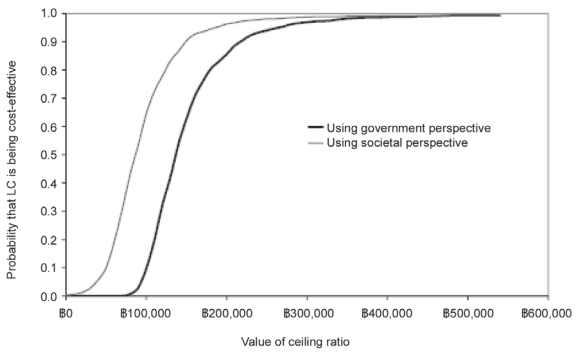
Fig. 6 Acceptability curve of trastuzumab for metastatic breast cancer

cost-effective if the WTP of the society is more than 5 million Baht per QALY.

With this same acceptability curve, the 95% CI for ICER of trastuzumab can be determined by the 2.5% and 97.5% acceptance levels. In this case, the lower limit of 95% CI for ICER is equal to 2.1 million Baht per QALY, whereas the upper limit is beyond the limits depicted by this curve.

The acceptability curve can be used to demonstrate the cost-effectiveness likelihood for varying scenarios used in CEA. Fig. 7 illustrates the CEA results from two perspectives, the government's and societal[18].

If there were no resources intended to be devoted to the incremental effectiveness delivered by an innovative health interventions (i.e., zero WTP), the



Source: Teerawattananon et al (2005)

Fig. 7 Cost-effectiveness acceptability curve for laparoscopic cholecystectomy

conventional open cholecystectomy (OC) would be more cost-effective for managing gallbladder-stone disease in Thailand than laparoscopic cholecystectomy (LC). Not until the WTP reaches 90,000 Baht based on the societal perspective (or 140,000 Baht based on the government's perspective) per one QALY gained that LC would be more likely to be cost-effective than OC. The likelihood of LC dominating OC would not be greater than 95% unless the WTP was greater than 190,000 and 270,000 Baht per QALY based on the societal and government's perspectives, respectively.

Recommendations

The best SA of the economic evaluation result due to parameter uncertainty is PSA. The PSA can be achieved if the mean (or proportion) values and the standard error (SE) of input parameters used in the CEA model are known. This is usually the case if the individual level observations are readily available. Otherwise, the mean (or proportion) and SE need to be reported. The assumed data distribution appropriate for the components related to cost and effectiveness will determine the variations in cost and effectiveness of the compared interventions facilitated by the iterative process of the Monte Carlo simulation. The WTP threshold set by society (in the case of using the societal perspective for an analysis) per unit gain in effectiveness will determine the likelihood that an intervention of interest would be deemed cost-effective. The NBA approach is the fundamental of this decision rule, which is reflected through a cost-effectiveness acceptability curve.

If the individual-level data is not available or there is no reported mean (or proportion) or SE, sensitivity of the CEA result can be analyzed using a conventional deterministic SA. The easiest approach is a one-way SA where uncertain parameters are set to vary one at a time, holding other parameters constant. A tornado diagram can help identify the most influential parameter on sensitivity of the CEA result.

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การจัดการกับความไม่แน่นอนของผลลัพธ์จากการประเมินความคุ้มค่าทางการแพทย์ภาวิเคราะห์ความไว

สุพล ลิมวัฒนานนท์

การประเมินความคุ้มค่าทางการแพทย์ของเทคโนโลยีและมาตรการด้านสุขภาพมักประสบกับความไม่แน่นอนของข้อมูลจากตัวแปรที่ใช้วิเคราะห์ในแบบจำลอง เพื่อแสดงให้เห็นถึงความไวของผลลัพธ์ซึ่งได้จากการวิเคราะห์ที่ค่าอ้างอิง นักวิจัยสามารถใช้วิธีทั้งแบบที่อาศัยและไม่อาศัยความน่าจะเป็น บทความนี้จะสรุปหลักการของการวิเคราะห์ความไวและเสนอแนะว่าการวิเคราะห์ความไวแบบอาศัยความน่าจะเป็นเป็นวิธีที่ดีที่สุดในการจัดการกับความไม่แน่นอนที่เกิดจากตัวแปรต่าง ๆ

Special Article

Presentation of Economic Evaluation Results

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In Thailand, economic evaluation results are being increasingly used for making health care resource allocation decisions. To assess the usefulness of economic evaluation information, users of studies such as policy decision makers or health care providers need to know whether the methods used in the study are appropriate and whether the results are valid. The quality of previous economic evaluation studies, however, was quite poor. The objectives of this article are to review the similarities and differences in reporting formats based on existing reporting formats suggested by published methodological guidelines for economic evaluation, and to provide recommendations for economic evaluation result presentation for Thai Health Technology Assessment guidelines. The article presents a recommended reporting format including ten key elements necessary for economic evaluation techniques. The recommended format will increase the transparency of studies as well as facilitate comparisons between studies. This may eventually lead to high-quality and reliable economic evaluation studies available for policy decision making in Thailand.

Keywords: *Result presentation, Economic evaluation, Thailand, Reporting format*

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Economic evaluation studies is used to improve decisions about the allocation of health care resources. In order to evaluate the usefulness of economic evaluation results, users of studies i.e., policy makers and health care providers, need to know whether the methods used in the study are appropriate, whether the results are valid and whether the results can ultimately be applied to their settings. Currently, some published methodological guidelines for economic evaluation recommend that reporting formats need to present results. There are a number of reasons why a standardized reporting format for economic evaluation would be useful[1]. The first reason is that the transparency of studies will be increased because it will be more straightforward to accurately evaluate whether the methods are proper and to determine what the researchers have analyzed[2]. Second, it may help to compare the results between studies. For example, if the results of cost-effectiveness ratios were presented in a similar format, the users or readers would be more certain that the differences in the ratios between studies indicated the characteristics of the interventions being evaluated rather than differences in study methodologies. Lastly, a standardized reporting format would improve the quality of studies as analysts will be required to specify the important methodological considerations in the report.

Consequently, the reporting format for presentations of economic evaluation results is tremendously important and necessary, especially in Thailand, a developing country where economic evaluation results have been increasingly used for policy decision-making. This is true because the quality of previous economic evaluation studies in Thailand was poor[3]. The objectives of this article are to review the similarities and differences in reporting formats based on existing reporting formats suggested by published methodological guidelines for economic evaluation, and to provide a recommendation for economic evaluation result presentations for Thai Health Technology Assessment (HTA) guidelines.

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Similarities and Differences of Existing Reporting Formats

Based on the published methodological guidelines for economic evaluation, there are a number of similarities along with several differences among available existing reporting formats. A number of reporting formats are used by the Commonwealth of Australia, the Ontario Ministry of Health[4], the Canadian Co-ordinating Office for Health Technology Assessment[5], and the National Institute for Clinical Excellence[6] for the provision of economic data before the reimbursement of pharmaceuticals. In addition, the reporting formats recommended by the US Public Health Service Panel on Cost-Effectiveness in Health and Medicine[7], and the British Medical Journal (BMJ) Working Party on Economic Evaluation[8], are more focused on the methodological standards in published studies and on how to interpret the results of economic evaluation by decision makers. Moreover, the reporting format proposed by the Task Force on Principles of Economic Analysis of Health Care Technology emphasises the importance of methodological issues and the relationship between researchers and sponsors[9].

Several reviews have compared the similarities and differences between economic evaluation guidelines[10-12]; even though there are differences among various proposed reporting formats, these reporting formats recommended by existing guidelines include common details regarding:

1) the background/rationale of the problem;

2) the viewpoint of the analysis;

3) the reasons for selecting the type of analysis;

4) the population to which the analysis applies;

5) the comparators being assessed;

6) the source of the medical evidence and its quality;

7) the range of costs considered and their measurement in physical and monetary terms;

8) the measure of effectiveness/benefits in the economic study;

9) the methods for adjusting the timing of costs and benefits;

10) the methods for dealing with uncertainty;

11) the incremental analysis of costs and benefits;

12) the overall results of the study and its limitations;

From the list above, there is a consensus on the requirement to report major components of study methodologies. However, there is no complete agreement on how each methodological issue should be handled. Based on the review of 25 published guidelines for economic evaluation, Hjelmgren *et al*[11] found that the guidelines were in agreement of about 75% of methodological aspects. Disagreement between guidelines was highlighted in the choice of perspective, resources, costs that should be included in the analysis, and methods of evaluation that resources used. These differences were due to the dissimilar health systems of each country and the different purposes of the guidelines. For example, Tarn *et al*[13] reviewed and compared 28 pharmacoeconomic guidelines from 23 countries based on 32 key features. Regarding the standard reporting format, they found that nine guidelines (the Baltic countries (Latvia, Lithuania, Estonia), Finland, France, Ireland, New Zealand, Scotland, Spain, Sweden, and, England & Wales) did not include a standard reporting format while eleven guidelines (the Baltic countries (Latvia, Lithuania, Estonia), Canada, Germany, Ireland, Poland, Portugal, Hungary, Sweden, Belgium, the Canadian Common Drug Review, and the US) recommended the disclosure of funding or an author's potential conflict of interest.

Recommendations on Thai Health Technology Assessment (HTA) Guidelines

Most guidelines specify a required reporting format to present the results from economic evaluations. Regarding the Thai HTA guidelines, a common recommendation is that all ten key elements should be clearly stated as follows.

1) Defining the scope of the study

2) Selection of comparator(s)

3) Defining the type of economic evaluation

4) Measurement of costs

5) Measurement of clinical effects

6) Handling time in economic evaluation studies

7) Handling uncertainty and sensitivity analysis

8) Presentation of the results

9) Discussion of the results

10) Disclosure of funding and author's conflict of interest

1) Defining the scope of the study

A framework is an introduction commonly providing the background of the study, the economic

and clinical importance of the study, and a description of the study design. The rationale of the problem should be addressed and the program or intervention being analyzed should be carefully described. Moreover, the objective of the study should be addressed. Enough details should be provided for readers to be able to evaluate the appropriateness of generalizing the results of the analysis.

The perspective of the study should be clearly indicated at the beginning of the report because it is an important part of the study which defines the costs and effects related to the analysis. In addition, the scope and boundaries of both the analysis and the time horizon should be clarified. The boundaries are defined by the groups of people included and the type of effects analyzed. The time horizon describes how long the resource use and effects are to be measured for.

2) Selection of comparator(s)

The explanation of the intervention contains the characteristics of the target population, the care settings, the mode of service delivery, and the timing of the intervention. The characteristics of the target populations may include age, gender, race, socioeconomic status, clinical history, geographic location or other descriptors. The care settings, such as hospitals, ambulatory clinics, or primary care practices should be described. The mode of service delivery such as equipment, personnel, and other aspects of the strategy used, should be also indicated.

The description of the comparators should be specified and the reason why the comparators are selected should be addressed. The comparators are the best available alternative as defined by clinical guidelines, an inexpensive alternative, or a "do-nothing" alternative. An explanation of these alternatives may help readers understand how they relate to current practice.

3) Defining types of economic evaluation

The type of economic evaluation used in the analysis (*i.e.* cost-minimization analysis, cost-benefit analysis, cost-effective analysis, or cost-utility analysis) should be reported including the strategy, structure, and important assumptions. It is also important to indicate the outcome(s) of interest.

If the mathematical or simulation model is used, the method (*e.g.* decision tree model, state-transition or Markov model, or a probabilistic simulation model) and all assumptions used in the model should be specified. If the Markov model is used, health states, cycle length, mechanisms for movement between states in simulation models, and the special features of the analysis should be explained. A diagram of the event pathway of the model and the software used should also be presented. In the case of using a model, the tests performed to demonstrate the accuracy of the programming and to establish the face validity of the model calculations should be described in brief. Moreover, the tests on the performance of the model using extreme assumptions will demonstrate to the readers that the model gives predictable results.

4) Measurement of costs

The cost section should include the year in which the costs are presented in the study and the type of currency used. The year will allow the readers to interpret the cost-effectiveness ratio, or compare it with the results of other studies. All costs due to the intervention and related events following the intervention in reference case-values, should be reported. Adjustments for inflation such as use of the medical component of the Consumer Price Index (CPI) should be specified where applicable. In addition, it is recommended that the types of costs, such as direct and/or indirect be stated. It is also suggested that the cost per unit of each resource, the number of units consumed, the method for cost valuation, and the source of data for each estimate in a table be presented. It is essential to report whether the cost or charge data have been used, and whether the ratios of cost to charge have been applied. It is also necessary to mention the quality of the cost data as well.

5) Measurement of clinical effects

An understanding of the source of effectiveness in the analysis is essential to evaluate the quality of the analysis and the appropriate use of its results. The effectiveness content should be discussed regarding the evidence of effectiveness of the intervention, the nature of the relevant disagreement, and the direction of the evidence. The rationale and necessary assumptions should be presented to provide estimates of effectiveness for the analysis when primary research or studies from supporting literature are used. Also the inclusion and exclusion criteria of the literature review should be notified. If program-specific primary data is utilized, the general strategy used and important assumptions made should be clarified. For example, to extrapolate survival beyond the end of the empirical data, survival analysis may

have been used. If this is the case, the assumptions should be addressed in the report. If a survey is used, the response rate should be reported. The effectiveness section includes the assumptions required and the mechanisms used to incorporate data into an analysis. It is helpful to summarize estimates of effectiveness at the reference case values used in the analysis in a table for convenient reference by the readers.

Information on health states or utility may have been collected previously by measuring health states directly within the study, or by asking experts to determine the health states. The instruments that have been used (*e.g.* the Health Utilities Index or the EuroQoL), the information explaining the measurement, as well as the methods used for value-outcomes (*e.g.* rating scale or time trade off), should be reported. It is recommended that the different health states used in the study and the related preference weight in a table format be presented.

In the analysis, if experts are required to provide input (*e.g.* estimate probabilities, costs, preference weights, etc.), the basis for selecting the experts, the source of their expertise, the number of experts contributing, the reason for using expert judgment, and the process used to obtain their input should be clearly described.

6) Handling time in economic evaluation studies

When a study period is longer than one year, it requires costs and health effects to be discounted. In these cases, it should be stated whether both costs and health effects are discounted as well as giving a statement of the discount rate.

7) Handling uncertainty and sensitivity analysis

Both the methods used to evaluate the effects of uncertainty in the analysis and the important results with confidence interval of the cost-effectiveness ratio should be presented. The choice of variables and the ranges used in the sensitivity analysis also should be reported. If the Monte Carlo simulation is used, the tests of the assumptions made concerning the distributions of variables and their statistical independence should be included.

8) Presentation of the results

Reference case results should be presented as a table of costs and effects of all the alternatives. For each alternative, it is recommended that per capita of total costs, total effectiveness, incremental costs, incremental effectiveness, and incremental cost-effectiveness ratios (ICER) be reported in an accompanying table. Although the discounted results using the discount rate at reference case are presented as the main results, the presentation should include both the discounted and undiscounted results.

If possible, the aggregate and disaggregate results on costs, outcomes and cost-effectiveness ratios should be presented to provide information about the effects of the intervention at both a population and individual level. It is suggested that years of life saved and quality adjusted life years saved (QALYs) should be reported in order to provide readers with an understanding of the relative importance of life-lengthening and the quality-enhancing benefits of the intervention. Additionally, costs and cost-effectiveness ratios should be presented in Thai currency (baht) on the cost per unit of effectiveness with the year of the cost calculation, for example 50,000 baht per QALY saved (2008 baht value). The costs and incremental cost-effectiveness ratios should also be rounded to whole baht or to the nearest thousand, and the effectiveness should be rounded, where appropriate. If there is a dominant option (*i.e.* a higher cost and lower effectiveness than other options), it should be specified in the table that the option is "dominant" instead of reporting the ratios. It is not recommended to report the average or absolute cost-effectiveness ratios for each alternative, because the readers may be confused and it may lead to a misinterpretation of the results[3].

It is also suggested that graphical presentations of the study results would be helpful for general readers. If the incremental cost-effectiveness results are presented graphically, the incremental costs (two consecutive interventions) should be displayed on the vertical axis and the incremental effectiveness (*i.e.* QALY) should be on the horizontal axis, so that the slope of the line segment represents the increment cost-effectiveness ratio. In addition, if a probabilistic sensitivity analysis is performed, cost-effectiveness acceptability curves, which present the relationship between the value of ceiling ratios (willingness to pay for a unit of outcomes) and the probability of favoring each treatment strategies, are also recommended.

9) Discussion of the results

This section should start with a descriptive interpretation of the quantitative results of economic evaluation followed by a discussion of the overall effect of important assumptions and the results from the sensitivity analysis of key parameters. The limitations of the study, for example the assumptions based

on expert opinions, theoretical models, or incomplete data, should also be stated to help the readers interpret and generalize the results.

A comparison of results from other economic evaluation studies of similar or related interventions should be included. In doing so, the currency year used in other studies should be converted to the year used in the author's study using the Consumer Price Index (CPI). If the year of analysis is not specified in the report, it is suggested that three years before the date of publication be used. It is also important that the similarities and differences of results between studies be clearly explained

The cost-effectiveness of an intervention can only be determined relative to other interventions. It is difficult to make certain statements regarding the incremental cost-effectiveness ratio of the intervention alone. Whether an intervention should be implemented depends on the resources available, alternative uses of resources, and other constraints considered by decision makers. As a result, researchers should be careful when stating that an intervention is "cost-effective" or "not cost-effective".

It is proposed that the potential budgetary impact on public and private healthcare expenditure should be estimated and discussed. This should include the impact on annual budgeting and the cumulative impact over a relevant period. It is also important to highlight the possible savings or additional non-monetary resources needed when the intervention is implemented. In addition, it may be important to discuss whether the introduction of the intervention will lead to increased or decreased need for related health care services. Equity or ethical considerations related to the introduction of the new intervention, for example access or utilisation of healthcare, reduced or increased inequality in health status, effect on a disadvantaged social group, should also be discussed.

10) Disclosure of funding and author's conflict of interest

The study should reveal the source of financial support of the study in order to make it transparent. The relationship between the authors and financial supporters and/or the authors' potential conflict of interest with the funding sources should also be specified.

Final remarks

Guidelines demand a uniform approach for reporting results from economic evaluation to increase the transparency of studies, facilitate comparisons between studies, or improve the general quality of the evaluation undertaken. A common recommendation is that all ten key elements discussed earlier in the guidelines be clearly stated in the report.

To help guide general readers, the authors have developed a report checklist (see Appendix) which summarizes the above recommendations. It is suggested that this checklist be used alongside the guidelines to facilitate assessment on whether the methods used in the study are appropriate and whether the results are valid. It is also considered that the guidelines and report checklist may be potentially useful if national or local health care authorities require a submission of the economic evaluation studies conducted by stakeholders in addition to clinical data for the consideration of the adoption of health technology in health care benefit packages.

Acknowledgement

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การรายงานผลการประเมินความคุ้มค่าทางการแพทย์

อุษา ฉายเกล็ดแก้ว, ยศ ตีระวัฒนานนท์

ในประเทศไทย ผลลัพธ์ที่ได้จากการประเมินความคุ้มค่าทางการแพทย์ถูกนำมาใช้สำหรับการตัดสินใจเพื่อการจัดสรรปันส่วนทรัพยากรด้านการดูแลสุขภาพเพิ่มมากขึ้น ผู้ใช้ข้อมูลได้แก่ ผู้วางแผนนโยบาย หรือผู้ให้บริการทางสุขภาพจำเป็นต้องทราบว่าวิธีวิเคราะห์ที่ใช้ในงานวิจัยมีความเหมาะสมหรือไม่ และผลลัพธ์ที่ได้จากงานวิจัยมีความถูกต้องและแม่นยำหรือไม่ เพื่อสามารถนำมาประเมินการใช้ประโยชน์ของผลลัพธ์ที่ได้จากการประเมินความคุ้มค่าทางการแพทย์ งานวิจัยด้านการประเมินความคุ้มค่าทางการแพทย์ที่ผ่านมาค่อนข้างด้อยคุณภาพ วัตถุประสงค์ของบทความนี้เพื่อทบทวนความเหมือนและความแตกต่างของรูปแบบรายงานที่เสนอแนะโดยคู่มือการประเมินความคุ้มค่าทางการแพทย์ที่ได้รับการตีพิมพ์แล้ว และเพื่อให้ข้อเสนอแนะสำหรับรูปแบบการรายงานผลการประเมินความคุ้มค่าทางการแพทย์ในคู่มือการประเมินเทคโนโลยีด้านสุขภาพสำหรับประเทศไทย บทความนี้เสนอแนะรูปแบบการรายงานผลที่ประกอบด้วยส่วนประกอบหลักสำคัญสิบประการซึ่งจำเป็นต่อการประเมินความคุ้มค่าทางการแพทย์ รูปแบบการรายงานผลนี้จะช่วยเพิ่มความโปร่งใสของงานวิจัย ทำให้สามารถเปรียบเทียบผลลัพธ์ระหว่างงานวิจัยได้ท้ายที่สุดจะนำไปสู่การได้มาซึ่งงานวิจัยที่มีคุณภาพสูง น่าเชื่อถือ และสามารถนำมาใช้เป็นข้อมูลที่เป็นประโยชน์สำหรับการตัดสินใจเชิงนโยบาย

Appendix. Checklist for economic evaluation report

Please tick (√), fill in the blank, and write the number of the page which contains the details of each following topic

Intervention .....
Compared with .....
Indication of intervention .....

Checklist for Economic Evaluation Report	√	Page
1. Framework		
1.1 State the background of the problem		
1.2 State the economic importance of the study		
1.3 State the clinical importance of the study		
1.4 State the design of the analysis		
1.5 State the objective of the study		
1.6 State the target population for intervention		
1.7 State the comparator programs or interventions		
1.8 State the time horizon		
1.9 State the perspective of the study		
1.10 State the type of economic evaluation methods (i.e., CMA, CBA, CEA, or CUA)		
2. Cost and effectiveness data		
2.1 Identify the outcome measured in the study		
2.2 State the sources of efficacy data		
2.3 State the sources of cost or charge data		
2.4 In the case of using data from expert opinion, state the sources and methods used to collect the data		
2.5 State the resource use separately from the cost data		
2.6 State the method of transforming charges into costs or costs into charges		
2.7 State the types of costs (e.g., direct, indirect)		
2.8 State the year of valuation for all costs		
2.9 State details provided of any adjustment for inflation/deflation for all costs		
2.10 In the case of exchanging money values, state the exchange rate		
2.11 State the valuation of cost		
2.12 State the valuation of effectiveness		
2.13 State the valuation of utility		
2.14 In the case of the study period being longer than one year, state whether discounting has been performed for costs and/or effects		
2.15 In case of the study period being longer than one year, state the discount rate		
2.16 State the reference case values used in the analysis		
3. Model (if applicable)		
3.1 State the choice of model (e.g., decision tree, Markov, etc.)		
3.2 State the description of the model used		
3.3 State the time horizon of the model		
3.4 For Markov models, state the cycle length of the model		
3.5 State all assumptions used in the model		
3.6 Describe the event pathway in the model		
3.7 Show a diagram of event pathways in the model		
3.8 State the software used in the model		
3.9 State the details of model validation that have been provided		
3.10 Present the results of model testing		

Checklist for Economic Evaluation Report	√	Page
4. Uncertainty or Sensitivity analysis		
4.1 Perform the sensitivity analysis method		
4.2 State the sensitivity analysis method		
4.3 State the choice of variables and the ranges used in the sensitivity analysis		
4.4 Present the results of sensitivity analysis		
4.5 State the summary of sensitivity results to assumptions and uncertainties in the analysis		
5. Result presentation		
5.1 Present the results of the reference case both discounted and undiscounted values such as total cost, total effectiveness, incremental cost and incremental effectiveness		
5.2 Present the disaggregated results of cost and effectiveness		
5.3 Present the aggregated results of cost and effectiveness		
5.4 Explain the summary of the reference case results		
5.5 Present the cost-effectiveness acceptability curve		
6. Discussion		
6.1 Discuss the analysis assumptions and important ethical implications		
6.2 Explain the limitations of the study		
6.3 Explain the relevance of study results for specific policy questions or decisions		
6.4 Compare the results with other studies' results		
6.5 State the impact on annual budgeting and the cumulative impact over a relevant period		
6.6 State the funding sources		
6.7 State the author's conflict of interest with the funding sources		

Title of the article .....

Name of journal, volume, year, page .....

Special Article

Health System and Equity Perspectives in Health Technology Assessment

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Economic evaluation is a useful and increasingly popular tool that helps policy makers and health practitioners in the assessment of new technology and health interventions. It is expected that careful assessment of the costs and benefits of all technology choices will guide one's decision in selecting the best mixture of cost-effective options, thus promoting allocative efficiency and increasing value for money within the limited resources available. The use of economic evaluation is also seen as a key step towards evidence-based medicine and evidence-based policy-making.

Nevertheless, value for money and allocative efficiency may not be the only or the most important issue to be considered in technology adoption. There are a number of factors that should be evaluated in addition to economic efficiency. These include safety, efficacy, and effectiveness of the technology or policy of interest. In addition, it is important to assess other external factors that could be impacted by the use of such technology or policy. This article presents two important areas of health technology assessment, in addition to economic evaluation, that must be considered as a part of any health technology assessment exercise. They are (1) health system feasibility and impact analysis, and (2) equity and fairness assessment.

Keywords: *Health systems, Health technology assessment, Equity, rationing, Feasibility analysis*

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With scarcity of resources, access to technology and health programs could be limited and may sometimes be restricted to certain groups of population. In many clinical settings, the choice of who will have access to the technology or drug is not decided explicitly. The rationing of health services could take several forms such as removing useful drugs or beneficial treatments from health insurance benefit packages to exclude some potential beneficiaries, having long waiting time to delaying access to services, requiring referral letters from primary providers to discourage easy access, etc[1]. Without the necessary information to guide decisions, it is difficult to choose between the different rationing methods. Also, the selected options may not produce the best-expected results for society. Economic evaluation is a tool that is increasingly popular, especially in health technology assessment (HTA) as it provides explicit information on the benefit or value a society could gain in relation to the cost involved in the adoption of an intervention or technology. It is expected that with better information from economic evaluation exercises, informed decisions to select the best mixture of cost-effective options will promote allocative efficiency and will increase value for money within the limited resources available.

Nevertheless, it is important to recognize that economic evaluation is not the only tool that has been used in HTA. The scope of HTA is not limited to evaluation of value for money of the new technology or innovation. In addition, increasing efficiency and maximizing value for money is not necessarily the only objective of health technology assessment. Evaluation of safety, efficacy, and effectiveness is seen as a necessary prerequisite to the economic evaluation of any technology. In addition, there are also other external factors, with regard to the technology of interest that should be assessed.

This article presents two important areas of health technology assessment, in addition to economic

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evaluation, that must be considered as a part of any health technology assessment exercise. They are (1) a health system feasibility and impact analysis, and (2) an equity and fairness assessment. The first section of the article explores health system-related issues that are relevant to HTA including the use of health system perspectives in HTA exercises. It also argues for the inclusion of health system implications and feasibility analysis in the assessment of technology. The second section explores the equity and fairness assessment of new technology and describes the use of these criteria in the reality of health care rationing and priority settings in the health system. The article ends with the conclusions and recommendations.

