



CHULABHORN  
ROYAL ACADEMY

# MODERNIZATION OF THAILAND HEALTH TECHNOLOGY ASSESSMENT

IDENTIFYING ALTERNATIVE  
APPROACHES IN THAILAND HEALTH  
TECHNOLOGY ASSESSMENT TO  
IMPROVE CANCER PATIENT  
OUTCOMES



# Chulabhorn Royal Academy

The Chulabhorn Royal Academy is a research, medical and higher educational institution established on January 19th 2016 by Professor Dr. Her Royal Highness Princess Chulabhorn Krom Phra Srisavangavadhana to commemorate and honour the wishes of His Majesty King Bhumibol Adulyadej in advancing the health and quality of life of the Thai people.

The Chulabhorn Royal Academy is a teaching and research center that teaches graduates and cultivates workers in healthcare, science, public health and the environment with knowledge, morality, ethics, volunteer spirit, commitment, and professional excellence for all life in society. It is also an institution that provides medical services with international standards to the public especially the poor and underprivileged to improve the quality of life of all Thai people in the country.

In the spirit of its commitment to improving quality of care for all Thai people, Chulabhorn Royal Academy recently organized a workshop to support the advancement of innovation in access to modern anticancer drugs in Thailand.

Cancer remains the major health problem in Thailand. As Thailand moves into upper-middle economy status, cancer is the major cause of premature mortality and accounts for nearly 0.5% of all GDP loss. Access to effective therapies remains one of the leading obstacles to helping cancer patients achieve cure, reduce mortality, improve quality of life, and contribute to growth of the country's economy.

To carry the vision of Professor Dr. Her Royal Highness Princess Chulabhorn Krom Phra Srisavangavadhana to improve the wellbeing of the Thai populace while ensuring growth and sustainability of the healthcare budget, Chulabhorn Royal Academy undertook the following report and workshop with a panel of Thai and international policymakers, researchers, and oncologists.

In this report Chulabhorn Royal Academy explored regional and global best practices, funding mechanisms and evaluation innovations from other countries to provide the most feasible and attractive policy recommendations for Thailand to strength the Thai healthcare system and improve patient wellbeing in oncology.

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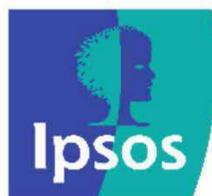
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# Table of Acronyms

ACRONYM	DESCRIPTION
APAC	Asia Pacific
ATMPs	Advanced therapy medicinal products
BIA	Budget impact analysis
CADTH	Canadian Agency for Drugs and Technologies in Health
CDF	Cancer Drug Fund
CEA	cost-effectiveness analysis
CED	Coverage with evidence development
CSMBS	Civil Servant Medical Benefit Scheme
DREC	Drug Reimbursement and Evaluation Committee
EMA	European Medicines Agency
EoL	End-of-life
FDA	Food and Drug Administration
HIRA	Health Insurance and Review Assessment
HITAP	Health Intervention and Technology Assessment Program
HTA	Health Technology Assessment
ICER	Incremental cost-effectiveness ratio
ISPOR	International Society for Health Economics and Outcomes Research
LICs	Low-income countries
LMICs	Low-to-middle-income countries
MCDA	Multi-criteria decision analysis
MEA	Managed entry agreements
NCCN	National Comprehensive Cancer Network
NCDs	Non-communicable diseases
NHSO	National Health Security Office
NICE	National Institute for Health and Care Excellence
NLEM	National List of Essential Medicines
PAP	Patient-access program
PCORI	Patient-Centered Outcomes Research Institute
QALY	Quality-adjusted life year
RSA	Risk sharing agreements
SSS	Social Security Scheme
UCS	Universal Coverage Scheme
UHC	Universal health coverage
WHO	World Health Organisation
WHO-EML	WHO essential medicines list
WTP	Willingness-to-pay

# Abstract

## Introduction:

Despite advances in achieving universal healthcare coverage, there are pervasive problems in reimbursable access to anticancer drugs in Thailand. Patients face delays in access to drugs and cancer remains a leading, preventable cause of premature mortality. The roots of the problem are twofold – the rapid pace of drug development, and current evaluation/funding methodologies in Thailand.