I. Health Systems, Health Technology Assessment, and Feasibility Analysis

The word 'health system' seems to be quite simple. However, it may mean different things to different people. Some may think of a health system as hospitals and clinics. Some may think of the Ministry of Public Health. It is therefore important to clarify the definition of 'health system' before we discuss further its goals and its interaction with health technology. The World Health Organization, in its World Health Report 2000, proposed the definition that the term 'health system' includes all actors, institutions and resources that undertake health actions - where the primary intent of a health action is to improve health. It is not limited to the health sector as programs such as environmental control, tobacco tax, and health education in schools are also included.

It is rather obvious that the goal of health systems is to improve health, *"a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"*[2]. However, the interest of health systems is not limited to individual health. The focus of health systems should be on population health, the level of health of the population as well as the distribution of health outcomes among them.

Several other goals of health systems in addition to population health have also been proposed. The World Health Report in 2000 suggested that the ultimate goals of health systems include level and distribution of health; level and distribution of system responsiveness; and fairness in financial contribution to health[3]. The Organization for Economic Co-operation and Development (OECD), and a few other countries, proposed additional dimensions of health system goals such as acceptability, accessibility, appropriateness, competence, continuity, effectiveness, efficiency, and safety [4]. To achieve these health system goals, the health system relies on its four main functions-service delivery, financing, resource generation, and stewardship-which are described in Table 1.

A. Health Technology and Health System Impacts

Health technology is defined as *"prevention and rehabilitation, vaccines, pharmaceuticals and*

Table 1. Four main functions of health systems

Functions	Description
Financing	Health system financing is the process by which revenues are collected from primary and secondary sources, accumulated in fund pools and allocated to provider activities. Health Financing is comprised of three subcomponents: revenue collection, fund pooling, and pur chasing.
Resource generation	Production of inputs, particularly human resources, physical resources such as facilities and equipment, and knowledge by various organizations to support the provision of health services
Service delivery	Service delivery refers to the combination of inputs into a production process that takes place in a particular organizational setting and that leads to the delivery of a series of interventions of both personal and non-personal health services.
Stewardship	Stewardship involves three key aspects: setting, implementing and monitoring the rules for the health system; assuring a level playing field for all actors in the system (particularly purchasers, providers and patients), and defining strategic directions for the health system as a whole. It can be subdivided into six sub-functions: overall system design, performance assessment, priority setting, intersectoral advocacy, regulation, and consumer protection.

Source: adapted from[3]

devices, medical and surgical procedures, and the systems within which health is protected and maintained"[5]. Within this broad scope, health technology is not limited to drugs or diagnostic machines. Innovative public health interventions, new health policy initiatives, and new clinical management techniques are all considered parts of health technology.

Health technology and interventions play a key role in health systems. They serve as a major resource, in addition to financial and human resources, for all health system functions. They are also inputs for health service delivery which can contribute to health system performance in the achievement of health system goals [6]. Technology changes the way health care is delivered and generally improves its health outcome.

Nonetheless, new technology and interventions are not always beneficial or risk-free. New pharmaceutical ingredients may create serious side effects to the patients. Some new appliances are not effective outside laboratory conditions and create no benefit to health. Inappropriate and over utilization of technology could also be harmful to an individual's health. Moreover, new technology and innovations may require additional financing and resources for their adoption or application. In the US, technology is seen as a major cost driver of health expenditure[7,8]. The introduction of new technology or interventions could also draw resources from other health programs and weaken the health system. It is therefore important for any new health technology to be assessed before its adoption.

B. Health Technology Assessment

According to Banta [9], the term HTA was first conceptualized in 1976 even though the practice of technology assessment predated that by several decades. Initial interest in technology assessment came from the area of pharmaceutical safety. The Elixir Sulfanilamide tragedy led to the promulgation of the US Food, Drug and Cosmetic Act of 1938, which requires safety approval for New Drug Applications before marketing[10]. The interest in efficacy and efficacy requirements only came in 1962. Therefore, most of the treatments recommended in medical textbooks in the early 20th century were found to be of dubious effect or even harmful[9].

The rapid diffusion of high cost technology, *e.g.* CT scanners, raised an important concern about the value for money of new technology and brought the interest in HTA to a higher level[11]. One historical landmark in HTA development was the release of the Cochrane's book titled "Effectiveness and Efficiency" in 1971[9]. Cochrane proposed the use of quality evidence, particularly from randomized-controlled trials, for medical intervention and health technology assessment. In the same year, the United States Congress established the U.S. Congressional Office of Technology Assessment which later became a key player in health technology assessment in the United States with a focus on effectiveness and cost-effectiveness.

Health technology assessment (HTA) has been defined as a form of multi-disciplinary policy research that systematically examines the short- and long-term, direct and indirect, intended and unintended, consequences of the development, diffusion, and application of a health technology, a set of related technologies or a technology related issue[5,12-14]. HTA involves the assessments of relevant available knowledge in various fields from medicine, social studies, ethics, and economics. Its main purpose is to inform decision-making[13]. According to Draborg et al, HTA *"systematically evaluates the effects of a technology on health, on the availability and distribution of resources and on other aspects of health system performance such as equity and responsiveness"*[6].

Despite its initial focus on pharmaceuticals and clinical procedures, HTA has a broad scope. It covers a whole range of interventions and technologies that are provided within the health system. Medical devices, surgical procedures, and diagnostic techniques are included. In addition, HTA also covers interventions that are implemented by the health system such as health financing policies or monitoring and evaluation programs[6].

There are also debates as to whether HTA should limit its scope only to assessment *("the scientific analysis, gathering and summarizing information and producing knowledge")* or extend to the area of health technology appraisal *("the political process of decision-making, taking into account information as well as values")*[15]. The latter requires that the knowledge acquired from assessment be considered at the policy-making level with an explicit framework of values and preferences[15,16]. The ten basic steps of HTA as proposed by Goodman are shown in Box 1 below.

C. Roles of HTA in Health Systems

HTA is a component of health system functions. It serves as a resource generation function

whose product – knowledge – benefits other health system functions including health service delivery. HTA informs priority setting and resource allocation processes as well as helps policy-makers in defining strategic directions for the health system.

McDaid *et al* and Goodman propose that HTA can help influence decisions in regard to health systems in many ways and at several levels[13,17]. At the clinical service level, HTA can be used to develop treatment guidelines to guide health workers' practice and patients' understanding of the proper use of health care technology. At macro policy level, it helps decision-makers in deciding on strategic directions of health care organizations including decisions to adopt or implement new policies or interventions. HTA is also frequently used by health insurers and national health program managers to guide decisions regarding benefit packages and resource allocations. In many countries, the knowledge gained from HTA has been used in pricing decisions such as health service charges and drug prices.

For its effective use, HTA should take into account the impact of technology adoption on health system functions in addition to clinical or economic aspects. There are several possible health system impacts from technology adoption such as financial, labor, and infrastructure needs, as well as the requirements for managerial and information system support. HTA should also consider the potential implications on health system goals beyond aggregate health gains *e.g.* the distribution of health, responsiveness, and fairness.

Box 1. Basic Steps of HTA

1) Identify assessment topics
2) Specify the assessment problem (including purpose and intended users)
3) Determine locus of assessment
4) Retrieve available evidence
5) Collect new primary data (as appropriate)
6) Interpret evidence
7) Synthesize and consolidate evidence
8) Formulate findings and recommendations
9) Disseminate findings and recommendations
10) Monitor impact

Source: [13]

D. Feasibility Analysis

A feasibility study is an initial study to determine whether a project or technology could be implemented with potential success and sustainability. They are frequently used in the business sector to initially evaluate a project of high investment value before carrying out a more detailed study. In the health

Box 2. Common tools for economic feasibility analysis

Indicator	Description	Calculation
Average rate of return (ARR)	average level of profitability as a percentage of investment	average profit / average investment
Average payback period	time required to obtain full investment amount	net investment / average annual cash inflow
Net present value (NPV)	profitability measure that uses the discounted cash flow techniques	present value of total inflows – present value of all investment
Benefit to cost ratio	Proportion of benefit in relation to cost	present value of cash inflows / present value of investment
Internal rate of return (IRR)	percentage profitability, or its percentage rate of return	discount rate which forces the NPV of the project to equal zero
Break-even volume	the volume needed to reach the financial break-even point	fixed cost / (net revenue per unit –variable cost per unit)

Source: [18,19]

sector, feasibility studies are particularly useful for projects that require extensive investment or have a broad impact on the overall health system. For example, broad implementation of expensive interventions, the purchase of big-ticket medical equipments, or the adoption of national programs deserve a full feasibility analysis-assessment as a part of HTA.

Several dimensions of feasibility should be assessed before the decision to adopt such technology or interventions. Four main types of feasibility analysis are described here. They are market feasibility assessment (demand analysis), economic feasibility assessment (financial analysis), technical and organizational feasibility assessment, and legal, environmental and cultural feasibility assessment.

Marketing Feasibility / Demand Analysis

In the business sector, market feasibility analysis is crucial to determine the success of a product. It involves the analysis of demand for the product, and the willingness to pay for it, in the population. It also needs to take into account other competitors in the business as well as other competing technologies that exist and that may emerge in the future.

In health, this issue is a little more complex as we consider not only the demand but also the need for the technology. The population in need of the technology is usually larger as demand only identifies expressed need. The analysis therefore depends on the type of technology and the types of purchaser, payer, and/or sponsoring agency. Usually this requires epidemiological data of the disease involved and the demographic data of the population of interest.

Economic Feasibility / Financial Analysis

Economic or financial feasibility analysis determines whether a project or a technology produces adequate monetary returns which merit its investment, as well as whether the health system has enough financial resources to invest in it. It is usually done in the event of an intensive capital or high price technology investment. The analysis usually looks at two major components of program finance: (1) return on investment; and (2) cash flow requirements. Common tools for economic feasibility analysis are provided in Box 2.

Return on investment considers the financial returns that can be collected over the life time of a product or a technology in relation to the investment costs. In health programs, the return may be in the form of usage charges or co-payments or nothing. The analysis is sometimes called budget impact analysis," and identifies the level of budget that needs to be prepared for this product or technology over a period of interest. For that technology with a stable demand or need, the required budget could be quantified on a periodic basis *e.g.* per year. However, for certain technologies or health programs where the users or beneficiaries could increase over time, the budget requirements could be continuously increasing and the overall budget requirements could reach an exorbitant amount. For example, an inclusion of hemodialysis for chronic renal failure patients in the reimbursement package would incur increasing costs to the health insurers as the number of eligible beneficiaries would increase each year during their longer life span and their prolonged demand for dialysis.

Cash flow analysis identifies the amount of money required for a certain period of time. It is important for big-ticket technology *e.g.* expensive diagnostic machines, where the cost of acquisition is high and may require expensive maintenance or even replacement. The level of cash required may not be stable over a prolonged period of time and there may be a surge in money requirement during certain periods i.e. for key component replacement, etc.

An economic feasibility analysis usually involves multiple time periods. It is therefore important that the use of adjustment factors or discount value is used to calculate net present value. The level of inflation could impact the financial requirements and the feasibility of the project.

To conduct full financial analysis for capital investment, Gapenski proposes five key steps: (1) estimate the total capital expenses; (2) forecast the operating cash flows including the incremental cash flows (cash flow if project undertaken minus cash flow if it was not), sunk cost, inflation, and the effect of the project on other parts of the system *e.g.* changing clinical or practice styles; (3) assess the riskiness of the estimated cash flows using tools such as break-even analysis or a calculation of the payback period; (4) estimate the project's capital costs given the level of riskiness; and (5) assess the profitability of the project using tools such as net present value (NPV) or internal rate of return (IRR). Decision-makers should consider the financial information from this analysis before investing in any capital-intensive projects.

Technical, Organizational, and Schedule Feasibility

For technology or projects to function effectively, there are other types of inputs that are required

in addition to monetary inputs. These include human managerial requirements.

As health programs or projects are largely labor-intensive and frequently require special skills, it is important to evaluate the human resource requirements for every program or technology to be implemented. Shortages in the health workforce could limit the feasibility of the program. An estimation of health workforce requirements should take into account both quantity and quality requirements. This involves the analysis of workforce capacity and competency, as well as skill-mix in comparison to the expected demand or need of the program or technology.

The decision to adopt a technology or intervention program should also consider managerial requirements and information system gaps. When a number of actors are required in technology adoption or project implementation, time analysis of key actors in relation to the project's time frame is also necessary.

Legal, Environmental, and Cultural Feasibility

There are also other dimensions of feasibility analysis that need to be considered. Legal feasibility requires a careful review of relevant laws, bylaws, and regulations in relation to the project or technology to be adopted. In Thailand since 1992, the Environmental Protection Act has required that a project in selected areas of the country or of a certain size need an Environmental Impact Assessment study before being approved. For example, an EIA study is required for any construction project to build a hospital above a 60-bed capacity in any area, or any river-side or beachside hospital that is above a 30-bed capacity.

In addition to legal and environmental requirements, there is a cultural dimension. This includes both the acceptance by the general Thai culture and also by the local or area-specific culture as well. The program adoption needs to be aware of and sensitive to the cultural and religious diversity in the area of implementation. For example, a policy to retain a newborn's placenta for laboratory investigation may face resistance in Muslim-dominated areas as a placenta is considered a part of the body that should be brought home to be buried properly.

II. Equity and Fairness in Health Technology Adoption Decision

With scarcity of resources, economic evaluation has been advocated as a tool to guide policy makers in their decisions on which technology to adopt based on the value for money of said technology and interventions. In a number of countries, cost-effectiveness is required - in addition to its efficacy, safety, and effectiveness - for a technology to be evaluated for adoption or funding. For example, the National Institute of Clinical Excellence in the UK and the Pharmaceutical Benefit Scheme in Australia both require economic evaluation for their decisions to adopt certain technologies or drugs into the health care program.

The use of economic evaluation as the only tool for technology assessment and adoption decisions, however, faces several limitations. These limitations are both methodological and operational. Methodological issues include the choice of comparators, the choice of incremental versus marginal analysis for non-constant or non-divisible interventions, the inconsistency of economic evaluation guidelines, and the constraint of economic evaluation tools in capturing externalities and non-health outcomes[17,20-22]. Operational limitations include substantive informational and time requirements needed for the assessment, perspectives and the ability to generalize the results, poor linkage with decision-makers, and the lack of a publicly acceptable, incremental cost-effectiveness threshold[1,22,23].

A stronger criticism on the focus on economic evaluation in health technology assessment and resource allocation lies at its ignorance of distributional aspect. Generally, economic evaluation practice aims to maximize health gains by treating everyone the same and ignores the distribution concern over individuals[24-26]. This could be against the principles of policy-makers or the public and results in a reluctance to use the economic evaluation results by policy-makers. Several studies have found that policy-makers and the public are willing to accept a certain degree of inefficiency in exchange for an improvement in equity or fairness[27,28]. In addition, they feel that several criteria should be used in health care rationing[1,29].

This part focuses on the important role that equity and fairness have in technology adoption decisions. It explores the meaning of equity and fairness with particular focus on health equity. It then explains how health equity has been prominently considered in health system rationing and priority setting. It then discusses how equity and fairness should be included in HTA as well as the possibility of integrating equity considerations with economic evaluation results.

A. Definition of Equity and Health Equity

Equity is not the same as equality. It is a moral

and ethical concept that is grounded in the principles of distributive justice[30]. An equitable society is not necessarily a society in which everyone is equal or has the same level of wealth and resources. The emphasis is on social justice or fairness in the society.

Similarly, health equity is a concept that is based on the equity concept. Health equity is not the same as health equality[30,31]. The differences in the level of health or health disparities in the population are not always unfair. An obvious example is the difference between young and old. Health inequities are defined as the *"differences in health that are unnecessary, avoidable, unfair and unjust"*[31] and health equity is therefore referred to as "the absence of socially unjust or unfair health disparities"[30].

The World Health Organization states that *"[e]quity in health implies that ideally everyone should have a fair opportunity to attain their full health potential and, more pragmatically, that no one should be disadvantaged from achieving this potential, if it can be avoided"*[32]. According to Sen, health equity is among the most important components of social justice[33]. Equity in health is an "ethical value, inherently normative, grounded in the ethical principle of distributive justice and consonant with human rights principles"[30].

Two main concepts of equity are frequently referred to in health: horizontal and vertical equity. Horizontal equity applies to people in the same status or situation. In the horizontal equity concept, people who are alike should be treated in the same fashion. For example, patients with the same health needs should receive an equal share of health care resource and treatments.

Vertical equity focuses on the difference between individuals or groups of people. In this concept, people who are unlike in relevant respects, *e.g.* income or health needs, should be treated differently in a just way. For example, people in lower economic groups should receive more priority in public support than higher economic groups and people with higher health needs should receive more treatments.

It is argued that the scope of health equity, both vertical and horizontal, should not be limited to the equity of health care access[33]. Recent debates on health equity have expanded its scope to the distribution of health of the population. Sen takes this further and argues for an even broader scope; equity in the opportunity to health. Health equity should also consider how *"resource allocation and social arrangements link health with other features of states of affairs"*[33].

B. Equity implications from the choices of economic evaluation techniques

Economic evaluation techniques are generally based on assumptions to quantify the gains or benefits and the costs into comparable units. The Thai Health Technology Assessment Guidelines propose a number of techniques and assumptions for economic evaluation for researchers in their analyses[34]. It is therefore very important for researchers and users of the evaluation results to realize the possible equity implications of these choices.

The choice of outcome measurement certainly has an implication on whose benefit will be counted more. For example, if improvement in life expectancy is used as the outcome measure, an intervention that benefits the elderly relatively more will be considered as less cost-effective than another intervention that benefits younger people more (when other aspects are the same). Similarly, some measurement techniques will value the benefit to disabled persons less because their potential gains from recovery (disability averted) from an intervention will be less than for non-disabled persons.

The selection of costing types could also give different value to different groups especially on the evaluation of economic cost *e.g.* loss of productivity. The use of 'willingness to pay' will put a higher value on those with the higher ability to pay (richer people). The guidelines suggest the use of a national wage average in the analysis, which means it will be insensitive to the difference in actual productivity lost by different population groups. Different perspective used in the analysis could also affect the inclusion or exclusion of certain costs or benefits. This may have different implications on different groups as well.

The level of 'discount rate' may also suit different groups differently. It was found that the rate of time preference is not the same for different income level populations, with low income households generally having a higher discount rate[1]. This means the use of a higher discount rate is more reflective of the poorer population preference.

C. Ethical perspective for health resource allocation

Economic evaluation techniques are generally based on utilitarianism which focuses on efficiency through maximizing gains or benefits in respect to cost. These benefits could be in the form of well being (cost-benefit analysis), health utility (cost-utility analysis, or health gains (cost-effectiveness analysis) and are valued equally irrespective of their distribution. This

creates criticism against its use by some especially those who do not want to provide relatively more resources to the rich or those already having an advantage in the society. This assumption of "distributive neutrality" used in the Economic Evaluation exercise is also against public respondents' and policy-makers' views as found in many studies[35]. Many of them believe that fairness should have a greater importance than the maximization of benefits[29,36]. In the equity approach, maximizing aggregate benefits to the society is not its primary concern.

Despite a strong interest in fairness of resource allocation, there is no consensus among the public or philosophers on a single set of allocation criteria which would be considered as a fair allocation[37,38]. On several occasions, the ethical and justice theories may be in conflict among themselves[39]. It is, therefore important to make explicit the decision criteria used in resource allocation decisions.

Several equity and fairness criteria have been used in resource allocation decisions. A number of studies have been carried out to explore the preference for these criteria in hypothetical allocation decisions by both the public and policy-makers[27,40]. Six major decision rules are discussed here: severity of health conditions, realization of potential health, rule of rescue, preservation of hope, concentration of benefit, and age-related preferences.

Severity of health conditions

Under this criterion, the priority of resource allocation should be given to the neediest i.e. those who have the most need. There are several ways to define health needs, each of which could be based on a subjective evaluation. In practice, it is common to use severity of health conditions as the criterion to reflect need[41] when patients or a population with more severe health conditions receive more resources irrespective of the value for money of the interventions or their capacity to benefit. Many previous studies have shown that people are willing to prioritize interventions that address severity of health over interventions that are cost-effective[27,40,42,43].

Realization of potential health

The use of capacity or potential to benefit from the intervention as a measurement of need in resource allocation decisions is another choice. However, this policy was not well received among the public as this approach unavoidably discriminates against those with disabilities or permanent injuries. There is abundant evidence from many countries which shows that people reject discrimination on the basis of disability, and that people want to avoid discrimination against those with disabilities or chronic illness[27,41].

Rule of rescue

Similar to the criterion based on severity of health conditions, the rule of rescue is a criterion that is based on one aspect of health need; the case of imminent and immediate life threats. Decisions based on this rule would choose to save "identifiable" individuals from life-or-death situations instead of other cost-effective non-lifesaving measures that may benefit statistical lives[42]. The allocation decisions would allow them to be saved or would leave them to die. The use of this criterion is common in clinical practice such as in the case of the retransplantation of organs in previously transplanted cases to save immediate life instead of giving these organs to other first time transplant candidates who may have a higher chance of success[40,44].

Preservation of hope

Empirical evidence from a number of studies suggests that people may not be willing to totally ignore patients who are left with only cost-ineffective therapy[44-47]. The case of allocation of scarce organs for transplantation is frequently raised. It is found that people do not want to restrict the allocation only to those who have the chance of the greatest health gains, thus leaving the others to die. They still want to preserve the hope of survival to those persons who may be less cost-effective candidates otherwise[46].

Concentration and dispersion of health benefits

A number of studies have shown that people prefer a more even spread of the distribution of health benefits [27,48,49]. For example, an experimental study by Nord *et al.* found that an intervention that can save 1 year of life for 10 persons (10 years in total) is considered the equivalent to another intervention that will prolong life for 5 years for 3.5 persons (17.5 years in total) despite the latter's higher aggregate years of life gains[49]. In this case, a health intervention that spreads the health benefits, in terms of life years to a broader population, is valued more highly than an intervention with concentrated benefits to a few individuals for the same level of total benefits. There seems to be a discounting of value of additional life years in this reasoning.

However, recent evidence shows that this preference for the dispersion of health benefits does

not always apply[43,50,51]. A few studies have found evidence of a minimum threshold level of benefit below which the public would prefer concentrating benefits to fewer individuals instead. For example, Choudhry, Slaughter and colleagues found that in the study of Canadian senior health officials, the same respondents could have differing preferences for concentrating or spreading benefits depending on the level of the benefits in consideration[52]. A study by Olsen in Norway also found a similar pattern. This threshold level varies based on the size of both the small and the big benefit in question[51].

Age-related social preferences

Many studies indicate that people are willing to give priority to certain age groups, usually the young, in competition for limited health care resources[27,49]. Three groups of reasons for the preferences to the young over the elderly have been proposed. Utilitarian ageism gives preference to younger patients because saving them means saving longer expected years of living. Productivity ageism considers the level of productivity as the basis of giving preference. Egalitarian ageism, on the other hand, aims to reduce inequality in age of death by favoring equal opportunity to live to a certain age. This last form of ageism is similar to the "fair innings" concept proposed by Williams on a social expectation for the achievement of a fair minimum length of life[53]. Because everyone can expect to pass through the different stages of the life span, giving different value to a year of life extension at different stages in the life span need not unjustly discriminate against individuals[54].

Other dimensions of social preferences

Fair distribution is not necessarily the same as equal distribution. Because the existing distribution of health and health opportunities in the population is generally not equal, priorities may be assigned to certain subgroups of the population who are currently underprivileged. For example, those who believe in the "maximin theory" of justice, which aims to maximize the minimum, would give priority of benefit to the worse-off population in the society. In some societies, preference may be given to a specific population with certain characteristics such as gender, geographical regions, or ethnicity. In a study of 80 economic students in Sweden, the respondents showed that an intervention that produces 1 quality-adjusted life year (QALY) gained in a healthier group is equivalent to an intervention that increases only 0.45 QALY for a health deprived group[48].

Evidence on public interest in fairness of resource allocation decisions reflects the willingness to trade efficiency or health maximizing goals with equity or fairness. In the context of a national health system, fairness or social justice plays a more important role as the main reason for a national health scheme is to primarily achieve fairness-related objectives[55]. Several methods have been invented to try to integrate equity-dimension into, or in addition to, the existing economic evaluation techniques as described below.

D. Integrating equity dimensions into health technology priority settings

Considering the public's and policy-makers' interest in integrating equity concerns into resource allocation decisions, a number of tools and methods have been introduced to allow for the integration of normative values in economic evaluation techniques. These can be done as part of the outcome measurements or separately in addition to the economic evaluation results.

One way of integrating equity dimensions into outcome measurements is by the choice of the evaluation technique. It is argued that the use of cost-benefit analysis instead of cost-effectiveness analysis allows the researcher to take other externalities, beyond health outcome, into consideration[20]. However, in practice there are still several methodological concerns about the valuation of health outcome and other benefits into monetary units to be used in CBA. Some of the methods, such as the human capital approach or the contingent valuation approach, also inherit equity concerns in themselves.

Another approach of integrating equity dimensions into outcome measurements is by adjusting total QALYs by some weights that reflect the public's value of certain population groups. This approach is sometimes called "cost-value analysis" to reflect that the outcome of interest has now changed from health utility to social value[56,57]. An example of this approach is the use of severity weight and potential weight to adjust for the social preference put on severity of health conditions and potential to benefit from interventions[43]. However, this approach is still far from practical to implement due to its weakness in methods, the current data gaps, and political acceptance in the real world[57].

Equity perspective could also be explicitly integrated into the decision-making process after economic evaluation analyses are done. One approach proposed by James et al, the Clarified Criteria Approach,

employs a model to estimate prioritization score. This allows policy makers to put weights on equity and efficiency explicitly[58].

Recent developments to integrate equity and fairness concerns into economic evaluation decisions involves the use of a "discrete choice experiment" – a form of multicriteria-decision analysis – to allow for the consideration of other attributes of health outcomes and social preferences into the priority setting decisions[59,60]. Under this approach, multiple allocation criteria *e.g.* severity of health conditions, the concentration of benefits, and efficiency, could be simultaneously considered using quantitative statistical techniques in a systematic and transparent manner. However, despite its attractiveness and feasibility as a priority decision aid, this approach and its method are still being developed and tested to gain a better understanding of the caveats and limitations[61,62].

E. Health system resource allocation in practice

Resource allocation and priority setting of health interventions occur at many levels in the health system. Clinicians are involved in bedside rationing. Health managers control the budget, staff, and time allocation for various health programs. Health insurance managers decide on benefit packages and reimbursement limits for new and old technologies.

At each level, the decisions can be made through explicit or implicit criteria and several factors may be considered altogether. Apart from efficiency and equity or fairness criteria, policy-makers may incorporate other factors into their allocation decisions. Financial factors, such as level of total financial investment and affordability and sustainability, are generally high on the agenda. Some technologies or drugs may be excluded from the benefit package or public subsidy if individual responsibility is expected. Additionally, most of the decisions are heavily influenced by the political situation and the environment surrounding the decision process.

It is also found that different levels of health care managers or decision-makers may have different concepts of equity. The public, doctors and health managers may have different view on priorities, and how to spend health resources[63,64]. Nevertheless, there is strong support for a pluralistic combination of different criteria in rationing[65]. A study in Thailand interviewing 36 key informants in the health sector - health authorities, health professionals, and academia - confirms that health maximization is not the only or the preferred criteria in health care rationing[29].

Additionally, the public wants to be involved in how priorities in the health sector are set[66-68]. There are several possible mechanisms where people's views can be heard such as through interviews, postal surveys, public consultations, or a system of citizen juries[66,69]. One caveat is that people's opinions may differ significantly when they are given enough chance to deliberate or discuss[70]. In other words, the instinctive view could be completely different from the considered view (after discussion) on any priority-setting issue. The public consultation process could also be costly and *"may result in an inefficient use of resources"*[71].

One major challenge in evidence based priority decisions is the lack of information. Health technology assessment and economic evaluation is a new field of the late 20th century with a limited number of studies available to inform decision-makers and the public. This applies globally as well as in the case of Thailand[29]. The evidence available is also of varying quality and requires careful and critical appraisal before its use[72,73].

IV. Conclusion

Economic evaluation is a tool to aid priority setting with the aim of increasing efficiency of resource allocation. It is a major component of the health technology assessment exercise that produces knowledge beneficial to the health system performance. However, economic evaluation alone is not sufficient in making health technology adoption and rationing decisions. Many other tools and criteria such as the use of feasibility analysis and equity perspective should also be employed.

This article describes the linkage between economic evaluation, health technology assessment and the health system. However, it has been found in many countries that the impacts of HTA in policy appraisal and the decision-making process are still very minimal[16]. One possible reason, as claimed by Oliver and colleagues, is that *"[m]any people from many different perspectives and for many different reasons remain skeptical of the relevance of current HTA activities for practical decision-making purposes"* [16]. Also, the assessment of the social, political, and ethical aspects of health technology remains limited, jeopardizing its popularity[11].

A number of suggestions have been proposed for the success of HTA in health system decision makings. They are:

- HTA should be considered as a

multidisciplinary approach that needs to consider all relevant aspects in addition to economic evaluation[16]. This includes political, social, equity, and ethical dimensions in the assessment process.

- For HTA guidelines, the process of development must be open and fair[39,67]. The criteria and the process used in the development should be explicitly explained. The final guideline products should be easily available to the public.

- Formal structures or institutions should be developed with mandates to advocate for the use of HTA and its results in decision making[16,74]. There should be regular communication and exchanges between HTA evaluators and stakeholders working in the health technology sector[11,16]

- The technology assessment process should be informed by a broad set of perspectives[11]. The involvement of the public in priority setting decisions could be beneficial but may come at a cost. Nevertheless, all the decisions and the rationales behind them must be made accessible to the public. Also, a system should be developed to allow for a change or challenge to these decisions by the public.

Opportunity exists for the development of HTA and its influence in policy decision-makings in Thailand. The challenge is the lack of quality evidence and the limitation of the resource available for HTA activities in the country. Optimistically, the emergence of newly established programs such as the Ministry of Public Health's Health Intervention and Technology Assessment Program (HITAP) and the Setting Priorities using Information on Cost Effectiveness (SPICE) Project will lead the country in HTA development and implementation which will result in a better health system performance and health outcomes for the population.

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มุมมองเชิงระบบและประเด็นทางจริยธรรมในการประเมินเทคโนโลยีด้านสุขภาพ

ปิยะ หาญวรวงศ์ชัย

การประเมินความคุ้มค่าทางการแพทย์เป็นเครื่องมือที่สำคัญซึ่งจะช่วยให้ผู้วางแผนนโยบายและบุคลากรทางการแพทย์มีข้อมูลเพิ่มเติมในการตัดสินใจเลือกใช้เทคโนโลยีทางการแพทย์หรือนโยบายสุขภาพต่าง ๆ โดยเฉพาะอย่างยิ่งการประเมินต้นทุนที่เกี่ยวข้องเพื่อเปรียบเทียบกับประโยชน์ที่ได้รับจากการเลือกใช้เทคโนโลยีและนโยบายนั้น ๆ ก่อนการตัดสินใจนำมาใช้ จะช่วยให้สังคมได้รับประโยชน์สูงสุด ภายใต้ทรัพยากรที่มีอยู่อย่างจำกัด ทั้งนี้ยังช่วยเพิ่มประสิทธิภาพ (efficiency) และส่งเสริมการกำหนดนโยบายและเวชศาสตร์เชิงประจักษ์

อย่างไรก็ตามความคุ้มค่าทางการแพทย์มิได้เป็นประเด็นที่สำคัญที่สุดเพียงประการเดียวในการตัดสินใจเลือกใช้เทคโนโลยีหรือนโยบายใด ๆ จำเป็นต้องมีการพิจารณาถึงปัจจัยต่าง ๆ อีกหลายประการ คุณสมบัติที่สำคัญอื่น ๆ ของเทคโนโลยีที่ควรได้รับการประเมินก่อนการเลือกใช้ ได้แก่ ความปลอดภัย (safety) ประสิทธิผล ทางคลินิก (efficacy) และประสิทธิผล (effectiveness) นอกจากนี้ ยังต้องมีการประเมินปัจจัยภายนอกที่มีความสำคัญต่อการเลือกใช้เทคโนโลยีหรือนโยบายเหล่านั้นด้วย บทความนี้ นำเสนอปัจจัยภายนอกที่สำคัญสองประการ นอกเหนือจากการประเมินความคุ้มค่าทางการแพทย์ที่ควรได้รับการพิจารณาในฐานะองค์ประกอบหลักของการประเมินเทคโนโลยีและนโยบายด้านสุขภาพ โดยปัจจัยสองประการนี้ได้แก่ (1) ความเป็นไปได้และผลกระทบในระบบสุขภาพ และ (2) ความเสมอภาคและความเป็นธรรม

Special Article

Policy Making and Roles of Health Technology Assessment

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The processes of policy development and implementation in the public sector are complex and dynamic as several actors with different interests are involved. To pursue their benefits, these individual and organizational participants compete with each other, and those with a relatively high degree of power can lead the policy decisions. Results of and recommendations derived from economic evaluation and other forms of health technology assessment (HTA) are expected to have an important role in policy making and professional practice. However, it appears that on many occasions, such scientific evidence is neglected. Complex calculations, arbitrary assumptions, debatable choices of whose perspectives to pursue, difficult-to-understand methods, research designs and underlying philosophy/concepts, and time-consuming processes are claimed as key factors discouraging policy makers and practitioners from making use of HTA findings. Ethical considerations and the perception that HTA-based clinical guidelines undermine professional autonomy are also crucial.

Keywords: *Public policy, Policy process, Health technology assessment, Economic evaluation, Priority setting, Evidence-based medicine, Ethics*

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The effort to examine the appropriateness of health policies and interventions in a systematic way is increasingly apparent at different levels of government: global, national, sub-national and even within health care settings. In some societies, largely in the developed world, health technology assessment (HTA) has been established and accepted as a tool for the better selection, procurement and use of health interventions[1]. At the global level, evaluation of health technologies in different facets, such as the efficacy, safety, implementation feasibility and financial consequences, is undertaken as a crucial step of policy formulation such as in the development of the World Health Organization (WHO) Model List of Essential Medicines, guidelines for prevention and management of diseases, as well as policy recommendations and best practices to address health problems[2]. Furthermore, HTA, as well as other research studies, can have a significant role in evidence-based medicine, which aims to ensure the quality of professional practice through the use of the best evidence currently available in making decisions about health care to be delivered to individual patients[3].

The literature illustrates potential policy utilities of HTA as its findings can be used to advise or inform the approval of pharmaceuticals, vaccines, devices and other technologies; the formulation of health benefit packages for reimbursement and coverage; the priority-setting of and resource allocation to public health programs; and the development of treatment guidelines. However, in real-life policy and professional decisions, HTA results are occasionally neglected, and this scientific evidence therefore, plays a less important role than the researchers and respective authorities have expected. The present paper reviews key features of public policy processes, and also discusses the nexus between policies and research including the evaluation of health interventions. It aims to provide better insights into the politics of policy making and actual roles of HTA in health sector reforms and professional practice.

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Fundamental concepts in policy study

The term 'public policy' has been defined differently by different scholars. Among others, Dye[4] describes public policy as *'Anything a government chooses to do or not to do'*. Public policies are the actions of governments including public organizations and individual government officials. The decisions to do nothing, i.e. to maintain a *status quo*, are also regarded as public policies. Generally, it is not difficult to understand the content of a policy introduced to address problems in the public domain. Nevertheless, the more important aspects, which are usually of interest to the general public as well as policy analysts, include why and how governments make decisions on some issues, in particular ways[5].

As policy processes are complex, involving several repetitive and interconnected steps, a stagist model is normally employed by policy researchers. Such an approach divides policy processes into simple phases for analytical purposes. For instance, Hogwood and Gunn[6] propose a framework of discrete stages, beginning with agenda-setting and option analysis, going on to policy formulation, implementation, monitoring, and evaluation. Another helpful model to understand public policy is the so-called 'policy triangle' which suggests the influence of actors and context on the development of policies in particular stages[7]. Actors or policy participants are different in terms of their position, power, roles and interests. Furthermore, different actors, as groups or individuals, command certain degrees of power, and those more powerful than others can take a leading role in policy making to meet their interests[8]. Meanwhile, interactions between policy participants and contextual environment such as economic status, natural disasters, technology, religions, culture, and international regulations can shape public policy content, processes and outcomes[9].

Agenda setting

The role of politics can be observed in every step throughout the policy development and implementation. In the agenda-setting stage, policy makers pay attention to problematic issues, so that the chance for the selection of corresponding solutions increases. Following Kingdon[10], if policy makers do not consider or recognize an issue as a problem, said issue cannot reach the government agenda. The high numbers of afflicted population, prevalence, Disability Adjusted Life Year (DALY) loss, and rapid transmission may draw attention of the public and the government to a disease, and encourage policy makers to seek the corresponding prevention/treatment measures. However, people consider a particular issue and construct it in different ways. As Baumgartner and Jones[11] put it, a condition may be recognized as a public policy problem if it has an image that indicates a demand for the government's intervention. The authors point out that such a perspective resembles what other scholars call 'problem definition'.

In addition, characteristics of available policy options and political factors are important in this phase. Major concerns of decision makers are placed on technical and management feasibility, affordability, social acceptability and the political desirability of policy alternatives. In the absence of an appropriate solution, problematic issues tend to be neglected[10]. Similar to the problems, solutions or policy choices are constructed and interpreted differently. Other than the recognition and definition given to particular issues, social movement, public opinion and shifts in key actors such as the regime and responsible committees/officials are crucial, driving or hampering changes in governments' agenda items. For instance, in HIV/AIDS policy over the past two decades, civil society organizations have gained widening access to medical services and social support for people living with the disease. From the mid-1990s, civic coalitions around the world put forth a strong, concerted effort to encourage international organizations and country governments to scale-up antiretroviral treatment in resource-poor settings[12].

Policy formulation

After the problematic issues reach government agendas, policy formulation is undertaken by governments. In this phase, respective officials or appointed task groups explore, examine and accept or reject a given policy option[13]. Particular public policies may come from the proposals posited at the agenda-setting stage, or may be developed later in government offices. In most situations policy makers tend not to seek fresh knowledge, i.e. conducting or commissioning research to inform policies, but to draw lessons on their past experiences, implementation feedback and other organizations[14]. When the information on potential policy prototypes has been gathered, policy makers need to consider whether or not, and how to introduce such lessons into their settings.

Lesson drawing may involve not only copying but also different degrees of adaptation, and therefore the policy innovations may be different from its template[14,15]. This is because the adoption of a policy

is contingent on several conditions, especially the internal factors of the policy importer setting, such as the effects of socio-cultural factors, policy legacies, political context and economic status[14]. Similar to the agenda setting stage, the benefits, feasibility and political consequences in introducing each policy option are assessed[16], and as a result, undergo some transformation. As policy formulation is carried out by government officials, their concerns, including bureaucratic implications, for example individuals' career objectives, competitive positions and budgets between governmental units, as well as administrative capacity, compliance and responsiveness may affect how far policies are adapted[17].

Policy implementation

The term 'policy implementation' refers to the process by which a policy is put into effect. During this stage, policy makers at the top of an administrative hierarchy, such as a government or parliament, expect bottom-level bureaucrats to carry out the policy as formulated[18]. In practice, however, owing to several factors such as unrealistic policy prescription, ambiguous policy objectives, poor communication and collaboration between responsible organizations, inadequate time and resources in implementation units and impeding work environment, the policy may be adjusted, elaborated upon or even rejected by government officials at a peripheral level[19]. As suggested by Hill[20], implementation gaps may stem from the differences in the interpretation and understanding of problems, policy goals and prescribed instruments between central-level policy makers and peripheral actors.

Public policy scholars emphasize the role of actors who are responsible for the translation of policy into practice: the implementation stage is part of a policy-making continuum: the policy is remade and fine tuned by those expected to be its implementers. As Walt (8:155) maintains, *'implementers often play an important part in policy implementation, not merely as managers of policy percolated downwards, but as active participants in an extremely complex process that informs policy upwards too'*. Meanwhile, many have pointed out that implementation is an interactive process, characterized by negotiation and conflict among participating actor networks, and therefore as political as the policy formulation stage[17]. Empirical evidence in the health sector shows that getting a policy into action involves many actors outside implementing units; for example, national and domestic politicians, representatives from a range of multi-level government agencies, private business, and civil society organizations, including professional organizations[21,22].

Lipsky's work on public servants' behavior suggests that *street-level bureaucracy* is where implemented policy is distorted from its prescription in several ways including in policy directions, guidance and in professional practice guidelines[23]. His study illustrates the discretionary practice in service delivery developed by public officials, which aim to address implementation constraints and complexity, excess demands, conflicting and ambiguous policy objectives, uncertainties about new jobs, and occupational stress. Eventually, such coping mechanisms become routine and then established practices in the organizations. Lipsky further argues that program managers and superior officials have found some difficulties in controlling the street-level bureaucrats' behavior and fostering policy compliance.

Integrating research into policy development

It is generally recognized that research findings including HTA, are beneficial in supporting evidence-based decisions at every policy stage, from agenda setting to the monitoring and evaluation when policies are implemented. This is, to some extent, in the same vein as that which a rationalist ideal argues; government agencies need comprehensive information on policy alternatives, and rational decisions are those drawn on the evidence objectively demonstrating cost minimization and benefit maximization of the selected options[13]. However, actual policy processes are not always rational since, as aforementioned, several elements, apart from research findings and other scientific information, collectively influence policy decisions[24].

An illustration can be drawn on the priority setting for reproductive health in Ghana, where breast cancer has been given a higher priority than cervical cancer despite the fact that available evidence on disease burdens and cost-effectiveness of screening and treatment interventions suggests that the government should invest in a cervical cancer program rather than the breast cancer initiative[25]. As this study points out, such debatable priority setting has resulted from campaigns run by women's groups at a national level who encourage breast-cancer problem solving, which are more powerful than those involved in the cervical-cancer counterpart. Even in developed societies such as the UK, where evidence-based decisions have been

promoted, the actual policy making in the health sector still faces the challenges of political imperatives and research evidence interaction[26].

Research-derived information may be employed by policy makers, interest groups and even researchers themselves to legitimize the policies they pursue[10]. In many instances, this requires a rigorous, tireless effort of 'policy entrepreneurs' who advocate particular policy choices. The case of universal health coverage policy development in Thailand offers a good example. In the early 1990s, groups of health economists started conducting domestic studies and also reviewing international experience on health system financing, different types of insurance plans and payment mechanisms, and their implications on the budget requirement and health care providers' responses[27]. The data on cost escalation of the fee-for-service scheme for government workers and inequitable spending per capita of beneficiaries of different health benefit programs in the country were highlighted as justification of these researchers' proposal to reshuffle the financing systems. After a long advocacy, the reformists succeeded in driving the universal health coverage issue on to the government agenda in 2000, and coupled their research findings with national policy decisions thereafter[28].

The concepts of policy communities and policy networks may help us to understand the research-policy nexus. Such notions maintain that public policies are decided and developed within closed policy subsystems, involving small numbers of actors including politicians, government officials, and representatives from interest groups, who have common goals and basic values[29]. Changes in members of policy communities, associated ideals, and therefore the interpretation of problems and solutions, can result in policy innovations. However, policy communities are well-integrated and not open for different interests to participate in their activities, including policy making. This is the major reason why radical shifts in public policies hardly happen[11].

Epistemic communities, including groups of experts, researchers and think tanks, are distinctive types of policy networks, of which the members share a professional background and expertise[30]. These scientists' goals are to promote their ideas on to the government agenda and integrate their detailed proposals into policy formulation. Policy alternatives proposed by experts, although based on sound research and evidence, inevitably compete with those pursued by other actor clusters with different ideals and preferences. Specialists in respective fields are usually invited by government agencies to work out program configurations, especially those in highly technical policy domains such as health and biomedical sciences. This is a channel to increase the chance for research-policy integration. However, on many occasions, problematic issues are constructed by other interests and conveyed to stakeholders as well as governments and the general public in particular ways, in which technical expertise and scientific information are not required in policy decisions[11]. This restricts the role of experts, and therefore hampers the impact of research on policies and practice. It is noteworthy that the contests between issue definitions, policy options and an explanatory role of the policy network model can be applied to understand policy making at global, national and domestic levels.

Scholars have discussed the reasons for the lack of research-policy integration at length. As Braybrooke and Lindblom[31] assert, the rational approach cannot address all problems in the real-world due to: a limited problem-solving capacity, inadequate information, unaffordable assessment costs, lack of reliable evaluative methods, the role of value in policy making, needs for effective strategies to convince policy makers, and a variation in the features of arising problems. Inefficient evidence production as well as poorly-performed monitoring and evaluation, which hinder the role of research in public health policy, are problems of not only resource-poor settings but also industrialized societies[26,32]. Meanwhile, Chunharas[33] maintains that different types of knowledge, not solely those derived from research studies, are helpful in guiding policy decisions. As the author further emphasizes, in addition to research findings, policy makers and other stakeholders may introduce lessons drawn on personal experience and those available in documents and other forms of databases in the policy formulation and implementation stages.

Others such as Trostle et al[24] provide insight into the promoting factors and impediments in applying research to policy making. Drawn on Mexican experience, this study suggests that these factors include: quality of studies perceived by policy makers; language used in research reports and communications; timelines of study results; the concreteness and applicability of research findings; the technical background of policy makers; the involvement of some interests in the research projects; (un)familiarity to use scientific evidence in policy decisions (this is referred to as 'political culture'); available channels for formal and

informal communication between researchers and policy makers; changes in top-level management of the health systems; excessive State centralization; and rotation of scientists into policy making positions. By this, it means that research with rigorous design, methodology and quality assurance is insufficient in guiding and shaping public policies. This is because other factors including policy makers, researchers, dissemination and communication of research findings, and health and political system environments also play important roles.

The Overseas Development Institute suggests that the links between research and policy are associated with three main groups of factors: the political context; the credibility of the evidence; and the relationships between policy and research communities[34]. The ODI framework sheds light on why the Thai researchers and policy makers were successful with their plans, resulting in the instigation of the universal health coverage plan. As Mills[35] puts it, the conducive elements of research-policy nexus in such cases include a strong political imperative behind the policy; highly credible research evidence; and longterm collaboration between politicians, bureaucrats and researchers, who shared common goals and trusted each other.

Health technology assessment and policy making

The needs for medicines, medical devices, therapeutic procedures and other health interventions which are safe, effective and, at the same time, offer the best value for money, are common in the health systems of developed and less-developed countries. HTA is expected to address these needs since its findings may serve as rigorous evidence to inform policy making and professional practice[36]. Following Banta and Luce[37], an HTA report can affect investment decisions; third-party payment policy; the adoption of new technology; the allocation of health care resources; clinician and patient behavior; and the rate of use of a technology. The literature, however, suggests that HTA results, though available, are underused and therefore have little impact. As van den Heuvel et al[38] note, for example, political arguments and interest groups played a crucial role in the introduction of new medical technologies in the Netherlands' health service, while HTA was less influential. Emphasizing the decisions made at the peripheral level, another illustration draws on a study by Hashimoto et al[39], and suggests that the adoption of coronary stenting in teaching hospitals in the USA and Japan was affected by payment systems and incentives, cultural attitudes, and local patients' characteristics.

Like policy utilization of research in other areas, HTA implications for policy development can be explained through the above-mentioned policy analysis models. In addition, HTA-informed and other research-based policy decisions are similar in terms of enabling and impeding elements. The body of literature with the focus on policy utilization of HTA of different approaches, especially economic evaluation, is expanding. However, it should be noted that the acceptance of HTA-generated recommendations among policy makers, professionals and the public varies across HTA studies with different objectives, methodologies and purposes. For example, the estimation of financial burdens of a new technology introduction seems to be less controversial than the cost-effectiveness or cost-utility analysis of said intervention. Moreover, the policy participants' interpretation of and response to 'assessment' findings and 'appraisal' results of the same policies/interventions may be totally different.

In Thailand and elsewhere, important barriers to using economic evaluation to inform health policies and care delivery are the perceptions towards economic analysis among policy makers and practitioners, who involve their knowledge of economic evaluation technique, trust in the methods, and the availability of information in the settings[40]. For some, cost-effectiveness analysis and pharmacoeconomics are viewed as 'non-science' or a 'pseudo-discipline'[35, 41]. Complex calculations, arbitrary assumptions, debatable choices of whose perspectives to pursue, difficult-to-understand methods, research designs and underlying philosophies/concepts, and time-consuming processes are among the reasons why politicians, health officials and professionals feel reluctant to adopt economic analysis as a policy making tool.

Following Cookson, Hutton[42] and Schultz[43], there are concerns about the validity of economic analysis evidence, especially the costs and effectiveness information, due to many limitations including unavoidable ethical and methodological difficulties. These include, for instance, incomplete economic data collection alongside clinical trials; a wide variation of economic assessment methodologies employed in different settings and studies; and exclusion of behavioral factors such as irrational prescription and utilization of health interventions from the estimations of costs and outcomes. The lack of confidence in the transferability of HTA across countries was one of the important barriers to use its findings among policy

makers (36). Critics of the transparency and peer review scrutiny in the reporting of research results are also significant.

Economic evaluation and its influence on priority setting and resource allocation have been scrutinized for their political aspects. As the major goal of the economic approach is to pursue 'efficiency' through the maximization of benefits and containment of resource use, such utilitarian-based analysis and its results contradict many ideologies, for example human rights, equity, ethics and professional autonomy[44,45]. Owing to the differences in these ideals, policy makers and some interests may disagree with, or hesitate to follow, the policy recommendations generated by the economic evaluation of health interventions. It is obvious that in health systems where the ultimate goals are to reduce health inequalities of underprivileged populations or to address illnesses with high burdens as the priority, cost-effectiveness evidence is likely to be ignored. In the absence of multi-criteria decision analysis, it would be difficult for policy makers to accommodate these conflicting goals of health care provision, and a trade-off between these policy goals seems to be inevitable[46].

Professionalism including autonomy, discretionary power and ethical concerns are crucial in making the decisions to provide or not to provide particular services[47]. As Teerawattananon[40] points out, it is uncommon for health professionals to consider efficiency or value for money as selection criteria of medicines and other treatment they prescribe. Moreover, the practitioners' awareness of social expectations on equitable access to health services and their professional role can affect their practice to a certain extent. While evidence-based policy/guidelines are concerned with the needs for and implications of particular treatment in the population, health workers have to relate the evidence to the conditions of their patients, and make decisions by weighing the pros and cons on an individual basis[48]. In many instances, physicians find it difficult to explain to patients and caregivers why some interventions are omitted. Negative reactions to the introduction of evidence-based medicine, including use of HTA findings, are generated through the perceptions that such ideas are 'dangerous to innovation', a tool for cost-containment, and suppress clinical freedom[3]. As Jacobson and Kanna[49] maintain, developing clinical guidelines on cost-effectiveness evaluation is an *'intrusion into physician autonomy'*. In essence, evidence-based medicine, when implemented in particular settings, allows for the participation of different actors, such as governmental authorities, purchasers and third-party payers, who can use their financial influence in clinical decisions[50].

Political policy makers are crucially concerned by the publicity of policy decisions and the expectations of the general public[1]. Although what is suggested on the grounds of anticipated clinical and economic consequences may be the best policy choice in certain situations, politicians normally take into account policy implications in wider aspects, especially in terms of social acceptability, the public preference and the political desirability of introducing particular health technologies/policies. If politicians take a leading role in policy formulation, they may choose these policies which are not only feasible to implement, but also attractive among their constituencies in order to gain popularity and be re-elected in later elections[51]. In addition, policy makers usually face competing requests for resource allocation to several technologies/programmes so that they have to make decisions in such a context on which no HTA evidence is available[48].

In addition to political motives, which drive the decisions against policy options recommended by HTA researchers, the structural context of the policy subsystems is crucial. In those societies where economic evaluation and other HTA activities are mistrusted by important institutions, such as legislative authorities and courts, it is difficult for the Health Ministry, public health program managers, insurance plans and professionals to use such analysis in decision making[1]. In some countries, health benefit plans are subject to legislation, and legislative bodies can mandate these health programs to provide certain services, which may or may not be proved cost-effective according to HTA processes[52]. These mandates are usually influenced by organized interests as well as pressure groups such as patient networks, professional associations and the pharmaceutical industry. Moreover, apart from sufficient funds, implementation feasibility which, in large part, involves health system capacity in terms of experienced workforces, knowledge, management and infrastructure are determining factors in policy choices[53].