Local success stories include the extensive use of managed entry agreements [MEAs] in Taiwan and South Korea, Cancer Drug Fund [CDF]-type funds in the UK and several Asian countries, coverage with evidence development [CED] and flexible ICER thresholds. Thailand makes minimal use of mechanisms that are concretely used elsewhere within Asia and globally. There is a growing need to design and implement novel evaluation and funding methodologies that respect healthcare system sustainability, rapid patient access, equity, and distribution of risk between payer, manufacturer, and other stakeholders in Thailand.

## Methods:

The current study aimed to elicit consensus on the evaluation and funding methodologies most likely to improve patient access in Thailand. An initial candidate set of solutions was identified through literature review and vetted with a panel of Thai, regional and global HTA/health economics experts to identify a final set of methodologies and mechanisms. A workshop convened by Chulabhorn Royal Academy with a panel of Thai policymakers, health economists and patient organizations (N = 21) was conducted to assess the feasibility and attractiveness of several solutions. Ratings and thematic analysis were conducted. Possible barriers, evidence generation needs, and implementation considerations were collected.

## Results:

Participants were most enthusiastic about financial mechanisms (e.g. MEAs, CDF, both potentially in combination with CED) as opposed to changes in evaluation methodologies (e.g. flexible ICER thresholds, application of End-of-Life criteria). These were seen as providing acceptable split of risk between payer and manufacturer, while ensuring access – balancing the needs of all stakeholders.

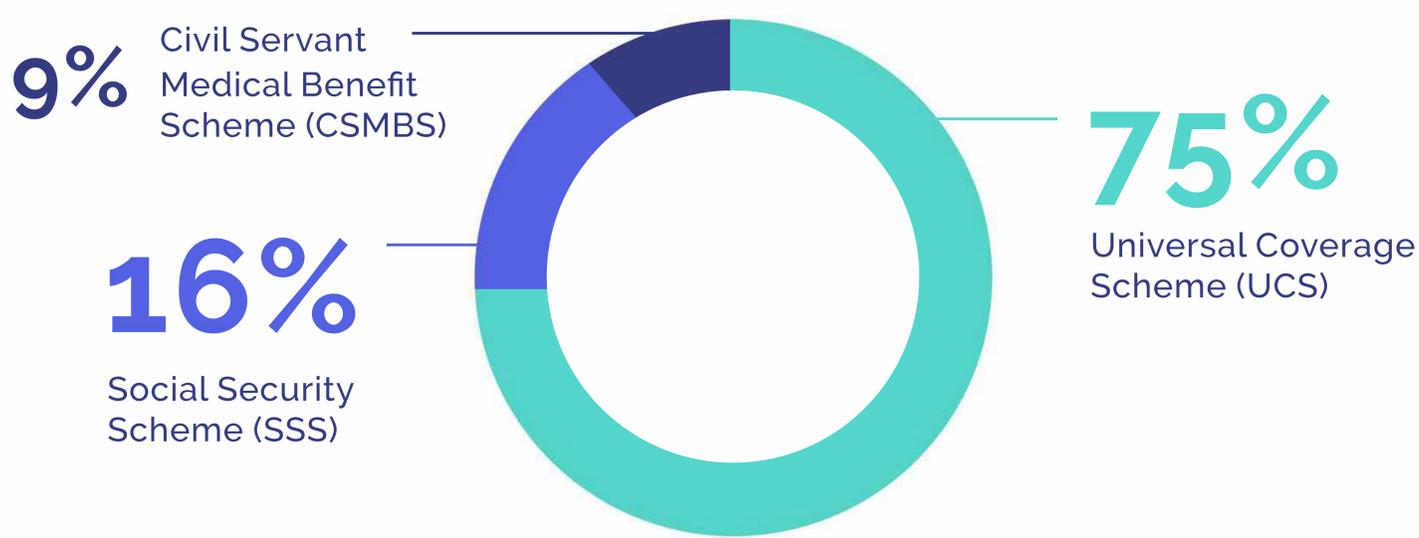
Participants were confident about combining MEAs or CDFs with CED to provide an environment where manufacturers are competitive in pricing, access is rapid, and Thai specific evidence-generation occurs. Participants recognized the difficulties of CED or outcomes-based MEAs but were confident regarding feasibility and the benefits of developing Thailand's evidence generation infrastructure and thought leadership in HTA and funding methodologies.