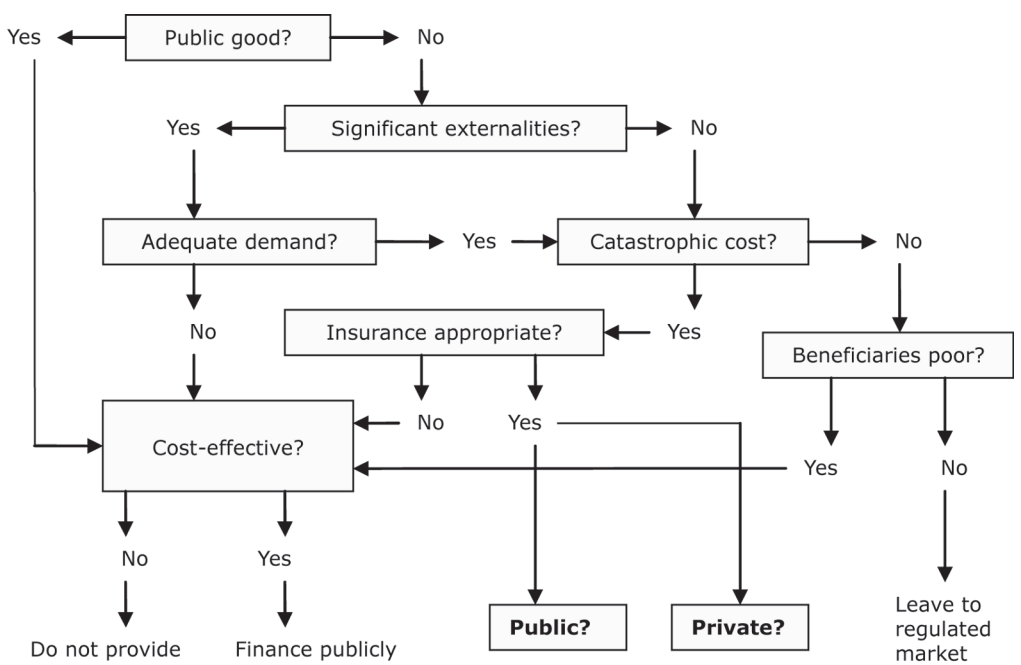
Recommendations made by the World Health Organization offer a clear illustration of the role of efficiency-oriented HTA. As suggested in the 2000 World Health Report (54), cost-effectiveness alone is not adequate to achieve a health system goal of inequality reduction. This means that other criteria are needed in deciding what technologies to invest in and

provide. Such criteria address different social elements through a set of questions: if interventions of focus are public goods, with significant externalities and adequate demand and whether or not they may cause financially catastrophic consequences, especially among the poor (Fig. 1).

Role of HTA evidence in Thailand: The case of antiretroviral policy development

To provide an illustration of how and to what extent HTA has been utilized in Thailand, the development of an antiretroviral therapy (ART) program[55] is presented as a case study. The HIV epidemic in this country started in the late 1980s, and had afflicted almost 1 million people by the mid-1990s. A publicly-funded initiative to deliver antiretroviral-based medication has been implemented since 1992, with two significant shifts in program features in 1996 and 2001. The first policy change was informed by an economic evaluation, suggesting therapy provision under the national initiative would soon be unaffordable as the numbers of AIDS patients continued to rise while antiretrovirals (ARVs) were expensive, and that ART was much less cost-effective than the use of zidovudine and infant formula to prevent mother to child HIV transmission. Owing to such calculations, the Health Ministry replaced the existing ART service with a clinical trial project, and maintained the number of treatment recipients at 2,000 a year.

The policy shift in 2001 took place when a newly-elected government decided to provide universal access to a highly active antiretroviral therapy (HAART), which meant the government had to expand the service to cover 100,000 patients at the least. According to Tantivess[56], such policy innovation was encouraged by several elements including local production of first-line ARVs and subsequent drug price reductions; campaigns run by non-governmental organizations (NGOs); involvement of health system reformists; and global efforts to promote access to HIV treatment in resource-poor settings. It is noteworthy that although drug costs had dropped significantly, HAART did not offer value for money when compared with to HIV prevention[57,58]. This suggests that the policy to scale up ARV therapy in Thailand, as well as other societies, has not been driven by efficiency-promoting ideal, but human rights, ethics and equity[55]. Furthermore, a concerted effort by NGOs, including people living



Source: World Health Report 2000 (54:55)

Fig. 1 Questions to be addressed in public resource allocation to health care

with HIV/AIDS, coalitions, health officials and HIV specialists had a crucial role in not only agenda setting and adoption of universal treatment policy, but also the processes of formulation and implementation thereafter.

As Tantivess and Walt[55] emphasize, this case study may not be generalizable since ART is unique. The demand for ARV-based medication is substantial, while the drugs are expensive. Treatment is indicated in incurable disease for which prevention measures are much more cost-effective. ART delivery is complex, and may cause both positive and negative spill-over effects. Finally, there has been global commitment to expanding access to ARVs. These features, to a certain extent, shaped the decisions of the national treatment initiative in Thailand, and are not comparable with decision making in other health interventions.

To sum up, the allocation of health care resources to ART delivery in Thailand over the past decade was largely shaped by the considerations of financial feasibility. In the first policy shift, the influence of economic information was obvious. On the other hand, the recent reforms were guided by other motivations and the strong advocacy of actor networks. However, the importance of affordability in association with ARV price reduction could not be ignored in both cases.

HTA and ethical dimension of resource use in health system

According to the American Heritage Dictionary of Cultural Literacy 2005 edition, ethics is referred to as *'the branch of philosophy that deals with morality. It is concerned with distinguishing between good and evil in the world, between right and wrong human actions, and between virtuous and nonvirtuous characteristics of people.'* When applying ethical principles in policy making, it means that the poor and other underprivileged groups will be given priority to obtain social benefits as well as being protected against financial risk. In the health domain, it is suggested that health care financing should be managed to achieve two objectives: the best attainable average level (or goodness) and the smallest feasible differences among individuals and groups (or fairness)[54].

In practice, however, it is difficult to develop a consensual framework to guide fair or ethically-sound resource allocation. This is because, as noted by Daniels[59], different arguments have been raised to debate, for example, what constitutes fair outcomes; what distributive principles should be used (e.g., to pursue best outcomes, to help the sickest patients, or to treat the most urgent needs; and how such principles should be interpreted in particular situations. In addition, there are dilemmas concerning responsibility for health needs, as some suggest that the scarce resources should not be allocated to therapy for the diseases responsible by individuals[60]. The lack of comprehensive theory of justice has resulted in unresolved issues not only in allocating resources across public health programs and interventions, but also in rationing treatment to individual patients[61].

As recently mentioned, the introduction of HTA, especially economic evaluation and ethical principles, is normally viewed as conflicting, in particular with the allocation and use of health-care resources where life or death is the consequence. While the economic approach seeks to maximize benefits to the population within available resources, the ethical counterpart mainly focuses on fairness, by seeking a fair distribution of available resources among competing health needs[62]. Also, people may view the resource allocation guided by economic assessment as unfair, because the cost-effectiveness analysis focuses on the sum of costs and benefits and mostly ignores their differences across affected groups of people[60]. Meanwhile, some scholars assert that the introduction of an economic approach in determining resource distribution violates the *'special moral importance of health'*, since the attempt to quantify everything in numbers transforms the discussion on ethics and human rights into a *'complex, resource-intensive, and expert-driven'* process, which neglects the debate concerning underlying values[63].

A chapter in the book titled 'Disease Control Priorities in Developing Countries' points out that resource allocation should meet two main ethical criteria[60]. First, the resources should be allocated to maximize the benefits for the population. It is argued that economic analysis can be regarded as a measure of one ethical criterion for HTA, since the benefit-maximization principle is underpinned by a moral concern: the numbers of beneficiaries of any cost-effective technology would be larger than investing in its alternatives, which are not cost-effective. Second, the distribution of costs and benefits to distinct individuals or subpopulations should be equitable. The authors maintain that although equity concerns may conflict with cost-effectiveness, sometimes efficiency and equity can coincide. Furthermore, the inclusion of cost and benefit components in economic analysis are not

value-free or exclusively a technical issue, but result from the analysts' ethical judgments.

Many researchers suggest reinventing the concepts of HTA into a more comprehensive form of evaluation research, and expanding the evaluation landscape to involve other dimensions beyond those of safety, efficacy and cost-effectiveness[45]. These include the application of ethical theories, principles and rules to assess particular interventions in order to offer morally-justified solutions. As ten Have[45] asserted, ethics can contribute to HTA in two ways, which are identifying the relevant moral issues to be addressed in the evaluation of a particular technology and expanding the conceptual framework and research questions by examining the relationship between technical and non-technical elements. To implement ethics-impregnated approaches in HTA, several groups of actors other than policy makers and experts, especially afflicted people and civil society organizations, need to be involved in the priority-setting and investment in health. Participation of a broader range of stakeholders in policy decisions is a rising trend in current political sphere of many developed and developing countries[64].

Dealing with stakeholders in health technology assessment

The previous sections have reflected, in part, the political aspects of HTA, especially the integration of HTA findings into policy making and practice. It can be seen that not many groups of key actors are involved closely in the upstream processes of evidence producing. This is because the examinations of the benefits, costs and other consequences of health interventions are highly technical and so complex that only those who have expertise and/or interests in this area are willing to participate. This means that researchers and the health technology industry are prime stakeholders, while policy makers are also important.

At present, as HTA is defined to cover research with a broad range of focuses such as studies in biomedicine, behavior, economics, and social sciences, the range of researchers with the necessary expertise required has widened accordingly. Meanwhile, private businesses, including pharmaceutical and medical device companies, can be affected by HTA results in either positive or negative ways; the sale of their products may increase if the assessments suggest the interventions are cost-effective and affordable by major purchasers, and vice versa.

HTAs may be influential as their results and associated policy recommendations can be used to guide priority setting and resource allocation. In essence, policy makers, at different levels, can be regarded as a cluster of HTA stakeholders. Examples of actors in this group include: politicians, health officials, managers of health benefits/insurance schemes, hospital administrators as well as decision-making panels in particular domains. Moreover, health professional organizations, such as physicians associations, royal medical colleges and other academic institutes, can be classified into this group as they may take part in some areas of policy development, for instance in the formulation and adoption of clinical practice guidelines and professional handbooks, all of which take into consideration certain forms of HTA findings. Another set of HTA stakeholders comprises practitioners and the general public who are expected to apply HTA findings and recommendations, mostly disseminated through intermediaries such as education and information campaigns, in their professional practice and health behaviors, respectively.

The understanding of policy participants, their perceptions and positions towards HTA and certain results, interests, roles and power is crucial in encouraging HTA utilization. Stakeholder analysis is a useful approach to examine all these facets, and helps policy makers and managers to detect and prevent potential misunderstanding or opposition to the introduction of the policy[65,66]. Following Roberts and colleagues[67], policy innovations and changes in practice and behaviors can be managed by employing strategies to address the positions of selective policy participants; the power of important stakeholders; the numbers of policy advocates and opponents; and the construction of problems and policy alternatives among key stakeholders. Lessons drawn on research-policy nexus in many settings as discussed above are also helpful to bridge the gaps between the research and policy-making arenas. Mills[35], for instance, emphasizes the importance of perceived quality of research as well as strong relationships and trust between policy makers and researchers. In a similar vein, many suggest that the use of HTA in policy making is a shared responsibility between evidence producers and end-users[68], and full engagement of end-users throughout the assessment process in order to identify problems and reflect needs and underlying perceptions in local perceptions will help to increase the impact of HTA for policy[69].

Conclusion

The present paper argues that the decisions to pursue particular policies and practices are not always rational, but complex and dynamic. Research-derived recommendations, including HTA evidence, are not the sole factor underpinning such decision making. Policy participants, in groups and individuals, with different ideals and interests, are crucial mechanisms driving the policy processes, through the construction of the problematic issues and corresponding solutions. In certain instances, HTA findings may be accepted by policy makers and practitioners. This increases the tendency of policy utilization. In most occasions, the integration of HTA in public policy development and implementation is difficult, but not impossible. It depends on the conformity to major norms and values of socio-political systems, credibility of evidence, practicality of policy recommendations, and policy makers-researchers relationships.

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บทบาทของการประเมินเทคโนโลยีด้านสุขภาพในกระบวนการนโยบายสาธารณะ

ศรีเพ็ญ ตันติเวสส

การพัฒนานโยบายและการนำนโยบายไปสู่การปฏิบัติในภาครัฐเป็นกระบวนการที่ซับซ้อน และเปลี่ยนแปลงอยู่ตลอดเวลา ในขณะที่ตัวแสดงจำนวนมากซึ่งมีผลประโยชน์ที่แตกต่างกันเข้ามามีส่วนเกี่ยวข้อง ตัวแสดงเหล่านี้ทั้งที่เป็นปัจเจกบุคคลและองค์กรมีการแข่งขันกันเพื่อที่จะให้ได้มาซึ่งสิ่งที่ตนต้องการ โดยผู้ที่มีอำนาจเหนือกว่าผู้อื่นจะเป็นผู้นำในการตัดสินใจเชิงนโยบาย ผลการวิจัยและข้อเสนอแนะจากการประเมินเทคโนโลยีด้านสุขภาพได้รับการคาดหวังว่าจะมีบทบาทสำคัญในการกำหนดนโยบายและเป็นแนวทางในการประกอบวิชาชีพ อย่างไรก็ตาม หลักฐานที่ได้จากกระบวนการทางวิทยาศาสตร์เหล่านี้มักจะไม่ได้รับความสนใจนำมาใช้ประโยชน์ ที่เป็นเช่นนี้เนื่องจากการประเมินใช้การคำนวณที่ยุ่งยาก การตั้งสมมติฐานที่ไม่ชัดเจน การเลือกมุมมองของบุคคลหรือสังคมซึ่งหลายฝ่ายมีความเห็นไม่ตรงกัน ระเบียบวิธีวิจัย แนวคิดและปรัชญาที่เข้าใจได้ยาก รวมทั้งใช้เวลานานในการศึกษาวิจัย ประเด็นด้านจริยธรรมและความรู้สึกที่ว่าแนวทางการบำบัดรักษาโรคที่กำหนดขึ้นจากผลการประเมินทำให้สูญเสียความเป็นอิสระของวิชาชีพก็เป็นปัจจัยที่มีความสำคัญ

A Determination of Topics for Health Technology Assessment in Thailand: Making Decision Makers Involved

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This study is to describe experiences and findings from the topic selection process for health technology assessment (HTA) conducted by Health Intervention and Technology Assessment Program. The process comprised of 5 stages namely: 1) determining objectives, scope and involved stakeholders; 2) requesting potential topics for assessment from decision makers at the national health authorities; 3) reviewing related literature on and prioritizing the proposed HTA topics by HITAP researchers; 4) selecting the HTA topics by decision-makers; 5) analyzing the strengths and weaknesses of the current topic selection processes by HITAP staff. The strengths of the topic selection were systematic and transparent. It also required participation from stakeholders; however, the limitations were topics prioritization methods and time constraints. Lessons learnt from this procedure can be useful for improving the next HTA topic selection in order to increase the usefulness of the future HTA results.

Keywords: *Health technology assessment, Health policy, Health priority, Health care rationing, Biomedical technology*

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Health Technology Assessment (HTA) is a comprehensive form of policy research that provides information on the consequences of the application of health technology. It is used primarily to guide health care resource allocation decisions[1,2]. Over the past few years, HTA programs have been introduced with strong commitment in many settings[3], and this is not exceptional in Thailand, where the Health Intervention and Technology Assessment Program (HITAP) was recently established in order to appraise a wide range of health technologies including pharmaceuticals, medical devices, procedures, individual and community health promotion and prevention interventions. Although the program is jointly funded by four public sources, namely; (1) the Thai Health Foundation, (2) the Health System Research Institute, (3) the National Health Security Office, and (4) the Ministry of Public Health, HITAP itself serves as a technical advisor for all public health authorities at national level who are responsible for the planning and management of health technology.

In general, the HTA process consists of three key features, (1) identification of technologies needing assessment, (2) assessment procedures and (3) technology appraisal (2). Given resource constraints in technology assessment, the procedure for the selection of HTA topics can be seen as a crucial part, because it is

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not only the first step of HTA, but also the topics for assessment themselves which need to be policy-relevant so that the assessment findings can properly assist decision-makers in making rational and effective policy decisions[4,5]. While there is a growing amount of literature addressing issues related to assessing and appraising health technology, very little literature demonstrates how the procedure for the selection of HTA topics works. For example, what criteria are actually used in the selection of HTA topics, and can the selection process be made in a transparent, scientific and socially acceptable way. The probable reason for this is that the methods of identifying priority areas for HTA are not well developed[6].

Goodman did the most extensive review on the potential criteria used for topic selection of HTA[2]. The criteria include disease burden, the cost of technology, variations in clinical practice, available findings not well disseminated or adopted by potential users, the need to make policy decisions, scientific controversy, public or political demand, sufficient research findings available upon which to base assessment, the timing of assessment relative to available evidence, the potential for HTA evidence to be adopted in policy and practice, and the feasibility for conducting HTA. Although his recommendations are comprehensive, many of the suggested criteria are subjective and, more importantly, he did not suggest how to apply these criteria to the selection procedure. Namely, who should be involved and how should they be involved in the selection process.

A growing concern is that all the processes of HTA, including the selection of HTA topics, are managed in a systematic and transparent manner. Teerawattananon and his colleagues demonstrated a poor distribution of research resources for HTA in Thailand, where HTA topics do not focus on major health problems, but rather are induced by the interests of individual scholars or private investment[7]. They requested a comprehensive and systematic way to prioritize areas of future HTA, to ensure that each investment would do the most good for society. In doing so, Batista and Hodge also suggested that the procedure should be well documented and involve end users and other relevant stakeholders[8]. Oxman and colleagues required openness and full participation from all parties in the group-decision-making process[9].

The purpose of this present paper is to report findings from the HTA topic selection process recently initiated in Thailand. It is intended to improve approaches in identifying priorities for HTA that are systematic, efficient and transparent. This is also part of HITAP activities in which its aim is to develop appropriate national strategies and plans for the future establishment of formal systems for the assessment, procurement and management of health technologies in Thailand. Recognizing rare literature on this, HITAP is expected to provide useful information to those involved in identifying candidate assessment topics in other settings.

Material and Method

This study makes use of the action research method with a view to understanding the social situation to improve for improving the strategies and practices of priority setting of research topics for HTA in Thailand. The overall procedure consists of five steps. First, HITAP consulted its staff to set the objectives and scope of the HTA topic process. This process was done with a series of meetings between August and November 2006 and agreement was reached that the procedure needs to be made in an explicit and transparent manner. It should also involve the intended users or target groups of an assessment. However, because the users of HTA can be very varied, ranging from clinicians, researchers, company executives, hospital directors, healthcare program managers and third party payers, who have different levels of expertise, interests and concerns about the effects or impacts of health technology, it was the intension of HITAP to involve, at this stage, only participants from groups of potential HTA users at the national level (healthcare program managers and third party payers).

Secondly, HITAP sent out an official letter dated December 27th, 2006 inviting public health agencies at the national level (Box 1) to submit their lists of 'interventions' including medicines, medical devices and procedures, and individual and community health promotion and prevention interventions, in which they consider they required assessment. Three sets of documents, namely a brochure introducing HITAP, and open-ended and close-ended self-administered questionnaires to gather the information, such as type of health interventions and their comparators, the impact on financial burden and health problem, and the magnitude of the problem, were enclosed with the invitation letter. The deadline for returning the completed questionnaires was set at January 19th, 2007. The representatives of these fifteen agencies were also invited to participate in a workshop which aimed at prioritizing the proposed health interventions in order

Box 1. List of organizations invited to participate in the HTA topic selection process in 2007

Third party payers
- National Health Security Office
- Ministry of Finance's Department of General Comptroller
- Social Security Office

Healthcare program managers at national level (Ministry of Public Health departments):
- Department of Medical Services
- Department of Disease Control
- Department of Health
- Department of Mental Health
- Department of Health Service Delivery Support
- Department of Medical Sciences
- Department of Thai Traditional Medicines
- Bureau of Policy and Strategy
- Department of the Food and Drug Administration including subcommittee for development of the National List of Medicines

HITAP funding organizations:
- Thai Health Promotion Foundation
- Health Systems Research Institute

to select the top ten most important items for the HITAP assessment process in 2007.

Thirdly, telephone calls were made to follow up on the questionnaires from the agencies. After receiving the returned questionnaires, HITAP researchers shortened the list of proposed HTA topics by excluding some interventions if they were: (1) interventions that should be assessed by the responsible authorized organizations rather than HITAP, (2) interventions that were recently assessed by other researchers, and (3) interventions that were not directly related to health. We also excluded some proposed topics which had no clear research questions e.g. giving unreasonable comparator(s) or not enough specific research questions.

Subsequently, each HITAP researcher was assigned to review literature related to the short- listed topics using PubMed and the database from The Centre for Reviews and Dissemination (CRD). The review was to set up a priority list of HTA topics for assessment using preset criteria in which each intervention item would be considered by 6 criteria: (1) the potential policy implications of the assessment results, (2) the magnitude of health problems to be addressed by the intervention, (3) the financial burden generated by the introduction of the intervention, (4) the duplication of assessment, (5) the variation in professional practice, and (6) the feasibility to use the assessment results to alter professional practice. A special meeting was held for all HITAP researchers on January 30th, 2007 when the results of the literature review were presented by each responsible staff member. Then HITAP researchers scored (only '0' and '1') each intervention item against the criteria set. The overall score was then summed up to make priority list 'A', which represents only the viewpoint of the HITAP staff.

Fourthly, the aforementioned workshop was convened on February 9th, 2007 from 9 am to 4 pm. According to the agenda, the following activities would be undertaken in series:

- Presentations of the background and importance of interventions by the proponent agencies, which was followed by comments and discussion by the audiences. An equal amount of time (2 minutes per item) was allocated to the proponents and discussants.

- Prioritization of interventions by the representatives of each participating health authority to make the priority list 'B' from the participants' perspective. This was planned to be carried out by scoring each item against the criteria set by the HITAP researchers.

- Presentations of priority list 'B', in comparison to priority list 'A', done by HITAP researchers.

- Discussion among the workshop attendants and the HITAP researchers, focusing on the differences in the top-ten priorities from the two lists, and potential modification.

- Final decision on the list of ten interventions to be appraised by HITAP in 2007.

However, during the workshop the actual process was modified slightly to accommodate the attendants' suggestions; namely, ten interventions were selected and listed by each participating agency, without scoring and ranking.

Finally, HITAP organized an internal meeting among its researchers and supporting staff to discuss the strengths, weaknesses and other aspects concerning the priority-setting and selection methods. All were encouraged to share their observations, analyses and recommendations. In addition, comments and suggestions made by the representatives of participating agencies, as well as empirical evidence on particular issues, came from evidence reviewed and inserted as results of this study.

Results

(Fig. 1) Illustrates the HTA topic selection process in Thailand. Of the 15 questionnaires sent out, 12 health authorities responded with 52 candidate HTA

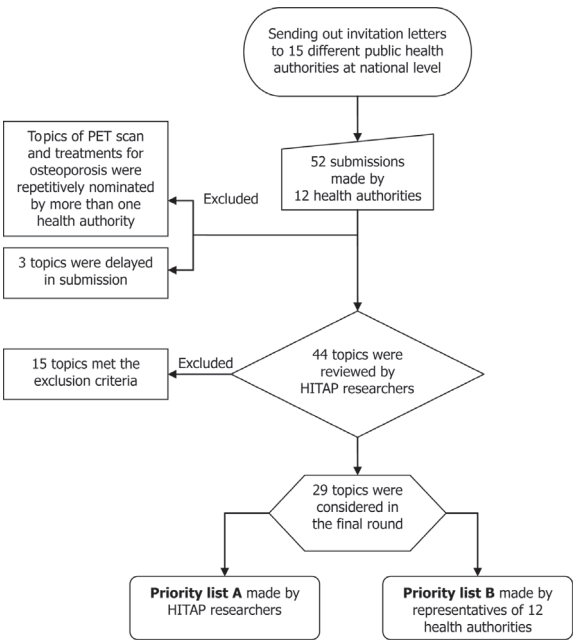

Fig. 1 Prioritization of health technology assessment topics in Thailand in 2007

topics submitted. However, two of them, namely the Department of Mental Health and the Thai Health Foundation, submitted no topic. The largest amount of submissions for the topics proposed for assessment were for pharmaceuticals and medical devices, accounting for 60% of the overall submissions (Table 1). Most pharmaceuticals topics (10 topics) were proposed by the subcommittee for development of the National List of Medicines (NLM), which is responsible for establishing a list of pharmaceutical products for public reimbursement, while all nine topics concerning health policy issues were submitted by Ministry of Public Health Departments. There were two topics; the Positron-Emission-Tomography-(PET) scanner and medical treatments of osteoporosis that were nominated by more than one public health authority (five nominations were made for the PET scanner and two nominations for the treatment of osteoporosis).

Three candidate topics proposed by one organization were initially excluded in the prioritization process due to the delay in submission (two weeks behind the deadline), resulting in only 44 designated to be put forward for further consideration. Consequently, after be reviewed by HITAP staff, 15 topics were excluded due to the following reasons:

- the proposed intervention and its comparators for assessment were not comparable *e.g.* 'Cardiac catheterization vs. echocardiography for investigating coronary arthrosclerosis';

- there were organizations that are formally responsible for the assessment *e.g.* 'the quality of condoms sold in Thailand' (Medical Device Control Division);

- the proposed topics had been recently assessed by researchers and the results would be available soon *e.g.* 'assessing cost-effectiveness of using nucleic acid amplification technology for screening blood components';

- the proposed interventions were not directly related to health e.g. 'cost-effectiveness analysis on interventions for mobile phone battery disposal';

Table 1. Proposed topics classified by types of agency and intervention

	Third party payers	Healthcare program managers	Subcommittee for development of the National Drug List	Funding organizations	Total (%)
Pharmaceuticals	6	-	10	1	17 (33)
Medical devices	6	7	-	1	14 (27)
Procedure	5	-	-	-	5 (10)
Service delivery	1	2	-	-	3 (6)
Health policy	-	9	-	-	9 (17)
Not applicable	-	4*	-	-	4 (8)
Total	18	22	10	2	52 (100)

i.e. health impact assessment of using insecticide in orange plantations in Thailand, cost-effectiveness analysis on interventions for mobile phone battery disposal, development of a method for assessing school child development, and assessing the impact of reporting false-positive or false-negative testing results (given no specific test)

- the scope of the study was not specific enough e.g. 'the use of antibiotics in Thailand'.

At final, 29 HTA topics were included in the final round of prioritization which was made independently on two different occasions by both HITAP staff and representatives from 15 health authorities, as specified previously in the methodology section.

Table 2 reveals results of the two top ten priority lists made by HITAP staff (list 'A') and representatives from 15 health authorities who participated in the workshop (list 'B'). There were six candidate-HTA topics that were in both priority lists. These included the PET scanner, medical management of osteoporosis, advanced management of Hepatitis B and C infection, medical management for Dementia/Alzheimer's disease, lipid lowering medications, and the use of erythropoietin for the treatment of advanced stage cancer. The HTA topics namely, percutaneous transluminal coronary angioplasty for the treatment of coronary heart disease, magnetic resonance imaging, commercial factors for treatment of Hemophilia and clopidogrel, were in the top ten of the list 'A', but not the list 'B'. In contrast, bone marrow transplantation in acute myeloid leukemia, cochlear implantation, HIV oral fluid testing for HIV diagnosis and insulin analogues were only in the top ten of list 'B'.