Implementation was noted as a central issue. Given Thailand's strong existing healthcare, HTA, clinical and academic infrastructure, implementation was seen as imminently possible. With political will and conversations with the correct stakeholders, sustainable, win-win solutions are possible for all stakeholders.

# 1. Current evaluation and funding of anticancer drugs in Thailand: what they mean for patient access and cancer burden

## 1.1. Burden of cancer in Thailand in the era of Universal Health Coverage and upper-middle income economy status

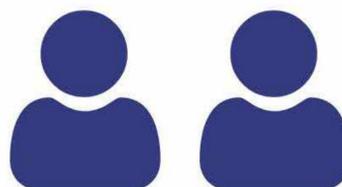
Thailand is an exemplary success story of a health system achieving universal health coverage (UHC). Since its introduction in 2002, the whole Thai population is essentially covered by one of the three public insurance schemes: 75% by Universal Coverage Scheme (UCS) and 9% by the Civil Servant Medical Benefit Scheme (CSMBS), 16% by the Social Security Scheme (SSS).<sup>1</sup>



Despite its success in achieving UHC, cancer continues to represent a serious and ever-growing health problem in Thailand. With prevalence on the rise, cancer has consistently higher rates of mortality than other non-communicable diseases (NCDs) such as heart disease and metabolic disorders. Notably, the pattern of higher cancer deaths than cardiovascular mortality mirrors patterns of mortality seen in high-income countries and upper-middle-income countries.<sup>2</sup>

With its remarkable social and economic development, Thailand moved from being a lower-income country to an upper-middle income economy in less than a generation, officially achieving the latter status in 2011.<sup>3</sup> As a result, Thailand faces a set of new and ongoing challenges such as a rapidly increasing burden of NCDs, among which cancer accounts for one of the highest and continuously increasing burdens.<sup>4</sup>

**36.1%**  
premature deaths



WHO data from 2016 suggests that premature deaths from cancer accounted for over one third (36.1%) of all NCD-related premature mortality in Thailand.<sup>5</sup>

## 1.2. Rapid pace of development in oncology and challenges in Thai patient access

Mirroring the increasing burden of cancer in Thailand is the rapid pace of innovation in oncology, with numerous high-efficacy, high-cost therapeutic breakthroughs entering the market yearly. 58% of new treatments approved by the US FDA in 2020 were for oncology, rare diseases and other similarly grouped drugs. These classes of drugs often receive designated breakthrough regulatory streams as breakthrough drugs by the US FDA, ATMPs by the European EMA or the SAKIGAKE pathway in Japan.<sup>6</sup> Table 1 summarizes the common characteristics of breakthrough drugs.

Table 1 Common characteristics of breakthrough drugs

<b>High efficacy</b>	High-efficacy for indications with no standard of care
<b>High innovation</b>	Considered innovative according to the definitions of the evaluating agency
<b>High cost</b>	Often at high cost, posing challenges to conventional notions of cost-effectiveness, willingness-to-pay, conventional HTA evaluation and value
<b>Targeted populations</b>	Increasingly targeted populations and disease groups, often defined by genotypic profiling

The rapid pace of development in oncology poses a problem not only for LMICs, but healthcare systems globally, followed by increasing efforts in balancing the sustainability and patient access.<sup>7</sup>

While numerous effective anticancer treatments are available, patient access remains a challenge in Thailand. Regulatory approval of anticancer drugs is generally high, with 97.5% of drugs on the WHO-EML's list and 78% of drugs on NCCN's guidelines being available on market.<sup>8</sup> However, reimbursable patient access is considerably lower, occasionally substantially so despite market approval. Patient access to cancer drugs is lower than 50% of the available treatments on the market, especially for the innovative drugs such as targeted cell therapies, which have better safety while providing a better quality of life to the patient.<sup>9</sup> Large numbers of cancer patients in Thailand die prematurely due to lack of access, including a substantial number under the age of 50.<sup>10</sup>

Concrete evidence of access affecting survival are seen when comparing differences in drug availability and survival outcomes between public insurance schemes in Thailand.

**For some cancers, reimbursable access (patient access) is lower than 20% of NCCN recommended drugs.**

**For some cancers, 0% of NCCN-recommended drugs are accessible despite receiving regulatory approval.**

Variations in patient access to high-cost anticancer medicines in Thailand under the three insurance schemes were reported and fully explored in a recent study.<sup>8</sup> The CSMBS was found to have greater patient access to reimbursable high-cost medicines treating cancers, especially advanced-stage cancers.<sup>8</sup>

Notably, there is poorer overall survival among UCS patients than CSBMB patients due to reimbursable access to treatments for colorectal cancer (74.6% VS. 84.3%, (p-value < 0.01)).<sup>11,12</sup> Similarly in the US, colorectal cancer patients with Medicare health insurance were reported to have a 32% higher risk of death than patients who were privately insured, indicating differences in survival linked to access inequality.<sup>13</sup>

Differences in access to effective cancer drugs between insurance schemes has been shown to result in significantly worse survival outcomes for patients with less avenues for access. The end result is that Thai patients face limited and delayed access to new oncology treatments, biologics, rare-disease therapies and similar therapeutics despite the existence of category E2-the high-cost medicines under the National List of Essential Medicines (NLEM) and the Oncology Prior Authorization program.

In summary, the clinical, humanistic and economic burden is substantial. Lost productivity and diminished workforce accounts for nearly half a percent of the whole Thai economy (0.4% of GDP loss), hindering economic growth of the country which has worked tirelessly in its development.<sup>10,14</sup>

### **1.3. Challenges in traditional HTA evaluation for oncology drugs**

While Thailand has achieved universal health coverage under its 3 insurance schemes, evaluating high-cost cancer drugs represents a challenge faced not only by Thailand but by all LMICs and HICs. Securing patient access to high-cost, high-efficacy and high-innovation while ensuring sustainability of healthcare budgets is a universal problem that has spurred the development of novel funding and evaluation methods across the Asia Pacific (APAC) region and globally.<sup>15</sup>

Evaluation for decision making using traditional health technology assessment (HTA), cost-effectiveness analysis (CEA) and budget impact analysis (BIA) methods is challenging for this class of assets. Novel oncology drugs often present problems of evidence generation as they receive regulatory approval in earlier phases of development. The value of such drugs is likely not captured in the conventional incremental cost-effectiveness ratio (ICER) and quality-adjusted life year (QALY) framework. As such, broader value concepts and novel evaluation/ financial models are required for advanced cancer therapies.<sup>16</sup>

Despite its status as a firm upper-middle-income power and the existence of a strong HTA agency, clinical societies and academic infrastructure, Thailand has faced challenges in securing equitable access to novel medicines in unmet diseases (Figure 1). While proven solutions have been implemented regionally and globally, pervasive challenges have resulted in a gridlock whereby finding modernization of evaluation and funding for modern drugs has been considered a lower priority by payers and various stakeholders.<sup>17</sup> Given the ever-increasing prevalence of cancer and the ever-increasing pace of oncology innovation, this problem will not resolve itself of its own accord. Thailand also spends less than 4% of GDP on healthcare, which is lower than the average spent by upper-middle income economies in general (5.8% in 2018)<sup>18</sup>, leaving it with less absolute spending power for all healthcare needs.<sup>19</sup>



Figure 1. Challenges in HTA system in Thailand <sup>17,20</sup>



### Capacity Building

Under the current model of HTA evaluation in Thailand, limited capacity for evaluation and evidence generation is a pervasive issue. Pragmatic models have been recommended in previous studies including previous Thai guidelines including public-private partnerships, or academic fellowship models with government and industry support.<sup>20</sup> Notably, academic partnerships are currently used consistently by NICE in the form of academic Evidence Review Groups (ERGs). CADTH also frequently partners with academics for HTA reviews.

### Multi-stakeholder engagement

The lack of the engagement of stakeholders, especially patients, medical societies and industry stakeholders in the HTA process was also seen as being sub-optimal for decision-making. Despite nominal inclusion of such stakeholders in the HTA process, there is a perceived lack of education or qualification regarding how best to engage with the process and raise issues with the panel.<sup>20</sup> Further, the engagement of clinicians was found to be quite limited in the HTA process, according to a complementary workshop we conducted, which will be described in below Section 5.