The anticipated utility of HTA from the perspective of the workshop participants varied across interventions. Economic evaluation and budget impact analysis of drugs and medical equipment and their comparators were generally requested by representatives of third party payers, with the purpose of recommending if particular interventions should be included in the benefit packages. Another use of HTA results was to inform the decision-markers of the most appropriate indications of health interventions, for example under what conditions the use of the PET-CT scan is appropriate given current available evidence. In addition, the assessments were anticipated to be helpful in devising effective measures for disease management as well as to regulate the distribution of high-cost equipment. The demands for management and financing mechanisms to promote the rational use of expensive technologies were also discussed.

Discussion

Although decision -makers, health professionals and academics are admirably interested in HTA[10], there is a general shortage of resources for

Table 2. Comparison health technology assessment topics identified by HITAP researchers (list A) and representatives from 15 national health authorities (list B)

	Priority list A			Priority list B	
Ranking	Topic for assessment	Ranking of list B	Ranking	Topic for assessment	Ranking of list A
1	PET scanner	1	1	PET scanner	1
1	Medical management of osteoporosis	2	2	Medical management of osteoporosis	1
1	Advance management of Hepatitis B and C infection	3	3	Advanced management of Hepatitis B and C infection	1
1	Medical management for Dementia/Alzheimer's disease	4	4	Medical management for Dementia/Alzheimer's disease	1
1	Lipid lowering medications	6	6	Lipid lowering medications	1
8	Erythropoietin for treatment of advanced cancer	6	6	Erythropoietin for treatment of advanced cancer	8
1	Percutaneous transluminal coronary angioplasty for treatment of coronary heart disease	16	4	Bone marrow transplantation in acute myeloid leukemia	11
1	Magnetic resonance imaging	22	6	Cochlear implantation	15
8	Commercial factors for treatment of Hemophilia	16	6	HIV oral fluid testing for HIV diagnosis	19
8	Clopidogrel	27	6	Insulin analogues	19

health research and it is not possible to undertake assessment for every single health technology. HTA studies often reflect the narrow interests of individual scholars and studies are sometimes initiated and supported by commercial sponsors[7,11]. As a consequence, it is necessary to ensure that HTA studies focus on topics that are relevant to the perspectives of its users, namely decision makers, and could subsequently have a substantial impact on decision making. This current paper offers a critical overview of plausible strategies and mechanisms employed by HITAP to advocate the involvement of the potential users in the prioritization process of HTA topics.

A review from international literature done by the authors indicates that many HTA agencies have attempted to include stakeholders into process for HTA topic selection (Table 3). While health care ad ministrators or public health insurers are the major sources for HTA topic nomination, only few HTA agencies allow industries to be involved. National Institute for Health and Clinical Excellence (NICE) of England and Wales is the most comprehensive that include the majority of stakeholders into its process for HTA topic selection.

The study suggests that this initiative was warmly welcomed by the responsible health authorities in Thailand, with twelve out of fifteen organizations returning the questionnaire and representatives from all fifteen health authorities participating in the workshop. Furthermore, during the workshop many participants expressed their gratitude and support of the good intentions of HITAP. They were aware that HITAP was trying to make HTA topic selection transparent and participatory. Also, they were willing to make the selection process worked, and learn together to improve it.

It was also found that the consultations were undertaken in a non-contested atmosphere even though the different health authorities had different perspectives and interests and they proposed different lists of interventions. For example, the subcommittee for development of the National Drug List submitted the topic of pharmaceuticals only and there was no one health authority that proposed topics covering all types of interventions. This may be explained by the fact that the short-time allocation allow to each presentation made it difficult for the workshop participants who were not familiar with some particular issues to follow and debate the content. As one workshop participant offered, one the way to improve the selection process was that HITAP should gather necessary information to support the assessment of certain

Table 3. Comparison of the sources of suggestions for health technology appraisals among various health technology assessment agencies

Settings	Health care administrators/ public health insurers	Health professional bodies	Industries	Academics/ Research institutes	General publics	Reference
Gezondheidsraad	✓					[13]
DAHTA		✓		✓	✓	[14]
SBU	✓	✓		✓	✓	[15]
CADTH	✓	✓			✓	[16]
VATAP	✓				✓	[17]
DACEHTA	✓			✓		[18]
MSAC	✓		✓		✓	[19, 20]
NICE	✓	✓	✓	✓	✓	[21]
HIRA	✓				✓	[22]
MRC	✓					[23]
HITAP	✓			✓		

Gezondheidsraad = Health Council of the Netherlands, **DAHTA** = German Agency for Health Technology Assessment, **SBU** = Swedish Council on Technology Assessment in Health Care, **CADTH** = Canadian Agency for Drugs and Technologies in Health, **VATAP** = Veteran Administration's Technology Assessment Program, **DACEHTA** = Danish Institute for Health Technology Assessment, **MSAC** = Medical Service Advisory Committee, **NICE** = National Institute for Health and Clinical Excellence, **HIRA** = Health Insurance Review Agency, **MRC** = Interim National Steering Committee on Health Technology Assessment, Medical Research Council, **HITAP** = Health Intervention and Technology Assessment Program

interventions from proponent agencies, and then circulate this information to all the attendants to study prior to the consultations.

In the workshop the presentations and discussion were closely relevant to the priority criteria set by HITAP, which mostly focused on: epidemiology, including the prevalence of diseases and estimations of demands for particular technologies in Thailand, current practice recommended by international associations and experts, clinical effectiveness in comparison with conventional interventions, variation in access to or coverage of technologies in the country, and anticipated financial burdens of the proposed interventions if provided to patients in need. The high costs of drugs and medical equipment were highlighted as crucial rationale to support the assessment priority. For some technologies, evidence on treatment outcomes and potential expenditure was drawn on studies in developed countries and Thai experience according to expert opinion.

While HITAP researchers scored each intervention item against the preset criteria, an important development of this workshop was that the attendants disagreed with HITAP's proposal to prioritize the interventions by scoring them in accordance with the six priority criteria. Many participants argued that such a process would not work well since it was subjective and not evidence-based, as the information provided in the presentations and discussion was brief and inadequate. Moreover, some participants commented that the methods were inappropriate because only two categories, 0 and 1, were allowed in the evaluation of interventions in each facet. As pointed out by one MOPH official, since most of the participants had a conflict of interest, they tended to give priority to their preferred lists, especially in the absence of sound methodology to prevent these biases. Therefore, the actual process allowed respondents from each health authority to name the top ten most important interventions without scoring or ranking them.

It can be seen that results from the two different approaches, of which one was done by HITAP researchers and the other by representatives from the fifteen health authorities, were similar, with six out of top ten items in priority list 'B' were in the top twenty of priority list 'A'. As a result, it was agreed that HITAP would select the topics identified by the representatives of the national bodies in priority list 'B' as its topic for further assessment.

And when we consider whether the priority topics have targeted major health problems based on the disease burden study in Thailand[12], it was found that five of ten priority topics for list 'A' and 'B' focused on diseases that were the twenty leading causes of disease burden (Fig. 2). Illustrates the proportion of overall disease burden, the proportion of economic evaluation publications that were published in PubMed, EMBASE (Ovid) and Academic Search Elite (EbscoH) between January 1982 and December 2005 for the top 20 major health problems, and HTA topics in priority list 'A' and 'B'. It is noteworthy that this priority setting could help HTA to focus on some particular health conditions where there were only a few (relatively to its disease burden) or no existing HTA studies.

There are some concerns regarding the HTA topic selection in this study. Firstly, that there were too many topics included in the final round of selection resulting in a short time allocation for presentation and discussion of each HTA topic. Also, this could prevent participants from understanding and debating the topics. Since this study found that all top ten in priority list 'B' were in the top twenty of priority list 'A', the final round of topic selection would have included only the top twenty of priority list 'A'. As a result of this, a longer time could have been spent on the presentation and discussion stages.

Secondly, since this is the first time that HTA topic selection was processed with involvement from potential users (national health authorities), it can be seen that there was some confusion regarding the scope of HTA conducted by HITAP. Even though this was the case, majority of health authorities have done well. There is a need for those health authorities to be well informed on the objectives and methods for HTA topic selection as well as the scope of the assessment. In addition, further research is also required to understand the ways in which each health authority identified its own priorities for HTA, and who were involved in the process.

Thirdly, the decisions made in the workshop are subject to potential bias in favor of health interventions that might benefit only health authorities at the national level. Because of this, it is probable that a wider group of stakeholders, for example, health professionals, patient groups or representatives from the public, need to be involved in setting the agenda for HTA to ensure that HTA can improve health technology resource allocation decisions with respect to various viewpoints from stakeholders in society.

Conclusion

The Thai health care system needs HTA to be

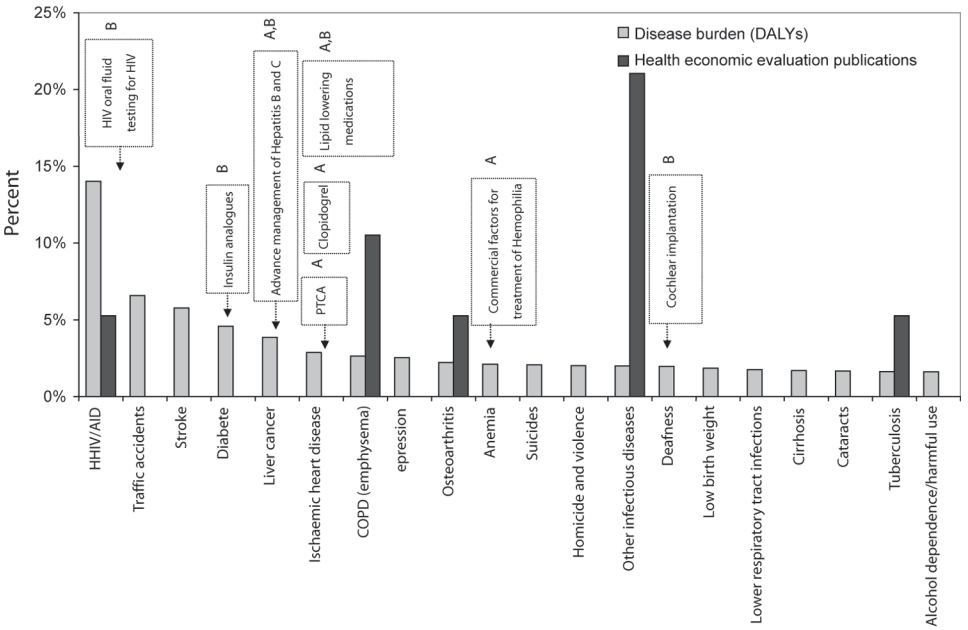

Fig. 2 Comparison of the proportion of disease burden of the top 20 major health problems, the proportion of economic evaluation publications and health technology assessment topics determined by HITAP researchers (A) and representatives from 15 national health authorities (B)

constructive to enable decision makers to make informed decisions with regard to the adoption of health technology. The development and promotion of clear criteria for selection of HTA topics is, therefore, essential to promote the efficient use of HTA information for decision making with respect to setting ultimate goals for HTA. Findings from this study illustrated the possibility of making the HTA topic selection process systematic, transparent and participatory. This will eventually increase the usefulness and credibility of HTA. In addition, it has emphasized a notion that HTA topic selection should not be seen as the sole responsibility of researchers but that decision-makers also need to be included in deciding upon the appropriate use of health technology.

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การคัดเลือกหัวข้อสำหรับการประเมินเทคโนโลยีและนโยบายด้านสุขภาพในประเทศ: กรณีศึกษาของการมีส่วนร่วมโดยผู้กำหนดนโยบาย

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รายงานนี้มีวัตถุประสงค์เพื่อนำเสนอประสบการณ์และสังเคราะห์บทเรียนจากการคัดเลือกหัวข้อเทคโนโลยีและนโยบายด้านสุขภาพสำหรับการประเมินในประเทศไทย ที่ได้รับการพัฒนาโดยโครงการประเมินเทคโนโลยีและนโยบายด้านสุขภาพ การคัดเลือกหัวข้อสำหรับการประเมินในครั้งนี้ประกอบด้วย 5 ขั้นตอน ได้แก่ 1) การกำหนดวัตถุประสงค์ ขอบเขต และผู้เข้าร่วมการคัดเลือก 2) การส่งแบบสอบถามให้หน่วยงานที่เกี่ยวข้อง เสนอหัวข้อที่ต้องการประเมิน 3) การจัดลำดับความสำคัญและคัดเลือกหัวข้อโดยทีมนักวิจัย 4) การจัดประชุมเพื่อคัดเลือกหัวข้อโดยตัวแทนจากหน่วยงานต่าง ๆ และการตัดสินผลการคัดเลือก และ 5) การจัดประชุมภายใน เพื่ออภิปรายจุดแข็งจุดอ่อน และข้อสังเกตต่าง ๆ ผลการศึกษาในครั้งนี้แสดงให้เห็นว่าการคัดเลือกหัวข้อมีจุดเด่น ที่เป็นระบบโปร่งใสและมีส่วนร่วมของผู้มีส่วนได้-เสีย อย่างไรก็ตามวิธีการคัดเลือกยังมีข้อจำกัดด้านวิธีการให้คะแนนและเวลา ทั้งนี้บทเรียนที่ได้สามารถนำไปใช้เป็นแนวทางปรับปรุงวิธีการคัดเลือกหัวข้อเทคโนโลยีด้านสุขภาพให้มีความเหมาะสม ซึ่งจะส่งผลให้ผลการประเมินมีแนวโน้มในการนำไปใช้ประโยชน์ในเชิงนโยบายได้มากขึ้น

Costs of Injuries Due to Interpersonal and Self-Directed Violence in Thailand, 2005

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Violence, a serious public health problem in Thailand, remains largely unknown for its economic costs. This study is a national-level economic cost-estimates of injury from interpersonal and self-directed violence for Thailand during 2005 using the World Health Organization-US Centers for Disease Control and Prevention's guidelines. Direct medical costs from self-directed violence totaled 569 million Baht (THB) while the cost of interpersonal violence was THB 1.3 billion. Productivity losses for injuries due to self-directed violence were estimated at THB 12.2 billion and those for interpersonal violence were THB 14.4 billion. The total direct medical cost, thus, accounted for about 4% of Thailand's total health budget while the productivity losses accounted for approximately 0.4% of Thailand's GDP. In summary, interpersonal and self-directed violence caused a total loss of 33.8 billion baht for Thailand in 2005. More than 90% of the economic loss was incurred from productivity loss and about four-fifths came from men.

Keywords: *Violence, Suicide, Economic cost*

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Globally, Disability Adjusted Life Year (DALY) loss from interpersonal and self-directed violence is about 4.2% and 1.7% of total DALY losses in men and women respectively[1,2].

In Thailand, violence accounted for a slightly higher burden than the world's average, at 5% and 2% of total DALY loss in men and women, respectively in 1999[3]. In addition to lives and health loss, violence places a massive burden on national economies. Various estimates of societal loss resulting from interpersonal and collective (civil war included) violence range from 0.3-90 per cent of annual GDP[4].

While our understanding of the epidemiological profile and the burden of violence in Thailand has improved, no study has investigated the economic costs of injury from interpersonal and self-directed violence in monetary terms.

To fill the knowledge gap, this paper estimated the costs of injuries due to interpersonal and self-directed violence occurring during 2005 in Thailand using guidelines from the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC)[5].

This study serves as an example for estimating the economic loss due to other diseases and risk factors for Thailand and also for other countries with similar levels of data sources available.

Material and Method

Economic costs of injuries from interpersonal and self-directed violence were estimated using the WHO-CDC Guidelines for estimating the economic costs of injuries due to interpersonal and self-directed violence. Table 1 provides detailed information on methods applied.

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Table 1. Information and formulas used in economic costing calculations

Parameter	Formula	Data source
Fatal incidence (I1)	= (reported deaths from self-directed and interpersonal violence) x (incomplete registration rate)	2005 National Vital Registry
Serious injury(I2)	= (injured inpatient admissions) x (utilization rates)	2005 National Health Security Office inpatient data and National Health and Welfare Survey
Slight injury (I3)	= (serious injury) x (ratio of non-admission to admission rate)	2005 National Health Security Office inpatient data and National Health and Welfare Survey
Direct medical cost	Serious Injury => {Serious injury incidence x (IP unit cost adjusted by charge weights for violence causes + OP unit cost adjusted weights for violence causes} Slight Injury => {Non-serious injury incidence x OP unit cost adjusted weights for violence causes}	
Indirect productivity cost	Fatal injury => { I1 fatal injuries x 365 x P5 x D1 } Serious => { (I2 short term injuries) x P3a x P5 } + { (I2 long term injuries) x 365 x P5 x D2 x Disability weight} Slight => { I3 x P4 x P5 }	
• Average age at death from violent injury (P1)		2005 National Vital Registry
• Average age at retirement / at which a person ceases to work (P2)		Formal national retirement age
• Average number of days a victim of a serious injury is unable to resume her/his normal activities (at the hospital and recovering from home) (P3a)		Global Burden of Disease Study, 2000
• Average number of years a victim of a serious injury is unable to resume her/his normal activities (at the hospital and recovering from home) for long term sequelae See D2 (P3b)		Global Burden of Disease Study, 2000
• Average number of days a victim of a slight injury is unable to resume her/his normal activities (recovering from home and during out-patient visits) (P4)		2006 National Health and Welfare Study
• Average income loss per capita per day, incorporates paid and unpaid work as described above (P5)		2006 National Labour Force Survey
• Ratio avg unpaid work hours to avg paid work hours		2004 National Time Use Survey
• Discount factor (D)	D1 = $1 / 0.03 - 1 / [0.03 \times (1.03)^{P2-P1+1}]$ D2 = $1 / 0.03 - 1 / [0.03 \times (1.03)^{P3b}]$	

Definition

Self-directed violence is defined as an act of violence inflicted upon oneself, whereas interpersonal violence is an act of violence inflicted by another individual or by a small group of individuals.

Violent injuries are categorized based on the severity of the injury into one of three groups. First, a fatal injury is defined as one in which the patient died as a result of that incident. Second, a serious injury is defined as one that did not cause the patient's death

within 30 days but was serious enough for the victim to be admitted into hospital as an in-patient. Third, a slight injury is one that required an accident and emergency department (A&E) visit but was not followed by hospital admission.

Incidence data and data sources

The data used in this study are derived from violent events occurring during 2005 and identified using existing national data. Violence-related injuries are classified using the International Classification of Diseases, 10th Revision Thai Modification (ICD-10-TM) codes (self-directed: codes X60-X84; interpersonal: codes X85-Y09) and were stratified by age and sex as well as by their intention either self-directed or interpersonal, related mechanisms and type of injury.

Fatal incidence is derived from national vital registration data classified by ICD-10-TM and redistributed for unknown causes of death. Mortality data from vital registry were compared with police data and other health reports.

The incidence of non-fatal violence-related injuries was estimated using the 2005 national inpatient dataset from the National Health Security Office and admission rate information from the 2005 National Health and Welfare Survey, a national representative household survey conducted by the National Statistical Office. The national inpatient database covers all patients entitled to national health security and civil service medical benefit regardless of hospital types.

Non-fatal incidence that did not require admission to hospital is derived from age-sex specific ratios of outpatient to inpatient utilization from the 2003 National Health Examination Survey. Information on the mechanism of violence (self-directed or interpersonal) was not available for non-hospitalized incident cases and was assumed to be similar to that for hospitalized incidence.

Cost data and estimation

The WHO guidelines provide a broad framework of cost categorized as direct and indirect cost. Direct cost is grouped into medical and non-medical cost. Direct non-medical costs include those incurred by the criminal justice system, costs of foster care, and private security contracts.

Indirect costs refer to resources and opportunities lost as a consequence of violence, both tangible and intangible. Productivity loss measures the loss of earning experienced by victims of violence and concerned family members, friends and employers. Other tangible costs include lost investments in social capital (e.g. education of the victim and perpetrator), life insurance costs, reduced productivity or output by the perpetrator, and macro-economic costs (e.g. reduction in property values or foreign investment due to violence). Intangible costs refer to reductions in quality of life.

Our study provides the estimates of 2 categories, namely direct medical cost, and productivity loss. All cost data is expressed in values of Thai Baht (THB). A lifetime approach is employed to estimate the economic cost of injury based on the incidence data described above and disaggregated national unit cost data.

Direct medical cost data is derived from health service utilization and costs occurring during the year 2005. Hospital unit cost (THB 2,537 per admission) was derived from reported national hospital costs for all causes adjusted by relative diagnostic related groups (DRGs) charge weights and length of stay for inpatient violence-related cases. Medical costs for fatal injuries were derived by applying the hospital unit cost to admission discharged as death.

Outpatient unit cost (THB 795 per visit) was also obtained from the same source and applied similar weights as that for in-patient cost to adjust for violence caused due to the absence of cause linkage to the outpatient unit cost. It should be noted that the database captured only public hospitals under the jurisdiction of the MOPH, there is no systematic data in non-MOPH hospitals. However, it covered more than 70% of total admissions nationwide. Direct medical costs are classified into fatal, slight and serious injuries.

Indirect costs are estimated for fatal, serious, and slight injuries using a human capital approach by measuring the value of time lost due to absence from work or reduced productivity. Future earnings are discounted at a rate of 3%. Age at death from violent injury was obtained from vital registry data. The average age at retirement was 60 years old, based on the formal national age at retirement. Inactive days caused by slight injuries were derived from the average number of days with limited daily activities ascertained from a 2006 National Health and Welfare Survey, and inactive days caused by serious injuries were derived from the average duration of injuries by body part provided by the Global Burden of Disease Study[6].

Average income loss per day due to violence was estimated by age and sex group. This estimate was derived from the summation of the product of the average national wage per day and the average number

of days of lost work; and the product of the average national wage per day and the average number of days of lost work weighted by the ratio of the average number of unpaid work hours to paid work hours.

Average national wages before taxes were obtained from the 2005 National Labor Force Survey conducted by the National Statistical Office, which incorporated formal and informal income but not unpaid or in-kind work. Days spent on unpaid productive activity were obtained from a national time use survey conducted in 2004. The unemployment rate, while known for the period (1.8%)[7], was not applied as we assumed that there was economic loss for the entire working population.

Results

In 2005, self-directed and interpersonal violence claimed 6,586 and 5,645 deaths, respectively, in total. They also resulted in 52,348 and 86,032 incidences of non-fatal serious injuries, and 270,418 and 332,133 incidences of non-fatal slight incidence respectively. Violent injuries claimed deaths among the prime of life, peaking at 30-44 in both men and women for self-directed violence, and at 15-29 in men and 30-44 in women for interpersonal violence (Fig. 1).

Self-directed violent injuries claimed 2% fatalities, 16% serious and 82% slight injuries. The profile is quite similar to the interpersonal violence injuries which claimed 2% fatalities, 20% serious and 78% slight injuries.

However, there is a specific, epidemiological profile type of violence by gender (Fig. 2). A high peak of self-directed violence among women was observed among those aged 15-29 years; this figure is twice as high as for men. In contrast, interpersonal violence, among men, peaked at the age of 15-29 years, and was three times higher than that of self-directed violence. Injuries damaged the health of prime age young adults, both men and women.

Poisoning was the most common form of serious self-directed injury for both men and women (84% men, 95% women). Sharp/blunt objects (men, 67%, women, 43%) and assault by bodily force (men, 15%, women, 35%) were the most common mechanisms of serious interpersonal injury; firearms accounted for 10% (n 8,275) of serious interpersonal injury.

When we combine serious and slight violent injuries, there was a gender specific mechanism (Fig. 3). More women applied poisoning than men, but more men applied sharp and blunt objects than women.

Direct medical costs for injuries due to self-directed and interpersonal violence totaled THB 1.9 billion in 2005 (Table 2).

The total direct medical cost for fatal and non-fatal injuries from self-directed violence was THB 569 million and that for interpersonal violence THB 1.3 billion. Nearly 75% (THB 1.4 billion) of direct medical costs were attributable to injuries among men.

The direct medical cost per incident event for THB 26,719 or 1.7 times greater than the overall

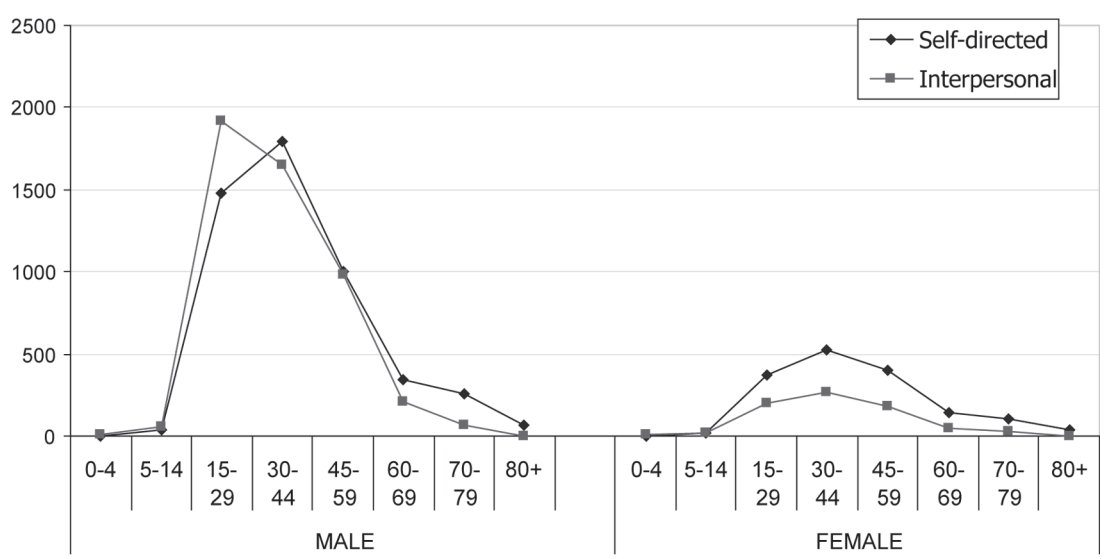

Fig. 1 Number of fatal violent injuries by types, 2005

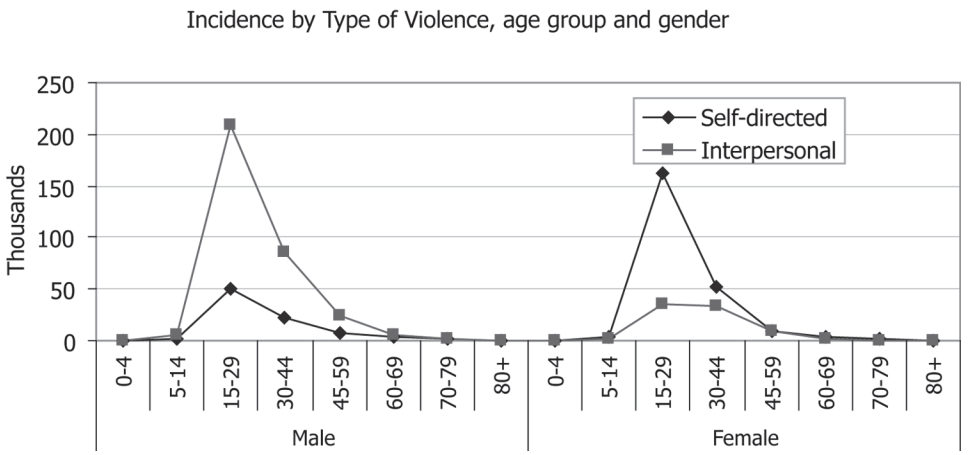

Fig. 2 Incidence of serious and slight injuries from violence by types, 2005

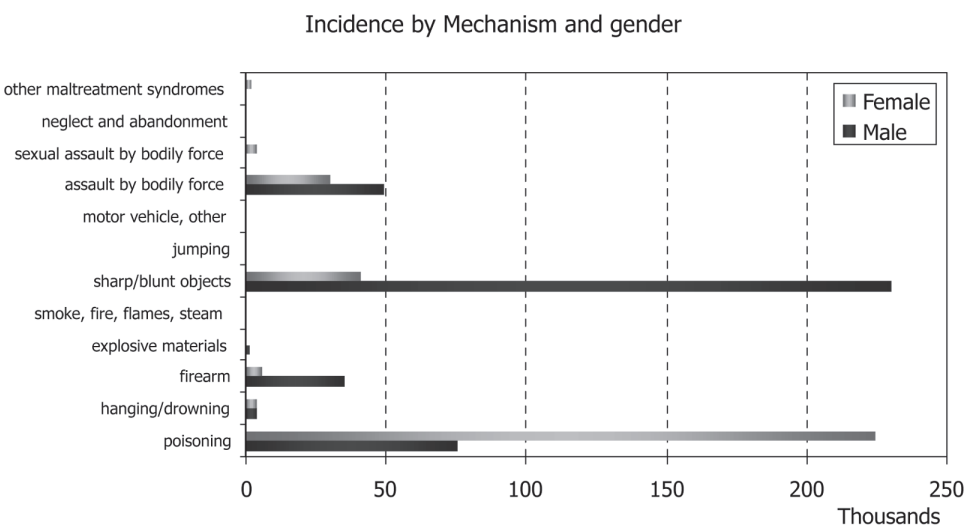

Fig. 3 Incidence of serious and slight injuries from violence by mechanisms, 2005

direct medical cost per incident event for serious interpersonal violent injuries (THB 15,911).