### Inequitable/variant patient access under different insurance scheme

The variance of patient access to cancer drugs under different health insurance scheme in Thailand was well recognized and discussed in above Section 1.2. Further concern stems from the lack of an appeal system under the Thai HTA process unlike the majority of HTA systems, leaving little recourse for assets that fail on initial submission – a situation that is not uncommon.

In summary, access to innovative drugs is an issue not only in LMICs and developing economies, but countries with higher ability to pay. As such, both in practice and in the academic literature, there is a move beyond traditional HTA approaches to increase access, including novel HTA methodologies, financing strategies, funding mechanisms and incorporating additional aspects of value.<sup>16,21</sup>

## 1.4. Existing regional and global solutions

Within Asia and internationally, success stories exist where flexible evaluation methods and innovative funding mechanisms allow the population to access innovative cancer drugs (Table 2). Examples include the use of end-of-life criteria and the cancer drug fund under the auspices of NICE, as well as extensive histories of managed entry agreements (MEA) and risk sharing agreements (RSA) in Taiwan and South Korea. Further innovations include coverage with evidence development and flexible ICER cut-offs.

Table 2. Example solutions in some HTA leading countries

Example countries	Solutions
	 Risk sharing approaches - Managed entry agreements (MEA) - Risk sharing agreements (RSA)
	 CEA waiver (exemption from CEA evaluation)
	 Cancer Drug Fund-type solutions, ring-fenced funding for oncology and rare-disease assets
	 Coverage with evidence development (CED)
	 End-of-life criteria
	 Flexible ICER

 Australia South Korea United States Germany Japan Taiwan United Kingdom Hong Kong Italy Singapore

For broader frame consideration, multi-criteria decision analysis (MCDA) and aspects of value beyond the ICER and QALY are also frequently being discussed and researched globally.

## 2. Study methodology

To address the challenges of improving access to innovative oncology drugs, Chulabhorn Royal Academy convened a panel of global, regional and Thai payers, academics and clinicians. An initial set of candidate approaches was selected based on literature review and discussion with a panel of academic and Thai policymaker experts with respect to their suitability to the Thai context. The final candidate solutions comprising a set of novel HTA methodologies, best practices, funding mechanisms and aspects of value were presented and subsequently explored during a workshop. Several promising approaches were evaluated for feasibility and attractiveness in the Thai context. Ratings, thematic analysis and next steps were conducted.

In addition, another complementary/ exploratory workshop was conducted with a group of practicing Thai clinical oncologists, to collect inputs from the clinical perspective and explore the roles of clinicians/ oncologists in HTA for cancer drugs.

## Objectives and goals

The overarching objective of this study is to evaluate several likely HTA approaches for the Thailand-specific context, to ultimately improve patient access to oncology drugs.

Specific stepwise goals are listed as below:

- Evaluate possible approaches/ solutions that could apply in the Thai context
- Identify possible barriers to these approaches, what evidence/ study is needed to support the recommendations, and how to implement them

## Targeted literature review and panel discussion to identify alternative approaches

Alternative HTA methodologies and funding mechanisms were identified via targeted literature review, followed by input from Asst. Prof. Suthira Taychakhoonavudh, PhD (Chulalongkorn University), Prof. Lou Garrison, PhD (University of Washington), Asst. prof. Raoh-Fang (Jasmine) Pwu, PhD (Ministry of Health and Welfare, Taiwan) and Assoc. Prof. Surachat Ngorsuraches, PhD (Auburn University) to finalize the set of candidate approaches for discussions. Ten approaches in several leading APAC and global HTA and funding/reimbursement countries were selected (Table 3), and the selected solutions were further narrowed down to 5, based on the pre-set criteria (Table 4) for the purpose of deep dive discussion in the multi-stakeholder workshop.

The selected 5 solutions will be presented below in Section 3.

Table 3. Reviewed solutions in various HTA leading countries

	<b>Country</b>	<b>Solutions</b>
<b>1</b>	South Korea, Taiwan, Australia, UK, majority of OECD/EU countries	Managed entry agreements/ risk sharing agreements (MEA)
<b>2</b>	UK	End-of-life criteria
<b>3</b>	UK, Hong Kong, Singapore, Australia, Italy	Cancer Drug Fund-type solutions
<b>4</b>	Germany, South Korea, Japan	Coverage with evidence development
<b>5</b>	South Korea, UK, Canada	Flexible ICER threshold
<b>6</b>	US	PCORI, Patient-Centered Outcomes Research Institute
<b>7</b>	Theoretical/in research	Augmented CEA
<b>8</b>	Theoretical/in research	MCDA, multicriteria decision analysis
<b>9</b>	South Korea	CEA waiver
<b>10</b>	Canada	Separate oncology and non-oncology HTA agencies

Table 4. Criteria of selecting solutions

<b>Feasibility</b>	<b>Attractiveness</b>
<ul style="list-style-type: none"> <li>• Successful in other countries</li> <li>• Data availability</li> <li>• Data analysis and capacity</li> <li>• Administrative and bureaucratic burden to implement and maintain</li> <li>• Funding/ investment required to implement and maintain</li> </ul>	<ul style="list-style-type: none"> <li>• High levels of buy-in from all stakeholders</li> <li>• Win-win for various parties (payer/ industry/ health care providers/ patients)</li> <li>• Delivers greater access to innovation, beyond conventional acquisition cost and QALY</li> <li>• Has scientific or literature supporting positive outcomes/ benefit</li> <li>• Attractiveness</li> </ul>

## Workshop approach

A workshop comprising a group of 21 Thai policymakers, clinicians, health economists, academic researchers and patient group representatives was conducted. Stakeholders were taken through a deliberative exercise into several established mechanisms used in APAC and globally when evaluating and reimbursing new oncology assets. The discussion was conducted in 3 separate groups, applying polling rounds after each discussion item. The full list of participants is available in Appendix 1.

Five solutions were considered in detail, and will be further presented in the next section:

1. MEAs/RSAs
2. Dedicated drug funds such as the UK's Cancer Drug Fund
3. NICE's End-of-Life Criteria
4. Coverage with evidence development
5. Flexible ICER thresholds

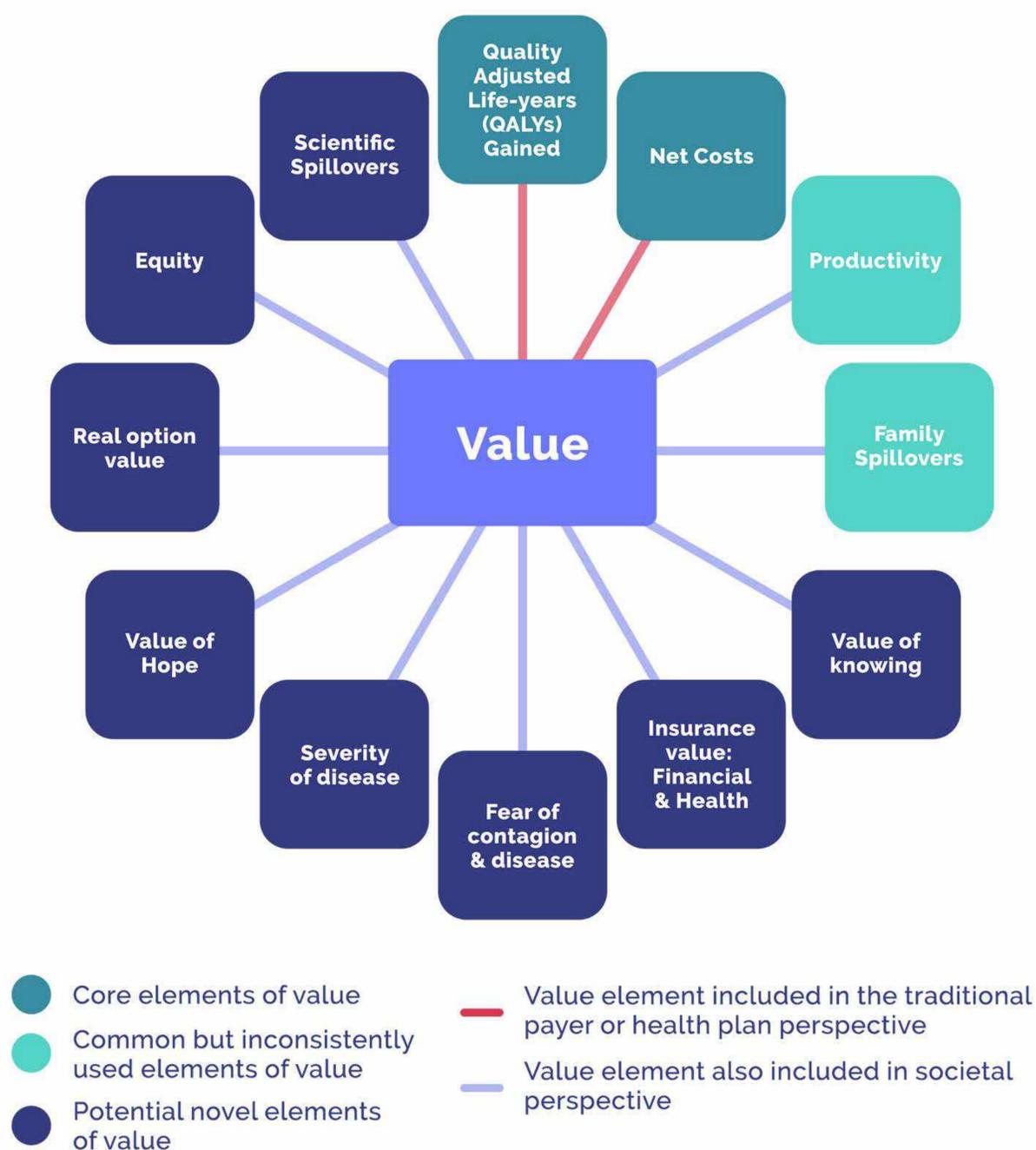
## Discussion, evaluation and ranking frameworks