The share of medical costs for all violent incidence are shown in Fig. 4. Among self-directed violence, poisoning incurred the largest cost both in men and women (72%, and 91% respectively). On the other hand, violence from sharp/blunt objects resulted in the highest medical cost for both men and women. Second to this were firearm in men (19%) and assault by bodily force in women (25%).

Productivity losses from injuries due to self-directed and interpersonal violence totaled THB 31.9 billion (Table 2). Indirect medical cost for self-directed injuries totaled THB 15.4 billion and that for interpersonal injuries was THB 16.5 billion. More than 80% of productivity losses were attributable to injuries among men, and as might be expected due to the incorporation of lost productivity due to premature death, productivity losses for fatal injuries were notably greater than those for serious or slight injuries.

The direct medical cost of injuries due to violence accounted for about 4% of Thailand's total health budget in 2005 (approximately THB 50 billion). Productivity losses due to violence related injuries

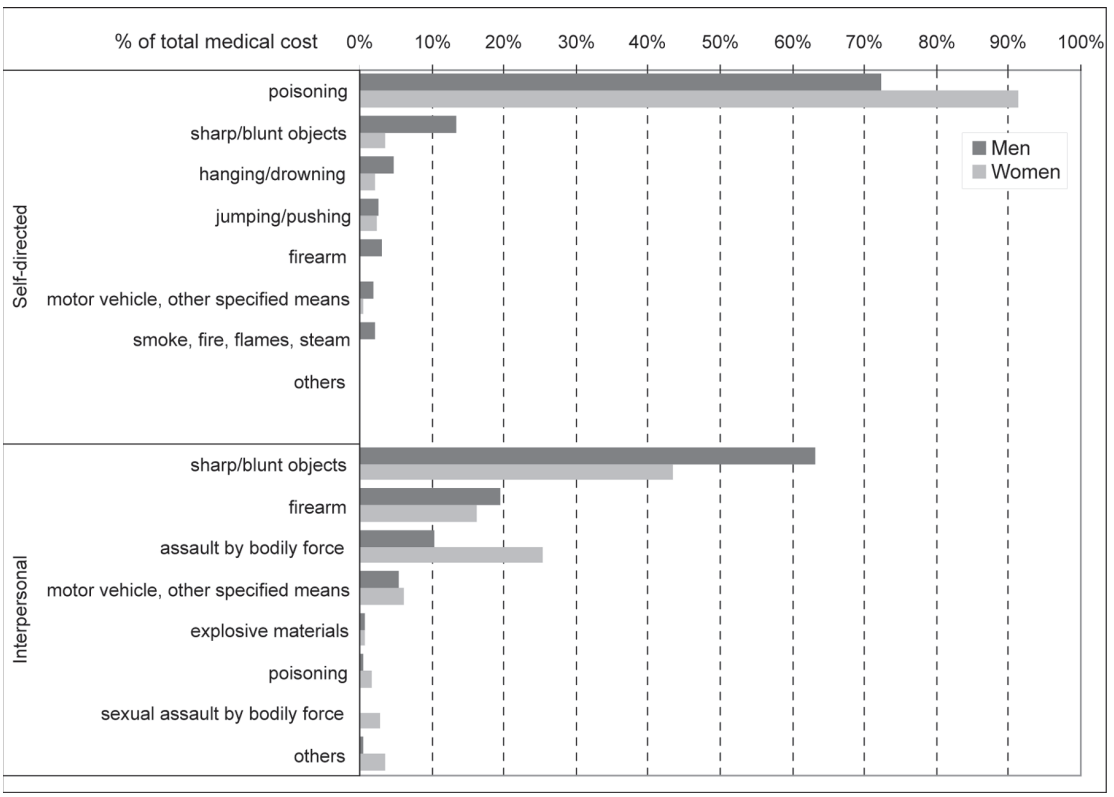

Fig. 4 Total direct medical cost by mechanism of injuries

accounted for approximately 0.4% of Thailand's GDP (THB 6.9 trillion) in 2005†. During 2005, estimated economic costs per incident violence related injury ranged from THB 795 for direct medical costs of slight injuries to nearly THB 2 million for productivity losses associated with fatal self-directed injuries among men.

Discussion and policy recommendations

Costs of violence across studies vary depending on the definitions applied, the types of costs included, and the methodologies used[8]. The US Department of Justice[9] reported the estimated direct costs of violent crime to victims resulting from short-term medical expenses and work loss at $1.8 billion, equivalent to 0.02% of the US GDP in 1994. When including indirect cost, the total amount is significantly higher. A study including psychological costs of pain and suffering into the estimate resulted in the cost equivalent to 6.5% of GDP, or $1100 per person in the US[10].

This study provides the economic loss from medical expenses and productivity loss due to self-directed and interpersonal violence in Thailand in 2005. It employs international guidelines with existing national data sources. Due to data limitation, we did not attempt to measure non-injury health effects, which are life-long and therefore likely to be many times greater in magnitude than the costs of treating physical injuries alone.

These cost estimates almost certainly underestimate the actual totals due to incomplete reporting systems and the illicit nature of interpersonal violence. Nevertheless, death estimates in this study are slightly higher than reported cases in police records. Information

† Evans and colleagues advise that only the indirect cost component involving market production (e.g., formal labour force) should be expressed as a percentage of GDP, and otherwise advise against such comparison. However, in the absence of a suggested alternative, readers will undoubtedly make comparisons to GDP; thus, the information is provided here with a note of caution. See also Evans DB, Chisholm D, Adam T, Tan Torres Edejer T. Cost of illness studies: counting what matters. Unpublished manuscript.

Table 2. Incidence of violent injuries and associated direct medical costs and productivity losses by age, sex, and severity and type of injury, Thailand, 2005

	Self-directed violence								
	Incident events			Direct medical cost (million THB)			Productivity loss (million THB)		
	Fatal	Serious	Slight	Fatal	Serious	Slight	Fatal	Serious	Slight
Total	6,586	52,348	270,417	16.0	337.5	215.1	14,272.7	663.2	469.2
Men	4,991	19,547	69,103	10.9	157.2	55.0	11,142.7	231.7	128.6
Women	1,595	32,801	201,314	5.0	180.2	160.1	3,130.0	431.5	340.7
Men									
0-4	-	188	633	-	0.6	0.5	-	-	-
5-14	40	240	808	0.0	1.1	0.6	-	-	-
15-29	1,477	10,641	40,030	2.4	76.8	31.8	3,728.7	135.2	60.8
30-44	1,799	5,247	17,766	3.1	43.6	14.1	5,455.8	66.2	42.1
45+	1,675	3,231	9,866	5.5	35.2	7.8	1,958.2	30.4	25.7
Women									
0-4	-	145	643	0.0	0.3	0.5	-	-	-
5-14	19	767	3,401	0.0	3.6	2.7	-	-	-
15-29	375	20,812	141,782	1.8	108.4	112.8	1,020.8	354.4	230.3
30-44	522	7,868	44,585	1.7	45.5	35.5	1,432.8	65.5	93.2
45+	679	3,209	10,903	1.5	22.4	8.7	676.4	11.6	17.2
	Interpersonal violence								
	Incident events			Direct medical cost (million THB)			Productivity loss (million THB)		
	Fatal	Serious	Slight	Fatal	Serious	Slight	Fatal	Serious	Slight
Total	5,645	86,032	332,133	25.9	1,090.5	264.2	13,395.3	2,495.4	603.1
Men	4,887	72,843	259,866	24.3	962.3	206.7	11,835.0	2,142.2	500.0
Women	758	13,189	72,267	1.6	128.1	57.5	1,560.3	353.3	103.1
Men									
0-4	8.0	151.0	508.0	0.2	2.5	0.4	-	-	-
5-14	59.0	1,271.0	4,279.0	0.3	11.9	3.4	-	-	-
15-29	1,916.0	44,030.0	165,637.0	10.2	579.5	131.7	4,925.1	1,132.9	265.8
30-44	1,646.0	19,602.0	66,372.0	7.4	258.4	52.8	4,913.3	666.5	163.1
45+	1,258.0	7,789.0	23,070.0	6.3	110.0	18.3	1,996.6	342.7	71.1
Women									
0-4	13.0	119.0	528.0	0.1	1.5	0.4	-	-	-
5-14	23.0	335.0	1,486.0	0.0	2.1	1.2	-	-	-
15-29	200.0	4,611.0	31,412.0	0.4	41.8	25.0	544.1	115.6	36.7
30-44	267.0	5,051.0	28,622.0	0.4	53.5	22.8	722.7	158.6	49.9
45+	255.0	3,073.0	10,219.0	0.7	29.2	8.1	293.5	79.1	16.5

Note: Amounts may not sum exactly due to rounding

on causes of death from vital registry suffered from a large proportion of undetermined intent causes which we assumed proportional redistribution back to the known causes. Although ICD-10-TM is able to classify violence by its mechanism, cause of death data presents incomplete information for this. Ambulance services are not fully included in the patient database and the estimates should be improved with availability of their incident and cost data.

Estimates regarding direct medical cost due to serious injuries should be improved for fatal injuries using health services prior to deaths provided that the

proportion of deaths at sites of deaths after being rescued is known.

In terms of family and intimate partner violence, incomplete information can be found from health services. In 2005, there were about 11,791 violent cases going to 109 sentinel public hospitals in the OSCC (One Stop Crisis Center) which covers only violence in children and women according to the 2003 Child Protection Act and the 1999 government's measure against violence to children and women. The figures, although reflecting only uncovered cases, provide information on ER and OPD visits in more detail than other reports.

The economic cost from our study is close to out-of pocket medical cost estimates of smoking-attributable diseases, which amounted to 9,857.02 million baht, 0.48% of GDP in 2006[11]. Compared with medical cost attributable to alcohol consumption[12], our direct medical cost yields one-third of that and approximately 87 times of the medical cost of alcohol-related self-directed and interpersonal injuries. Without a standard protocol of direct medical cost, results from different studies can hardly be compared and are even more difficult for further decision-making among cost-effectiveness studies.

What this study contributes to our knowledge gap is that it provides cost and incident data of self-directed and interpersonal violence in great detail of the both nature and mechanism of injuries. This is useful for policy in priority setting and directing appropriate measures relevant to where problems exist.

The availability of accurate and reliable data of the highest quality from information systems, particularly health-related information systems, is critical in providing useful information on the burden of violence and injury to decision makers at local, regional, and national levels. As ministries of health take a leading role in violence and injury prevention[13], data collection and information systems must play a central role.

In conclusion, this study uncovers and confirms the existing problems concerning the accuracy of the cause of death in vital registration and inadequate information on epidemiology profiles of non-fatal, non-severe outcomes of violence which do not followed by hospital admission. Discrepancies of figures across different data sources prompt policy attention to improve the foundation for better estimates in the future.

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ความสูญเสียทางเศรษฐกิจของการบาดเจ็บจากการทำร้ายกันและทำร้ายตนเองในประเทศไทยในปี พ.ศ. 2548

กนิษฐา บุญธรรมเจริญ, ภัทรพรรณ อดทน, สุวรรณา มูเก็ม, สิรินทร์ยา พูลเกิด, กัญจนา ติษยาธิคม, เดวิด ว. บราวน์, วิโรจน์ ตั้งเจริญเสถียร

ความรุนแรงเป็นปัญหาทางสาธารณสุขที่สำคัญปัญหาหนึ่งในประเทศไทย อย่างไรก็ตาม การศึกษาภาระทางเศรษฐกิจของการบาดเจ็บจากความรุนแรงในระดับประเทศยังคงมีจำกัด การคาดประมาณความสูญเสียทางเศรษฐศาสตร์จากการกระทำความรุนแรงทั้งการทำร้ายผู้อื่นและการทำร้ายตนเองในประเทศไทย ปี พ.ศ. 2548 ครั้งนี้ใช้ระเบียบวิธีศึกษาจากคู่มือขององค์การอนามัยโลกและศูนย์ควบคุมและป้องกันโรคของสหรัฐอเมริกาเป็นแนวทาง ผลการศึกษา พบว่า ค่าใช้จ่ายตรงทางการแพทย์เพื่อการรักษาการบาดเจ็บจากการเจตนาทำร้ายตนเองคิดเป็นมูลค่าประมาณ 569 ล้านบาท และค่าใช้จ่ายจากการบาดเจ็บจากการทำร้ายกันคิดเป็นมูลค่าประมาณ 1.3 พันล้านบาท ความสูญเสียกำลังผลิตจากการทำร้ายตนเองมีมูลค่าประมาณ 12.2 พันล้านบาท และ 14.4 พันล้านบาทจากการทำร้ายกัน ซึ่งมูลค่ารวมที่เกิดจากความรุนแรงคิดเป็นร้อยละ 4 ของงบประมาณด้านสาธารณสุขของประเทศไทยในปี พ.ศ.2548 หรือคิดเป็นร้อยละ 0.4 ของมูลค่าผลิตภัณฑ์มวลรวมภายในประเทศ โดยสรุป ในปี พ.ศ. 2548 ประเทศไทยมีภาระค่าใช้จ่ายที่เกิดจากการกระทำความรุนแรงทั้งจากการทำร้ายกันและการทำร้ายตนเองคิดเป็นมูลค่ารวมทั้งสิ้น 33.8 พันล้านบาท ซึ่งมากกว่าร้อยละ 90 ของค่าใช้จ่ายดังกล่าว มาจากการสูญเสียกำลังผลิตและประมาณ 4 ใน 5 เป็นความสูญเสียที่เกิดในผู้ชาย

Cost-Utility Analysis of Recombinant Human Erythropoietin in Anemic Cancer Patients Induced by Chemotherapy in Thailand

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Objective: *To conduct a cost-utility analysis on recombinant human erythropoietin (rHuEPO) for treating anemic cancer patients induced by chemotherapy compared to blood transfusion alone under the Thai health care setting.*
Materials and Methods: *A health care provider's perspective was used to examine relevant costs and outcomes using the Markov model. Cost data were estimated based on the reference price set by the Ministry of Public Health. The effectiveness data were obtained from a systematic review of published literature. The results were presented in terms of incremental cost-effectiveness ratio (ICER) in Thai Baht per Quality Adjusted Life Years (QALYs) gained. A probabilistic sensitivity analysis method was performed.*
Results: *The ICERs of rHuEPO compared to blood transfusion alone were 3.7 and 2.7 millions Baht per QALY for patients with hemoglobin less than 8 g/dl and 8-9 g/dl, respectively. The rHuEPO required additional resources (more costly) with less benefit compared to blood transfusion for patients with hemoglobin 9-10 g/dl.*
Conclusions: *The rHuEPO may be cost-ineffective for the treatment of anemia caused by chemotherapy in cancer patients in Thailand.*

Keywords: *Anemia, Cost-utility analysis, Erythropoietin, Blood transfusion, Cancer, Thailand*

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Similar to other health care settings, an increase in the number of cancer patients with anemia has been observed in Thailand due to an increase of cancer patients and the use of chemotherapy for treatment of cancers that cause bone marrow suppression[1]. Although blood transfusion is an effective way of increasing the hemoglobin level in anemic patients, several limitations do exist with this approach. These limitations include: a severe shortage of blood donations and the high cost of screening of blood donations. This screening is carried out in order to reduce the residual risk of transmission of bloodborne viruses including hepatitis and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)[2].

As a result, an innovation recombinant human erythropoietin (rHuEPO) has been considered as an alternative choice for the treatment of anemia caused by chemotherapy. However, the adoption of rHuEPO has been limited owing to inadequate evidence regarding cost-effectiveness. The findings from a study conducted by the Health Technology Assessment (HTA) program of England suggested that rHuEPO was unlikely to be cost-effective due to the high price of rHuEPO[3]. However, these results may not be applicable to the Thai setting because of the availability of the generic version of rHuEPO, which is much less expensive.

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At present, cost-effectiveness evidence of rHuEPO for the treatment of anemia caused by chemotherapy is not available in Thailand. A primary objective of this study is to assess the value for money of rHuEPO for the treatment of anemia caused by chemotherapy among cancer patients compared to blood transfusion alone in Thailand. Although rHuEPO has been included in the National List of Essential Drugs (NLED) for the treatment of anemia caused by endstage renal disease, it is not included for anemia caused by chemotherapy in cancer patients. The results obtained from this study will be used as an information source for making a decision on whether to include rHuEPO in the NLED for the treatment of anemia due to chemotherapy among cancer patients.

Material and Method

A Markov model was constructed to estimate relevant costs and consequences of rHuEPO treatment compared with blood transfusion alone. The study adopted a health care provider perspective. The results were presented in terms of incremental cost, incremental Quality Adjusted Life Years (QALYs) gained and incremental cost-effectiveness ratio (ICER) in Baht per QALY.

Analyses and model assumption

A schematic diagram of the Markov model is shown in Fig. 1. The model was modified based on the model developed by Wilson *et al*[3] in order to incorporate treatment guidelines for anemia caused by chemotherapy. These guidelines have been recommended by the Food and Drug Administration of the United State (USFDA)[4], Rodgers *et al*[5], and the National Health Services of the Northern and Yorkshire[6]. Health states are denoted in the solid line ovals. Six mutually exclusive health states were defined by hemoglobin levels (including death) in the rHuEPO arm and five health states in the blood transfusion arm. An arrow indicates the probability of moving from one state to another. It is determined by transitional probabilistic parameters.

A fixed 4-week cycle length was assigned. The time horizon of the analysis was 7 months, in which the patients received chemotherapy for one week in each six consecutive month period. It was also recommended to continue the treatment for a month following the end of chemotherapy. Costs and QALYs gained were calculated as patients went through the model. Patients were characterized by their hemoglobin level in order to determine which health state to enter. A full dose (150 IU/kg three times weekly) and a half dose of rHuEPO were given when the hemoglobin level was less than 10 g/dl and 10-11 g/dl, respectively. The target result was that the patient's hemoglobin level reached 12 g/dl.

The response to rHuEPO was defined as a 2 g/dl increase in hemoglobin level meaning that patients would move up two states. No response in the first cycle was allowed, which implied no response within the first 4 weeks after treatment**.** It was assumed that once a patient responded to rHuEPO, he/she would continue to respond to rHuEPO until the treatment was stopped**.** The response to rHuEPO treatment was assumed to be independent of their hemoglobin level and dose escalation was not considered in this model. Non-response was defined as there being no increase in the hemoglobin level within three cycles (12 weeks), after which patients were treated with blood transfusion and they had to follow the same pathways as those in the blood transfusion arm. Some patients might die anytime at the end of each cycle.

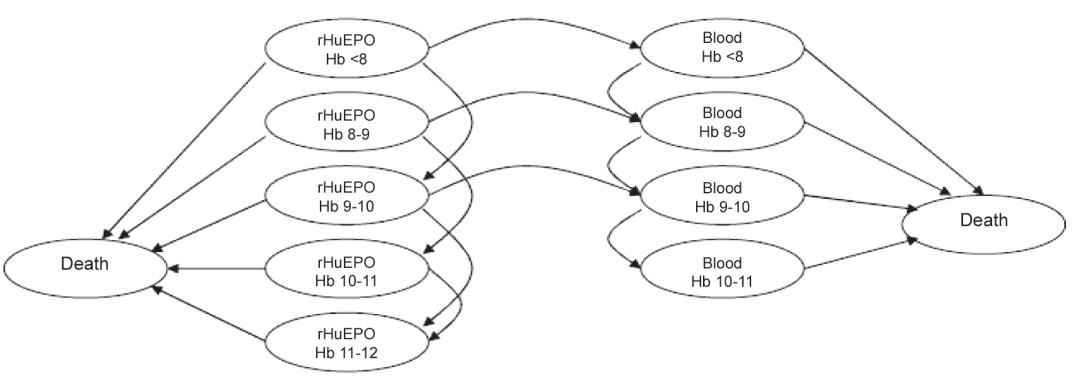

Fig. 1 Schematic diagram of the Markov model

Patients started to receive blood transfusions when their hemoglobin level fell below 10 g/dl. A response was defined as a 1 g/dl increase in a given hemoglobin level. A response was assumed immediately at the end of the cycle but lasting for only one cycle. If the patient was not given a blood transfusion in the following cycle, the patient's hemoglobin level dropped down to the previous level. If another transfusion was given, the patient stayed in that state. Some patients might die anytime at the end of each cycle.

Input parameters

Although the systematic reviews of literature published in several databases, namely Medline, the National Coordinating Centre for Health Technology Assessment (NCCHTA) and the Cochrane library, were carried out, all transitional probabilities and utility parameters used in this study were obtained mainly from a report made by Wilson *et al*[3]. This report was the most up-to-date and comprehensive study that provided information from a systematic search of both clinical and cost-effectiveness measures. It was found that there was no relationship between the use of rHuEPO and the increase/decrease in a patient's mortality. All input parameters are shown in Table 1. The probabilities of patients achieving a hemoglobin response in rHuEPO and blood transfusion groups were 0.53 (0.40-0.55) and 1.00, respectively[3]. The probability of dying in each cycle for both the rHuEPO and blood transfusion groups was 0.49 (0.010-0.095)[3].

The utility scores were obtained from a submission of cost effectiveness data of Neo-Recormon® (epoetin beta)[3] and epoetin alpha by the Roche and Ortho Biotec Company, respectively[3]. The time trade off (TTO) technique was used to elicit the patient preference on different hemoglobin levels. A higher level of hemoglobin resulted in a higher utility value. The lowest utility value was 0.474 for patients with hemoglobin less than 8 g/dl, and for patients with hemoglobin 8-9 g/dl, the utility value was 0.589. For patients with hemoglobin 9-10 and 10-11 g/dl, the utility were 0.623 and 0.737, respectively. The highest utility value was 0.765 for patients with a hemoglobin level of 11-12 g/dl.

It was assumed that thromboembolic events, which might occur among patients with a high-dose rHuEPO, were not included in the model because rHuEPO was recommended at a lower dose. The target

Table 1. Mean and standard error (SE) of effectiveness input parameters

Parameter	Mean	SE	Parameter distribution	Data source
Transitional probabilities				
Monthly probability of dying	0.49	0.02	Beta	3
Monthly probability of response to rHuEPO in the first cycle	0.00	-	Beta	3
Monthly probability of response to rHuEPO in next cycle	0.53	0.04	Beta	3
Monthly probability of response to blood	1.00	-	Beta	3
Utility parameter				
Utility of patient with hemoglobin less than 8 g/dl	0.474	0.007	Beta	3
Utility of patient with hemoglobin between 8-9 g/dl	0.589	0.026	Beta	3
Utility of patient with hemoglobin between 9-10 g/dl	0.623	0.008	Beta	3
Utility of patient with hemoglobin between 10-11g/dl	0.737	0.045	Beta	3
Utility of patient with hemoglobin between 11-12 g/dl	0.765	0.016	Beta	3
Cost in blood arm				
Monthly cost of Pack Red Cell (PRC) screened by NAT	797	797	Gamma	9
Monthly cost of cross-match testing by gel test	153	153	Gamma	9
Monthly cost of blood administration	716	716	Gamma	9
Monthly cost of laboratory monitoring	100	100	Gamma	**
Cost in rHuEPO arm				
Monthly cost of rHuEPO alfa based on patient 70 kg	38,891	11,565	Gamma	9
Monthly cost of rHuEPO administration	100	100	Gamma	Assumed
Monthly cost of laboratory monitoring	100	100	Gamma	**

* Reference price of multiple brands, Ministry of public health, Thailand 2007
** Assumed to be equal in both arms

for the hemoglobin level was set at 12 g/dl, which would make patients safe from complications[4]. Likewise, the probability of patients being infected with blood borne diseases such as hepatitis B, hepatitis C and HIV/AIDS was not included in the model because the blood products used were assumed to have been screened for blood borne diseases by nucleic amplification testing (NAT). This is very effective in detecting blood borne organisms[7]. In addition, the incubation periods of such infections were much longer than the average life expectancy of the cancer patients. This meant that they would die long before the complications of blood borne infections appeared.

The relevant direct medical care costs were considered using the reference prices from the Ministry of Public Health in the year 2007 and the Civil Servant Medical Benefit Scheme (CSMBS) in the year 2006. The medical costs included the costs of drugs, labor and materials. All costs were converted and reported in 2007 Thai Baht using the consumer price index (CPI). Discounting was not performed since the time horizon was shorter than one year. For international comparison, costs could be converted into international dollars using purchasing power parity (PPP) (US$ exchange rate at 1US$ (2007) = 12.615 Thai Baht[8]). This was not shown in the report.

Uncertainty analysis

A probabilistic sensitivity analysis was performed using a second order Monte Carlo simulation. It was carried out using Microsoft Office Excel 2003 (Microsoft Corp., Redmond, WA). All input parameters were assigned probability distributions according to their attribute to reflect the feasible range of values that each input parameter could attain. Beta-distribution was the choice of distribution for probability and utility parameters, which were bounded zero-one, Gamma-distribution, which ensures positive values, was modeled for all rates and unit cost parameters. The simulation drew one value from each distribution simultaneously and calculated cost and effectiveness pairs. This process was repeated 1,000 times to provide a range of possible values given the specified probability distribution. The results were expressed as average value of all costs, QALYs and ICER in the Results section[9].