After a presentation of each solution and an interactive discussion in each group based on questions listed below, the multi-disciplinary groups were asked to evaluate the above solutions in terms of their feasibility and attractiveness in the Thai context, considering the criteria presented above (Table 4).

- How feasible is this solution?
- How attractive is this solution?
- What evidence or resources are needed for this solution?

Finally, in addition to the concrete, previously implemented mechanisms examined above, we examined ISPOR's 'value flower' framework as generated by their dedicated task force (Figure 2).

Figure 2. ISPOR Value Flower Framework



Adapted from Lakdawalla et al.<sup>2</sup> QALY indicates quality-adjusted life-year.

Source: ispor.org

The participants were asked which aspects of value from ISPOR's value flower framework were most relevant for the Thai oncology context after the presentation and discussion on the topic, beyond QALY gain and net costs as considered in conventional CEA.

### 3. Discussion and results

Below, the results of the discussion are presented in sequence of ranking result during the workshop. Participants were provided with summarized information of each solution in a case study, as per the boxes below. As seen below in Table 6 (Appendix 2), the rankings of feasibility and attractiveness were correlated with each other: solutions that were seen as feasible were also seen as attractive.

#### Ranking result sequence:

- 1 MEAs/RSAs (most feasible and attractive) 
- 2 CDF-type solutions
- 3 Coverage with Evidence Development (CED)
- 4 Flexible ICER thresholds
- 5 EoL

### 3.1 MEAs & RSAs

#### Brief Description of MEA

- Under risk sharing schemes/ MEAs, payers and manufacturers share the burden of the risks of financial impact
- Allows access to drug and better health outcomes, often with manufacturer reaching a confidential discount or other financial-based agreement with payer
- Almost entirely based on financial mechanisms. Outcome-based agreements are possible, but difficult to implement
- Widely used with different names, arrangements, eligibility and frameworks in different countries
- Over two-thirds of the Organization for Economic Co-operation and Development and European Union countries have been utilizing or had utilized RSAs by 2019

#### Success Case



RSA was introduced in South Korea since 2013, to improve patient access to new drugs, it is particularly relevant for cases involving costly anticancer drugs and orphan drugs that lack alternative drugs or treatments. In Taiwan, in some years 100% of drugs approved for reimbursement were approved subject to MEA, despite only 16% of drugs submitting a CEA. As a result, Taiwanese treatment generally adheres closely to NCCN guidelines.