Results

The total costs and QALYs gained from each treatment options, and the incremental costs per QALY gained from providing rHuEPO in comparison to blood transfusion alone, are shown in Table 2. The costs of providing blood transfusions alone were fixed at every hemoglobin levels (each patient needs one unit of blood transfusion for each cycle regardless of their hemoglobin level) while the lower the hemoglobin levels the higher the costs of rHuEPO. As a result, for patients with hemoglobin less than 8 g/dl, 8-9 g/dl and 9-10 g/dl, the incremental costs of providing rHuEPO compared to blood transfusion alone were 116,503, 101,187 and 85,707 Baht, respectively. The incremental QALYs gained for patients with a hemoglobin levels less than 8 g/dl, 8-9 g/dl and 9-10 g/dl were 0.03, 0.04 and -0.01, respectively. The ICERs of rHuEPO were 3.7 and 2.7 millions Baht per QALY for the patients with hemoglobin lelvels less than 8 g/dl and 8-9 g/dl, respectively. Providing rHuEPO was less effective at a higher cost than blood transfusions alone for those patients with hemoglobin levels 9-10 g/dl.

Uncertainty analysis

The results of the probabilistic sensitivity analysis are presented in terms of cost-effectiveness acceptability curves, and are shown in Fig. 2. If policy makers were willing to pay at 100,000 or 300,000 Baht per QALY gained, providing blood transfusions alone was appropriate at all hemoglobin levels. However, at

Table 2. Cost-effectiveness results obtained from the analysis (probabilistic results)

Hemoglobin (g/dl)	rHuEPO		Blood transfusion		Incremental cost (Baht)	Incremental effectiveness (QALYs)	ICER (Baht/QALY)
	Total cost (Baht)	Total effectiveness (QALYs)	Total cost (Baht)	Total effectiveness (QALYs)			
less than 8	127,937	0.31	11,434	0.28	116,503	0.03	3,789,762
8-9	112,621	0.34	11,434	0.30	101,187	0.04	2,746,506
9-10	97,141	0.34	11,434	0.35	85,707	-0.01	dominant

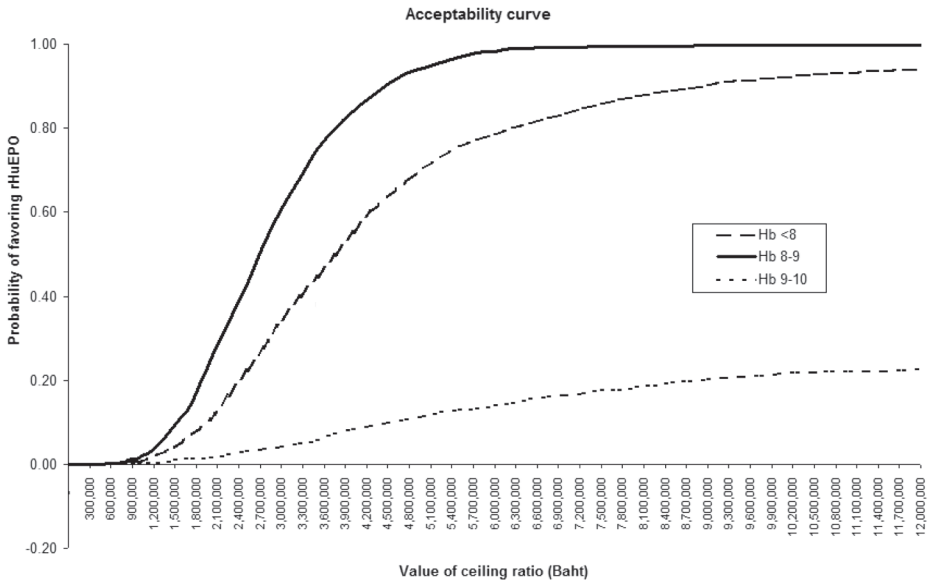

Fig. 2 Cost-effectiveness acceptability curve

the ceiling ratio of 3 million Baht per QALY, providing rHuEPO for patients with a hemoglobin level less than 8 g/dl and 8-9 g/dl was an optimal choice. Providing rHuEPO for patients with hemoglobin 9-10 g/dl was cost-ineffective for every ceiling ratio ranging from 0 to 12 million Baht per QALY.

Discussion

Based on the recommendations made by the Macroeconomics and Health Committee, it was suggested that technology is considered to be cost-effective if its ICER is lower than three times that of the Gross Domestic Product (GDP) per capita[10], This implies a ceiling threshold of 300,000 Baht per QALY in Thailand. The results of this study clearly indicated that rHuEPO is cost-ineffective for treating anemia caused by chemotherapy among cancer patients in Thailand regardless of their initial hemoglobin level. These findings were also in line with the findings from Wilson et al[3]. However, it is noteworthy that some economic evaluation studies that assumed a benefit of rHuEPO concerning the patient's mortality, suggested that rHuEPO was cost-effective[3,11]. As a result, we recommend that a high quality of study or evidence synthesis on whether rHuEPO is beneficial to the patient's mortality should be conducted.

There were several reasons that could explain why rHuEPO appeared to be inferior to blood transfusions for treatment of anemia among cancer patients. First, rHuEPO can be very effective in the treatment of anemia if the patients have depletion of serum erythropoietin such as patients with end-stage renal disease. Nevertheless, anemia in cancer is commonly caused by cytokines blunting erythropoietin response or chemotherapy inducing bone marrow suppression or both[12]. The patients tend to have a normal or high blood level of erythropoietin[13]. As a result, cancer patients would gain less benefit from being treated by erythropoietin. Second, there was no linear relationship between hemoglobin levels and the increase of the patient utility[14]. For instance, the utility increases the most for a shift from hemoglobin levels less than 8 g/dl to 8-9 g/dl, while it increases the least for a move from hemoglobin level 10-11 g/dl to 11-12 g/dl. Thus, treating anemia for patients with relatively high hemoglobin levels yields a lower benefit than treating those with relatively low initial hemoglobin levels.

At present, the subcommittee for development of the NLED has decided not to include erythropoietin for the treatment of anemia among cancer patients from the NLED because it proved cost-ineffective and also the recent cancer treatment trials reported that a maximum dose of erythropoietin was associated with decreased survival, especially when rHuEPO was used to maintain hemoglobin at a level higher than 12 g/dl or 13 g/dl[15]. Furthermore, we hope that this study can be

used as an example for those interested in using economic evaluation as a tool for priority setting of health interventions and technology. Using such a tool in decision-making not only makes policy decisions transparent and evidence-based but also increases the use of health care resources more efficiently in the Thai health care setting where the scarcity of health care resources is increasingly causing concerned.

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การประเมินต้นทุน-อรรถประโยชน์ของการใช้ยาอีริโทรโพอีตินเพื่อแก้ไขภาวะโลหิตจางที่เกิดจากยาเคมีบำบัดในผู้ป่วยมะเร็งในประเทศไทย

จิราพรรณ เรืองรอง, ยศ ตีระวัฒนานนท์, อุษา ฉายเกล็ดแก้ว

วัตถุประสงค์: *เพื่อวิเคราะห์ต้นทุน-อรรถประโยชน์ของการใช้ยาอีริโทรโพอีตินเพื่อแก้ไขภาวะโลหิตจางที่เกิดจากยาเคมีบำบัดในผู้ป่วยมะเร็งเปรียบเทียบกับการให้เลือดเพียงอย่างเดียว*

วัสดุและวิธีการ: *ต้นทุนและผลลัพธ์ที่เกี่ยวข้องพิจารณาจากมุมมองของผู้ให้บริการ ตัวแปรต้นทุนได้จากอัตราค่าบริการและราคายาอ้างอิงจากกระทรวงสาธารณสุข ข้อมูลตัวแปรด้านประสิทธิภาพได้จากการทบทวนวรรณกรรมอย่างเป็นระบบ แบบจำลองมาร์คอฟและวิธีวิเคราะห์ความไม่แน่นอนแบบความน่าจะเป็น (probabilistic sensitivity analysis) ถูกนำมาใช้สำหรับการวิเคราะห์*

ผลการศึกษา: *อัตราส่วนต้นทุนประสิทธิผลของการให้อีริโทรโพอีตินเปรียบเทียบกับการให้เลือดเพียงอย่างเดียวมีค่าเท่ากับ 3.7 และ 2.7 ล้านบาทต่อปีสุขภาวะ ในผู้ป่วยที่มีระดับฮีโมโกลบินต่ำกว่า 8 กรัมต่อเดซิลิตรและระหว่าง 8-9 กรัมต่อเดซิลิตร ตามลำดับ สำหรับผู้ป่วยที่มีระดับฮีโมโกลบินระหว่าง 9-10 กรัมต่อเดซิลิตร ต้องใช้งบประมาณที่สูงกว่าแต่ให้ปีสุขภาวะที่น้อยกว่าการให้เลือด*

สรุป: *การให้อีริโทรโพอีตินอาจไม่คุ้มค่าสำหรับการแก้ไขภาวะโลหิตจางที่เกิดจากยาเคมีบำบัดในผู้ป่วยมะเร็งในประเทศไทยเมื่อเปรียบเทียบกับการให้เลือดเพียงอย่างเดียว*

The Cost-Effectiveness Analysis of Initiating HIV/AIDS Treatment with Efavirenz-Based Regimens Compared with Nevirapine-Based Regimens in Thailand

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Objectives: *The aim of this study is to evaluate the cost-utility of the treatment, starting with EFZ-based therapy, compared with NVP-based therapy in Thai HIV/AIDS patients.*
Material and Method: *The study adopted a health care provider perspective. A probabilistic Markov model was applied to Thai HIV/AIDS patients aged 15 to 65 years. Input parameters were extracted from a cohort study of four regional hospitals. The study explored the effects of uncertainty around input parameters.*
Results: *For those patients with a different baseline CD4, initial therapy using EFZ-based regimens was the preferable choice for all subgroups. Given a maximum acceptable willingness to pay (WTP) threshold of 300,000 Baht/DALY averted starting with EFZ-based regimens was cost-effective for patients with a baseline CD4 count less than 250 cells/mm^3 and in all patient age groups, except those who were 20 years old.*
Conclusions: *The results suggest that starting with EFZ-based regimens was the preferable choice and it should be used as the first line regimen for Thai HIV/AIDS patients.*

Keywords: *Cost-effectiveness, HIV/AIDS treatment, Efavirenz-based regimens, Nevirapine-based regimens, Thailand*

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Even though the introduction of highly active antiretroviral treatment (HAART) has dramatically reduced the number of deaths and AIDS-related opportunistic infections in developed world, the availability of antiretroviral therapy for HIV infected patients is still limited in developing settings[1]. The World Health Organization has estimated that more than 1 million people living with HIV/AIDS (PLWHA) in Asia are in need of HAART, but only 6-7% of them can access to this expensive therapeutic regimen[2]. In Thailand, despite the declining incidence of new HIV transmission, due to the efforts of the Thai government in the early 90's, including extensive and intensive campaigns to promote condom use and HIV education in susceptible populations, the estimated numbers of HIV-infected and AIDS cases were 600,000 and 70,000, respectively in 2005[3].

Although the accessibility to HAART among Thai PLWHA has dramatically improved since 2003, when the universal coverage to HAART was implemented[4], the negative consequences of the treatment raised concerns among health care providers. Six standard ARV regimens were approved for use in this program, including an NVP-based regimen, which was used as the first drug of choice, while an Efavirenz (EFZ)-based regimen and a Protease Inhibitor (PI)-based regimen were set as alternative regimens[5]. Empirical evidence revealed that NVP could cause serious

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and life-threatening adverse events such as cutaneous hypersensitivity reactions, including Steven Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN) and severe hepatic toxicity. These adverse events became an emerging cause of mortality in HIV-infected patients[6-10]. These serious adverse events not only affected the patients' quality of life and success of treatment, but also increased the budget of the program. Therefore, substitution with a less toxic alternative such as EFZ is warranted. EFZ was recommended as a substitute for NVP in the treatment regimen. It had less severe toxicity but was reserved for patients who had a severe adverse event because of its higher cost.

The purpose of this study is to appraise value for money, using the cost-effectiveness and cost-utility analyses, on initiating treatment with the NVP-based regimens compared with initiating treatment with EFZ-based regimens. It has developed an economic model to estimate long-term effects on both costs and outcomes of these two alternative treatment options.

Material and Method

Overview options

The standard antiretroviral treatment for eligible patients who had a baseline CD4 count less than 200 cells/mm^3 was to start with NVP-based regimens, which are composed of Nevirapine, Stavudine and Lamivudine. Switching to other combinations was allowed if the patients developed negative consequences, such as adverse events, drug resistance or major opportunistic infections. The second and third regimens were two nucleoside or reverse transcriptase inhibitors (NRTI) plus a non-nucleoside reverse transcriptase inhibitor (NNRTI) regimens and Protease Inhibitor (PI)-based regimens, respectively.

The other choice of treatment that was compared was starting with EFZ-based regimens instead of NVP-based regimens. Switching to other combinations was allowed if the patients developed negative consequences such as adverse events, drug resistance or major opportunistic infections. The second and third regimens were the 2NRTI+1NNRTI regimens and PI-based regimens, respectively.

Analyses and model

An economic model was created to estimate the long-term effects of the treatment of HIV disease progression. The main principle of the model was that, to be effective, antiretroviral regimens must not only reduce viral loads, but also be tolerated by patients who are willing to adhere to it over a long period of time. The model evaluated the effect of the initial choice of triple therapy on the progression of an HIV positive population through 4 states, starting with the naÔve to the treatment state (1st regimen), switching to the 2nd regimen, the 3rd regimen, and then death (Fig. 1).

The target population of this study was HIV/AIDS patients aged 15-65 years. The Markov model structure (shown in Fig. 1) illustrates the mutually exclusive health states that a patient commencing treatment from either NVP-based regimens or EFZ-based regimens might go through. Health states are denoted by the solid oval-lines. The model also includes sub-states (dotted oval lines) to reflect the difference in the rate of complications between the two treatment modalities. An arrow indicates that movement from one state to another is possible. The likelihood of movement between each state ("transition probability") was determined using data from a retrospective cohort study in four regional hospitals namely Lampang Hospital,

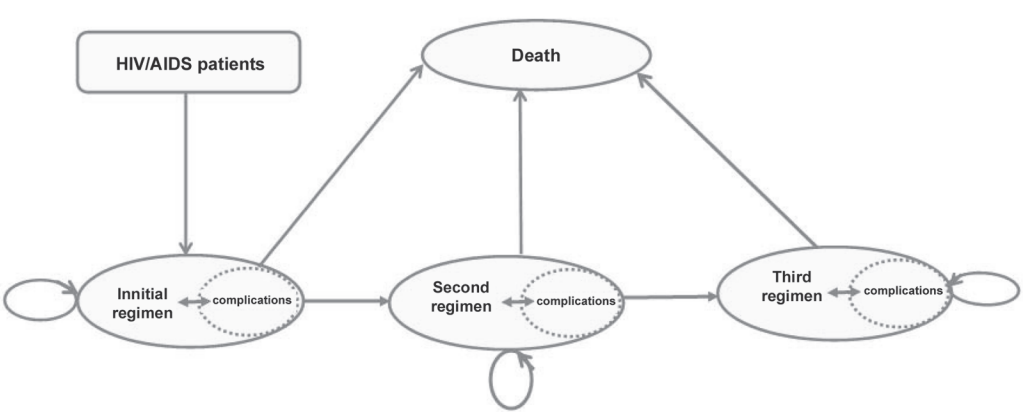

Fig. 1 Schematic diagram of the Markov model

Had-Yai Hospital, Chonburi Hospital and Sappasittiprasong Hospital. Initiating treatment with either NVP-based or EFZ-based ART was modeled for the remaining lifetime of the prevalence cohort. Cycle lengths of 1-year for the full health states and one or two months for the sub-states were used for the analysis.

The model was used to quantify the costs and effects of two long-term alternative treatments for HIV/AIDS patients in each age group and each baseline CD4 level. In the model, patients might start either with NVP-based or with EFZ-based ART and remain on the same treatment until the next cycle. Moving to other health states (second and third regimens) was dependent on the development of complications during treatment such as moderate or severe adverse drug reactions, opportunistic infections, or drug resistance. Moving to the final state (death) might or might not be related to the occurrence of complications since patients could die from non HIV/AIDS causes, such as cardiovascular disease. In each case, it was assumed that the event would only happen at the end of each cycle. The simulations were conducted to model cost and events over a 99-year period to cover the maximum total period over which the whole cohort could reasonably be expected to survive.

A probabilistic sensitivity analysis using a second-order Monte Carlo simulation was carried out. All input parameters were assigned a probability distribution to reflect the feasible range of values that each input parameter could attain. This process was repeated 1000 times to provide a range of possible values given the specified probability distributions. To comply with the Thai HTA guideline for conducting heath economic analyses, all costs and outcomes were discounted at a rate of 3 %[11].

Outcome measures

Probability of moving to next health states

The probabilities of moving to the next health state (from first regimen to second regimen, third regimen and death) were estimated using the survival analysis of a hypothetical cohort of patients from a retrospective cohort study of HIV/AIDS patients in 4 regional hospitals. To adjust the survival rate, CD4 at baseline, the age of patients and ordering of ARV regimens were used as covariates of disease progression.

This data consisted of 408 records of patients who started with NVP-based regimens and 116 records of patient who started with EFZ-based regimens. In the follow up period of 3 years, no one died in the group of patients who started with the EFZ-based regimens. Therefore, the existing data were not applicable to calculate the survival rate of the patients starting with the EFZ-based regimens. From a Cochrane review[12], the finding from a 2NN study, (a large randomized control trial), was that NVP-based regimens had a higher death rate compared with EFZ-based (RR [95%CI] = 1.33 [0.50, 3.53]). Thus, it was assumed that the HIV/AIDS patients who started with NVP-based regimens had 1.33 times (SE 0.49) higher death rate in the first health state compared with HIV/AIDS patients who started with EFZ-based regimens.

Using the statistical software package STATA (Stata Corp, College Station, TX), this study initially applied a non-parametric Kaplan-Meier approach[13] to fit Kaplan-Meier curves and plotted graphs of log against log (time) which were generally linear and indicated that a Weibull survival model would adequately fit the data[14]. The study consequently used the "streg" module of STATA to perform the maximum likelihood estimation for parametric regression of the Weibull survival models.

For the Weibull distribution, for example, the survival function, which describes the probability of survival as a function of age,[15] is:

$$S(t) = \exp[-H(t)]$$

and

$$H(t) = \lambda t^{\gamma}$$

Where H(t) is the cumulative hazard; λ (lambda) is the scale parameter; t is time in days; and γ (gamma) is the shape parameter that describes the instantaneous hazard rate h(t), which increases with age if $\gamma > 1$. The λ depends on the covariate and age, according to the formula:

$$\lambda = \exp[(\text{age\_coefficient} \times \text{age}) + \text{cons}]$$

The transitional probability of dying during the cycle, *tp(c)*, is therefore estimated from the following formula (where c is the number of cycles):

$$tp(c) = 1\text{-}\exp[H(t\text{-}c)\text{-}H(t)]$$

Disability-adjusted survival

This study measured outcomes in disability-adjustedlife years (DALY) by using the disability weight (DW) from Global Burden of Diseases (GBD)[16], an Australian study[17] and expert opinion. For co-morbidities in this model, such as AIDS patients who developed tuberculosis, the multiplicative adjustment method, which was used to calculate the disability weight for co-morbidities in Health-adjusted life expectancy (HALE) calculation[18], was applied. The concept of this is that it assumes that the increase in disability due to co-morbidity disability is proportional.

Total disability for an individual having more diseases could be written as:

$w(1,2)=1-(1-w1)(1-w2)$

$w(d) = 1-\pi_d(1-wd)$

Where: $w(1,2)$ disability weight of an individual with disease 1 and 2

$w(d)$ disability weight of an individual with d diseases

Costs

Using the health care provider perspective, the cost of treatment in this study was the direct health care cost. The costs of treatment in this study included the cost of ARV drugs, the cost of laboratory testing, the cost of medical services, the cost of hospital services and the cost of treating complications such as adverse events and opportunistic infections in out-patient and in-patient visits. The costs of treatment were derived based on the cost data from the retrospective cohort of HIV/AIDS patients in 4 regional hospitals. The costs of adverse events and opportunistic infections treatment were the average cost of treatment from the four hospitals. Only costs of ARV regimens were adjusted by the reference cost of ARV drugs from the Bureau of AIDS, Tuberculosis and Sexually Transmitted Infection, Ministry of Public Health and the Thai Government Pharmaceutical organization (GPO)[19,20] to minimize the variation of cost of ARV drugs. All costs were reported in 2006 Thai Baht, using the Consumer Price Index[21].

Uncertainty analysis

A probabilistic sensitivity analysis, with second-order Monte Carlo technique, was carried out using Microsoft Office Excel 2003[15]. All input parameters were assigned a probability distribution to reflect the feasible range of values that each input parameter could attain[22]. The beta-distribution was the choice of distribution for probability parameters which were bounded by zero and one. The gamma distribution, which ensured a positive value, was modeled for all rates and unit cost parameters. Normality, on the log-odds scale with a covariance matrix and using the Cholesky decomposition, was applied for survival parameters[23]. The simulation chose one value from each distribution simultaneously and calculated cost and effectiveness pairs. This process was repeated 1000 times to provide a range of possible values given the specified probability distributions. The means and standard error (SE) of input parameters are shown in Table 1. The incremental cost and incremental effects were represented visually by using a cost-effectiveness plane and cost-effectiveness acceptability curves based on the concept of net-benefit approach suggested by Stinnett and Mullahy[24] and Briggs *et al*[25]. To quantify the ceiling ratio for the Thai population, although there is no such accepted threshold for adopting health technologies in Thailand, we applied the threshold that is recommended by the commission on Macroeconomics and Health. This suggests the use of three times the gross domestic product (GDP) per capita as the threshold for consideration in developing countries[26]. In addition, this ceiling was used to assess the cost-effectiveness of HIV prevention in Thailand[27]. This would indicate a ceiling value in Thailand of 300,000 Baht per quality-adjusted life years (QALY) based on Thai GDP and population.

Results

Table 2 presents the lifetime-treatment costs and effectiveness of initiating the two different antiretroviral regimens using the health care provider perspective. The lifetime-treatment cost of the patients with baseline CD4 count of 200 cells/mm^3 that started with the EFZ-based regimens, was lower in all age groups compared with those treated by the NVP-base regimen, except for those patients aged 20 years old. It was shown that starting with NVP-based regimens for the patients with baseline CD4 at 200cell/mm^3 offered slightly more LYs gained in all age groups, except patients aged 20 years old, but offered less DALY averted in all age groups.

Table 3 presents the lifetime-treatment costs and effectiveness of initiating NVP-based and EFZ-based regimens for patients aged 38 years (average age of the Thai cohort) with a different baseline CD4 count. It can be seen that starting with EFZ-based regimens was cheaper in all baseline CD4 groups. In terms of effectiveness, starting with EFZ-based regimens offered more LY gained among the patients who initiated the regimen at a low CD4 count baseline (*i.e.* 50 to 100 cells/mm^3). In patients with higher baseline CD4 counts, starting with EFZ-based regimens offered slightly less LY gained compared to NVP-based regimens. However, starting with EFZ-based regimens provided more DALY averted compared to NVP-based regimens in all baseline CD4 groups.

Incremental cost-effectiveness ratios of initiating with EFZ-base regimens compared with NVP-based regimens were presented in Table 4. In patients with a baseline CD4 at 200 cells/mm^3, the incremental costs of providing the EFZ-based regimens as the first option ranged from 6,082,000 Baht per LY gained for

Table 1. Means and standard error (SE) of input parameters

Parameter description	Mean	SE	distribution	Data source
Weibull survival				
Weibull survival in NVP group: death				
Constant value for baseline hazard	-5.0534	1.1441	Lognormal	Thai cohort
CD4 baseline coefficient for baseline hazard	-0.019	0.0061	Lognormal	Thai cohort
Regimen coefficient for baseline hazard	-1.2305	0.5623	Lognormal	Thai cohort
Ln (g)	-0.3856	0.2024	Lognormal	Thai cohort
Weibull survival in NVP group: switching from Reg1 to Reg2				
Constant value for baseline hazard	-6.1716	0.525	Lognormal	Thai cohort
CD4 baseline coefficient for baseline hazard	0.0031	0.0011	Lognormal	Thai cohort
age coefficient for baseline hazard	0.0282	0.0106	Lognormal	Thai cohort
Ln (g)	-0.493	0.0715	Lognormal	Thai cohort
Weibull survival in NVP group: switching from Reg2 to Reg3				
Constant value for baseline hazard	-10.2941	1.2661	Lognormal	Thai cohort
age coefficient for baseline hazard	0.0602	0.0192	Lognormal	Thai cohort
Ln (g)	0.0127	0.1378	Lognormal	Thai cohort
Weibull survival in EFZ group: switching from Reg1 to Reg2				
Constant value for baseline hazard	-7.141	1.2231	Lognormal	Thai cohort
CD4 baseline coefficient for baseline hazard	0.0005	0.0022	Lognormal	Thai cohort
age coefficient for baseline hazard	-0.0021	0.0198	Lognormal	Thai cohort
Ln (g)	-0.1448	0.1524	Lognormal	Thai cohort
Weibull survival in EFZ group: switching from Reg2 to Reg3				
Constant value for baseline hazard	-6.8363	3.0088	Lognormal	Thai cohort
age coefficient for baseline hazard	0.0108	0.056	Lognormal	Thai cohort
Ln (g)	-0.4629	0.4716	Lognormal	Thai cohort
Transitional Probability				
Relative risk of NVP compared to EFZ: Outcome death				
Relative risk of EFZ-based compared with NVP based regimens	1.33	0.499	Gamma	Ref [12]
Annual rate of having complications				
Probability of Meningitis in 1st regimen in NVP-based regimens	0.0196	0.0069	Beta	Thai cohort
Probability of TB in 1st regimen in NVP-based regimens	0.0417	0.0099	Beta	Thai cohort
Probability of MAC in 1st regimen in NVP-based regimens	0.0098	0.0049	Beta	Thai cohort
Probability of Toxoplasmosis in 1st regimen in NVP-based regimens	0.0172	0.0064	Beta	Thai cohort
Probability of CMVR in 1st regimen in NVP-based regimens	0.0245	0.0076	Beta	Thai cohort
Probability of PCP in 1st regimen in NVP-based regimens	0.0294	0.0084	Beta	Thai cohort
Probability of skin reaction grade 2 in 1st regimen in NVP-based regimens	0.1299	0.0166	Beta	Thai cohort
Probability of SJS in 1st regimen in NVP-based regimens	0.0123	0.0054	Beta	Thai cohort
Probability of Hepatitis in 1st regimen in NVP-based regimens	0.0245	0.0076	Beta	Thai cohort
Probability of Hepatotoxicity in 1st regimen in NVP-based regimens	0.0221	0.0073	Beta	Thai cohort
Probability of HighTG in 1st regimen in NVP-based regimens	0.0294	0.0084	Beta	Thai cohort
Probability of Hepatotoxicity in 2nd regimen in NVP-based regimens	0.0025	0.0024	Beta	Thai cohort
Probability of HighTG in 2nd regimen in NVP-based regimens	0.0123	0.0054	Beta	Thai cohort
Probability of HighTG in 3rd regimen in NVP-based regimens	0.0025	0.0024	Beta	Thai cohort

Table 1. Means and standard error (SE) of input parameters (Cont.)

Parameter description	Mean	SE	distribution	Data source
Probability of TB in 1st regimen in EFZ-based regimens	0.0085	0.0085	Beta	Thai cohort
Probability of CMVR in 1st regimen in EFZ-based regimens	0.0085	0.0085	Beta	Thai cohort
Probability of skin reaction grade 2 in 1st regimen in EFZ-based regimens	0.0085	0.0085	Beta	Thai cohort
Probability of HighTG in 1st regimen in EFZ-based regimens	0.1624	0.034	Beta	Thai cohort
Resource cost parameter				
Direct medical care costs i.e. direct costs of treatment				
Monthly Cost of drug 1st regimen in NVP-based regimens	1750	519.221	Gamma	[19-20] and survey
Monthly Cost of drug 2nd regimen in NVP-based regimens	2657	732.8054	Gamma	[19-20] and survey
Monthly Cost of drug 3rd regimen in NVP-based regimens	9552	7000.449	Gamma	[19-20] and survey
Monthly Cost of drug 1st regimen in EFZ-based regimens	3067	537.373	Gamma	[19-20] and survey
Monthly Cost of drug 2nd regimen in EFZ-based regimens	4223	2280.822	Gamma	[19-20] and survey
Monthly Cost of drug 3rd regimen in EFZ-based regimens	9552	7000.449	Gamma	[19-20] and survey
Average cost of Meningitis treatment	14184.125	2199.5206	Gamma	Survey
Average cost of MAC treatment	20048.5	2213.2468	Gamma	Survey
Average cost of Tuberculosis treatment	9266.1538	1162.5913	Gamma	Survey
Average cost of CMV rhinitis treatment	25064	4213.4115	Gamma	Survey
Average cost of Toxoplasmosis treatment	5167.7143	2134.7126	Gamma	Survey
Average cost of PCP treatment	6506.7273	1245.32	Gamma	Survey
Average cost of ADR treatment(skin grade 2)	437.7925	184.1442	Gamma	Survey
Average cost of ADR treatment(SJS)	3420	346.1545	Gamma	Survey
Average cost of ADR treatment(Hepatitis)	1797.4	194.2507	Gamma	Survey
Average cost of ADR treatment (Hepatotoxicity)	6159.375	2402.079	Gamma	Survey
Average cost of ADR treatment (HighTG)	3650	1245.52	Gamma	Survey
Utility parameter				
Disability weight for AIDS without complications	0.5600			[17]
Disability weight for AIDS with meningitis & toxoplasmosis	0.9617			[17]
Disability weight for AIDS with TB	0.6898			[16]
Disability weight for AIDS with MAC and PCP	0.8064			Expert opinion
Disability weight for AIDS with CMVR	0.7492			[17]
Disability weight for AIDS with grade 2 skin reaction	0.6150			Expert opinion
Disability weight for AIDS with SJS&TEN	0.7593			Expert opinion
Disability weight for AIDS with Hepatitis	0.6524			[17]
Disability weight for AIDS with Hepatotoxic & cirrhosis	0.7092			[16]
Disability weight for AIDS with HighTG	0.6150			Expert opinion

patients aged 20 years to 28,772,000 Baht per LY gained for patients aged 30 years. However, in older patients, the incremental costs of providing the EFZ-based regimens as first option decreased from 7,967,000 to 15,510,000 Baht per LY gained. In terms of incremental costs per DALY averted, starting with EFZ-based regimens proved less costly with more DALY averted in all age groups except for those aged

Table 2. Lifetime cost and the effectiveness of starting with NVP-based and EFZ-based regimens classified by age-group (a baseline CD4 count at 200cell/mm^3)

Age (year)	Lifetime cost*		LY gained		DALY averted	
	NVP-based regimens	EFZ-based regimens	NVP-based regimens	EFZ-based regimens	NVP-based regimens	EFZ-based regimens
20	1,744,000	1,954,000	24.10	24.13	6.08	6.25
30	1,969,000	1,758,000	22.10	22.09	5.82	5.98
40	2,027,000	1,532,000	19.68	19.62	5.45	5.59
50	1,892,000	1,277,000	16.70	16.66	4.90	5.02
60	1,560,000	982,000	13.26	13.21	4.14	4.23

* Cost are given to nearest 1,000 baht, 2006 price level

Table 3. Lifetime cost of starting with NVP-based and EFZ-based regimens classified by baseline CD4 group (age at initial of treatment at 38 years-old)

Baseline CD4 count(cell/mm^3)	Lifetime cost*		LY gained		DALY averted	
	NVP-based regimens	EFZ-based regimens	NVP-based regimens	EFZ-based regimens	NVP-based regimens	EFZ-based regimens
50	1,521,000	1,349,000	17.12	17.25	4.80	4.95
100	1,736,000	1,514,000	19.07	19.08	5.26	5.41
150	1,882,000	1,535,000	19.82	19.81	5.45	5.59
200	2,051,000	1,595,000	20.22	20.19	5.54	5.69
250	2,130,000	1,624,000	20.37	20.34	5.58	5.72

* Cost are given to nearest 1,000 baht, 2006 price level

Table 4. Incremental cost-effectiveness ratio (ICER) of starting with EFZ-based regimens compared with NVP-based regimens classified by age group (baseline CD4 count at 200cell/mm^3)

Age (year)	Incremental cost-effectiveness ratio (ICER)	
	Baht per LY gained	Baht per DALY averted
20	6,082,000	1,200,000
30	28,772,000	Dominate (1,342,000)
40	7,967,000	Dominate (3,677,000)
50	15,510,000	Dominate (4,900,000)
60	10,578,000	Dominate (5,912,000)

( ) = negative ICER

20 years old.

On the other hand, the group of patients aged 38 years at initial treatment, at the low level of CD4 (50 and 100 cells/mm^3), starting with EFZ-based regimens, dominated NVP-based regimens in terms of baht per LY gained (Table 5). In patients with a high baseline CD4 level, the incremental costs of providing EFZ-based regimens as first option ranged from 33,509,000 baht per LY gained for patients with a baseline CD4 at 150 cell/mm^3 to 13,859,000 Baht per LY gained for patients with a baseline CD4 at 250 cells/mm^3. In terms of incremental costs per DALY averted, starting with EFZ-based regimens proved less costly with more DALY averted at all baseline CD4 levels (Table 5).

Uncertainty analysis

Uncertainty in cost-utility analysis classified by age-groups

The cost-effectiveness planes of the incremental costs and DALY averted for starting with EFZ-based regimens compared with NVP-based regimens, classified by age group, are presented in Fig. 2(a-e). The figures indicate that for patients who had CD4 200 cell/mm^3 at the baseline, starting with EFZ-based

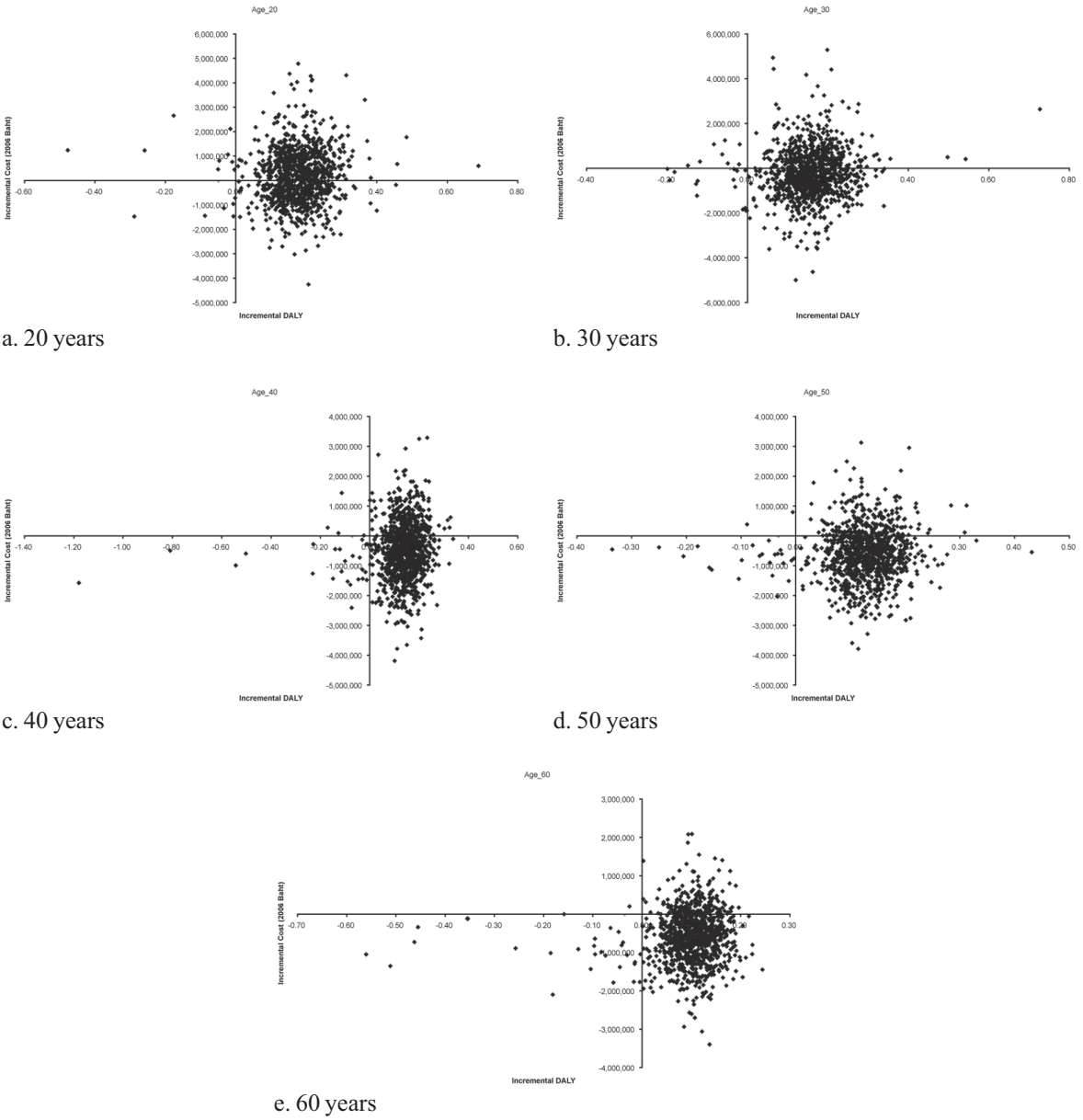

Fig. 2 Cost effectiveness plane of disability-adjusted life years (DALY) averted of EFZ-based regimens compared with NVP-based regimens classified by age group

regimens yielded more DALY averted than NVP-based regimens. However, the differences in the treatment costs between the two regimens depended on the patient's age. In younger age groups (*e.g.* 20 years old), introducing EFZ-based as first line regimens was more expensive than NVP-based regimens. In contrast, in middle to old age groups (*e.g.* 30 to 60 years old), introducing EFZ-based as first line regimens was cheaper than NVP-based regimens.

The cost effectiveness acceptability curve of DALY averted presented in Fig. 3 reveals that with no extra budget available it is more likely that starting with EFZ-based regimens is a preferable choice, except in patients aged 20 years. However, in this age-group, the higher the WTP threshold the lower the likelihood that an NVP-based regimen is still cost effective. Starting with

Table 5. Incremental cost-effectiveness ratio (ICER) of starting EFZ-based regimens compared with NVP-based regimens classified by baseline CD4 group (age at baseline treatment at 38 years)

Baseline CD4 count (cell/mm^3)	Incremental cost-effectiveness ratio (ICER)	
	Baht per LY saved	Baht per DALY averted
50	Dominate (3,133,000)	Dominate (1,144,000)
100	Dominate (19,454,000)	Dominate (1,460,000)
150	33,509,000	Dominate (2,344,000)
200	15,881,000	Dominate (3,149,000)
250	13,859,000	Dominate (3,603,000)

( ) = negative ICER

EFZ-based regimens in this age group is preferable when the WTP is above 1,200,000 Baht/DALY averted. Given a maximum acceptable WTP of 3 times per capita GDP or 300,000 Baht/DALY averted, starting with EFZ-based regimens is cost effective in all age groups except those who were 20 years old at baseline treatment when a NVP-based regimen is the preferred choice.

Uncertainty in cost-utility analysis classified by baseline CD4 groups

The incremental cost per DALY averted for those patients aged 38 years old indicated that starting with EFZ-based regimens yielded more DALY averted than NVP-based regimens in all age-groups (Fig. 4(a-e)). However, the differences in the treatment costs depended on the baseline CD4 count. With a low level of baseline CD4 (e.g. 50 cells/mm^3), introducing EFZ-based regimens as first regimens was more costly than NVP-based regimens. In contrast, with a higher level of baseline CD4 (*e.g.* 100 to 250 cells/mm^3) introducing EFZ-based regimens as first-line regimens was less costly than NVP-based regimens. The findings of the cost-effectiveness acceptability curve presented in Fig. 5 shows that for patients who were 38 years old at baseline treatment, starting with EFZ-based regimens dominated NVP-based regimens for all baseline CD4 counts.

Discussions and Conclusion

This study explored the value for money of initiating an EFZ-based regimen for the treatment of PLWHA at a CD4 count less than 250 cells/mm^3 compared to the current practice that uses an NVP-base regimen as the first line treatment. The patient's age and the levels of CD4 count were taken into account when considering additional costs and additional effectiveness in terms of DALY averted from the new regimen. Although the drug cost of initiating an EFZ-based regimen was higher in the model, the results indicated that starting with EFZ-based regimens was more cost effective for all baseline CD4 counts, and in

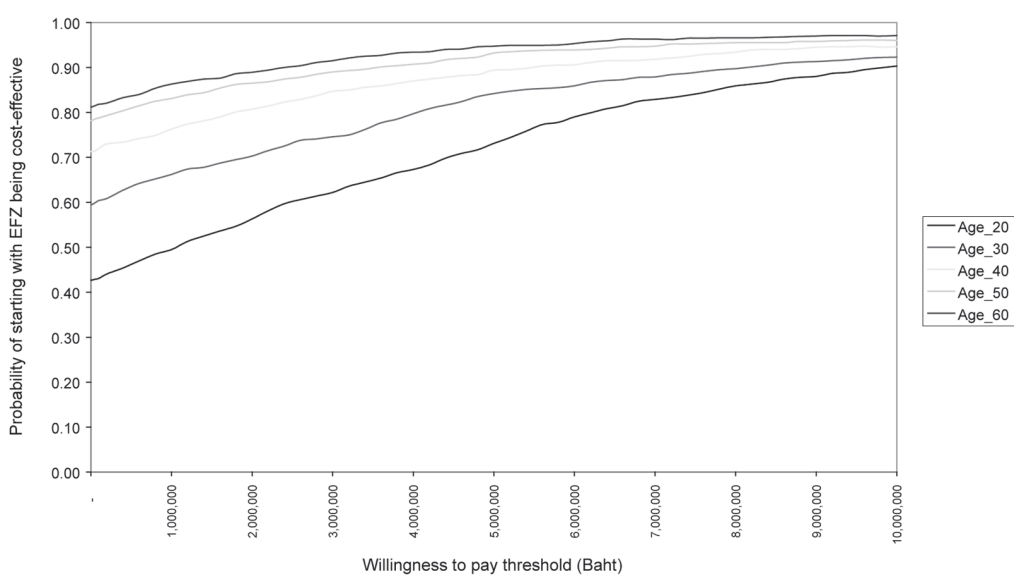

Fig. 3 Cost effectiveness acceptability curve of DALY averted of EFZ-based regimens compared with NVP-based regimens classified by age groups

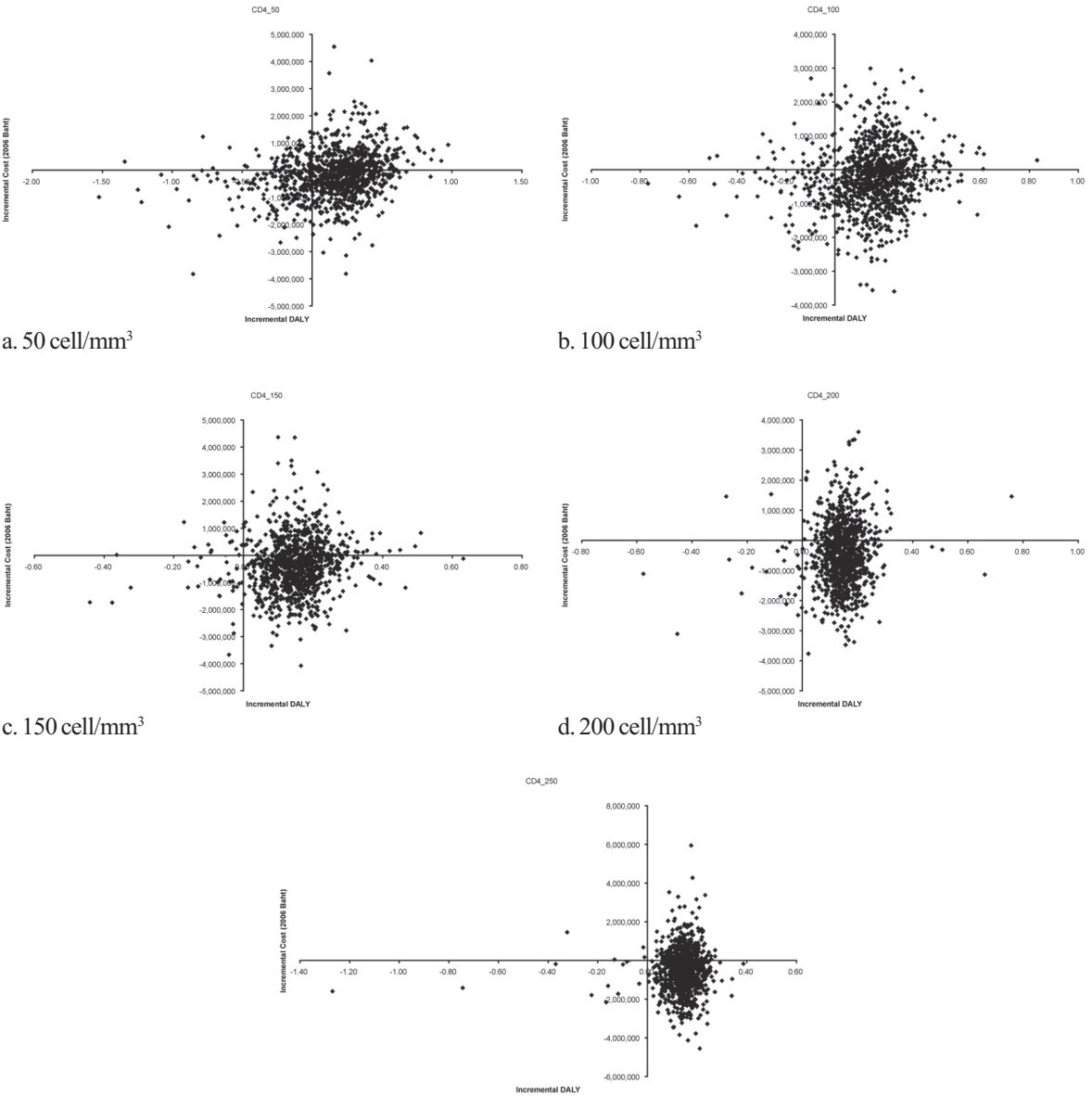

Fig. 4 Cost effectiveness plane of DALY averted of EFZ-based regimens compared with NVP-based regimens classified by baseline CD4 group

all age groups, except in the young patients i.e. those patients aged 20-29. These findings suggest that EFZ-based therapy should be used as the first line regimen for treating PLWHA.

These results are in agreement with the study conducted by Freedberg et al.[28]. The two studies found that the baseline CD4 cell count was the most important determinant concerning the costs, clinical outcomes, and cost effectiveness of HIV/AIDS treatment. Although the national guidelines for HIV/AIDS treatment stated that a patient with a CD4 count less than 200 cell/mm^3 must receive HAART, in reality many eligible patients do not have access to medications. The findings from this study showed that the higher initial CD4 cell count the better the effectiveness of the treatment in terms of LY gained, as well as DALY

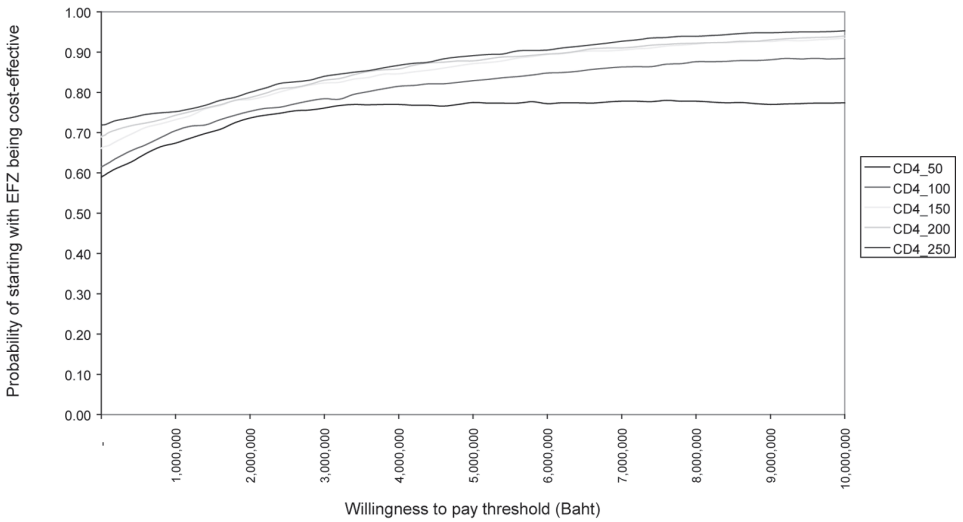

Fig.5 Cost effectiveness acceptability curve of DALY averted of EFZ-based regimens compared with NVP-based regimens classified by CD4 at baseline group

averted. Thus, the problem of the delay of treatment must be seriously considered by decision-makers. It also raised another question whether to start the treatment at an earlier stage, *i.e.* a CD4 cell count of 250 cells/mm^3, than that indicated in the current guidelines, a CD4 cell count of 200 cells/mm^3. It should be noted that the Thai government issued compulsory licensing (CL) for EFZ in November, 2006[29] which would substantially affect the treatment cost of EFZ-based regimens and might lead to a more preferable option to the initial treatment with an EFZ-based regimen.

There were some limitations regarding the availability of the data used in the model. This study intends to conduct subgroup analyses based on the level of CD4 cell count at the start of treatment and the patient's age. As a result, it was carried out by modelling CD4 level- and age-specific survival from the three-year cohort data, which was a relatively short period of the follow-up time, to determine the difference in mortality between the two treatment modalities. Based on the data, none of the patients who started with EFZ were dead within this follow-up period. The mortality rate of patients with EFZ-based regimen was, therefore, adjusted using the relative mortality between EFZ-based regimens and NVP-based regimens from the literature and the baseline mortality of the cohort patients with NVP-based regimens. It is also noteworthy that the relative mortality was derived from the Cochrane database, where the systematic search and meta-analysis were properly employed.

Furthermore, the disability weights used to estimate DALY gained from this study were derived from different sources[16-17] and where there was no disability weights available in the literature for some health states, e.g. Steven Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) , expert opinions were sought to elicit the weights. This limitation should be treated with care, and future studies to determine the missing disability weights are welcome.

Competing interests

The authors declare that they have no competing interests.

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การประเมินต้นทุน-ประสิทธิผลของการเริ่มต้นใช้ยาต้านไวรัสเอดส์ด้วยสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบเปรียบเทียบกับสูตรที่มียาเนวิราปีนเป็นองค์ประกอบในประเทศไทย

อุษาวดี มาลีวงศ์, วิทยา กุลสมบูรณ์, ยศ ตีระวัฒนานนท์

วัตถุประสงค์: *เพื่อประเมินต้นทุน-อรรถประโยชน์ของการเริ่มต้นการรักษาด้วยยาต้านไวรัสเอดส์สูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบเปรียบเทียบกับยาสูตรที่มียาเนวิราปีนเป็นองค์ประกอบสำหรับผู้ติดเชื้อและผู้ป่วยเอดส์ในประเทศไทย*
วัสดุและวิธีการ: *การศึกษานี้ใช้มุมมองของผู้ให้บริการ แบบจำลอง Markov ถูกพัฒนาขึ้นสำหรับผู้ติดเชื้อและผู้ป่วยเอดส์ในประเทศไทยที่มีอายุระหว่าง 15 ถึง 65 ปี ตัวแปรที่ใช้ในแบบจำลองมาจากการศึกษาไปข้างหน้าในโรงพยาบาลศูนย์ 4 แห่งในประเทศไทย ในการศึกษาทำการประเมินผลกระทบของความไม่แน่นอนของตัวแปรต่าง ๆ*
ผลการศึกษา: *สำหรับผู้ป่วยที่มีค่าซีดีโฟร์เริ่มต้นแตกต่างกันการเริ่มต้นการรักษาด้วยยาต้านไวรัสสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบจะมีความคุ้มค่ามากกว่ายาต้านไวรัสสูตรที่มียาเนวิราปีนเป็นองค์ประกอบ ในทุก ๆ ค่าซีดีโฟร์ หากกำหนดให้ประเทศไทยมีค่าสูงสุดที่ยอมจ่ายเท่ากับ 300,000 บาทต่อ 1 ปีสุขภาวะที่ปรับด้วยความบกพร่องทางสุขภาพที่กลับคืนมา การเริ่มต้นการรักษาด้วยยาต้านไวรัสสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบ จะมีความคุ้มค่ามากกว่ายาต้านไวรัสสูตรที่มียาเนวิราปีนเป็นองค์ประกอบ ในทุก ๆ ค่าซีดีโฟร์เริ่มต้นที่ต่ำกว่า 250 เซลล์ต่อมิลลิลิตร และในทุกกลุ่มอายุยกเว้นในกลุ่มอายุ 20 ถึง 29 ปี*
สรุป: *การศึกษานี้บ่งชี้ว่าการเริ่มต้นการรักษาด้วยยาต้านไวรัสสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบจะมีความ คุ้มค่ามากกว่ายาต้านไวรัสสูตรที่มียาเนวิราปีนเป็นองค์ประกอบ และควรเสนอให้ใช้ยาต้านไวรัสสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบเป็นยาสูตรเริ่มต้นในการรักษาผู้ติดเชื้อและผู้ป่วยเอดส์ในประเทศไทย*

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