Source: Lee et al., 2021,<sup>23</sup> Akhtar and Gras 2020,<sup>24</sup> Kuo et al., 2020<sup>25</sup>

Risk sharing approaches such as RSA, MEA, were considered the most attractive to the participants, given its capability to address clinical and financial uncertainties. MEAs were seen as minimizing risk to the government healthcare budget while expediting access. Furthermore, MEAs may increase competition between manufacturers where drugs of similar classes target similar indications – the launch PD-L1 inhibitors and the subsequent competition for market share was cited as an example. During the discussion, participants supported more widespread use of financial-based outcomes, with simple discounts, rebates and refunds and other finance-based outcomes being noted as especially feasible and attractive.

Considerations for implementation raised were:

- Complexity of the arrangement is expected for implementing a national wide MEA, which will increase the administrative burden of the system. As such, simple arrangements are likely preferred if possible
- Attempting to minimize patient out-of-pocket spend
- Some interest was also seen in outcomes-based arrangements. It was noted that centres such as Chulabhorn Royal Academy may have the infrastructure to regularly collect outcome data that can be leveraged for the implementation. Notably, outcomes-based arrangements are typically seen as complex. However, Thai stakeholders are enthused at this prospect and Thai evidence generation, with strengthening of evidence generation infrastructure, was noted as highly desirable not only for MEAs but for several solutions under discussion (e.g. CED, CDF)
- Requires more conversations and sustainable framework between budget-holders and manufacturers to implement. Implementation emerged as a pervasive theme, regardless of solution discussed.

## 3.2 Dedicated drug fund to innovative high-cost drugs/ Cancer Drug Fund (CDF)

### Brief Description of CDF



- CDF is a separate source of funding for cancer drugs in the UK, initially introduced as a stop-gap measure to provide for drugs for rare cancers
- It plays a significant role in patients' access to drugs, provides patients with faster access to new cancer treatments, and offers pharmaceutical companies a fast-track route to NHS funding
- Drugs with clinical potential can be provided temporarily using the CDF, in cases where either NICE is yet to issue final Guidance, or where there is insufficient evidence for a proper assessment
- Often used to provide access while further evidence is collected, i.e. in conjunction with CED
- Has recently seen extensive uptake in APAC region. Hong Kong, Singapore and Australia have all established ring-fenced funds for oncology and rare diseases in the past 2-3 years.
- Most notably, Australia and Italy have dedicated considerable funds to rare diseases and oncology in the midst of the COVID-19 pandemic, demonstrating that this class of assets requires unique funding considerations even under the distinct circumstances of the current pandemic

Source: National Health Service (NHS) UK <sup>27</sup>, Australian Pharmaceutical Benefit Scheme 2021 <sup>28</sup>, Jommi et al., 2021<sup>29</sup>

The participants were enthusiastic about the idea of a dedicated drug fund for novel high-cost, high-efficacy drugs. It was a solution previously proposed to the government by researchers, according to the participants – however a lack of multi-stakeholder implementation efforts hampered realization of such a fund.

- Stakeholders acknowledged that a certain subset of high-efficacy, high-cost, high-innovation drugs may require measures to help support access, and would also help avert catastrophic spending among patients

- However, there were concerns about equity across different diseases, as well as the sustainability and the source of funding, while acknowledging that disease severity is also a consideration

- This may benefit from a study evaluating WTP amongst the Thai population for different diseases, accounting for disease severity

Recent theoretical work in health economics supports the argument that WTP is higher for more severe diseases than less severe conditions.<sup>30</sup> Further, implementation of such funds in APAC and globally during the pandemic suggests that countries acknowledge the need for measures specifically aimed at high-cost, high-efficacy oncology assets even against the backdrop of competing health priorities, suggesting that equity concerns and sustainable budgets are achievable with the right set of measures. Finally, in combination with ongoing evidence generation, CDF-type solutions may provide rapid access while providing payers with a mechanism for disinvestment for drugs that prove to be ineffective with more mature data.

### 3.3 Coverage with Evidence Development

#### Brief Description of CED

- In coverage with evidence development (CED), innovative drugs with uncertain clinical data (e.g., early phase trials) can be reimbursed and patients can gain access
- The positive coverage decision requires that manufacturers provide more evidence in the coming months and years, e.g., larger trials or real-world data
- Manufacturers can receive market access that otherwise would be denied due to insufficient evidence at time of product launch
- Notably, CED can be integrated with an MEA or CDF-type solution. This can be used to provide a stopping rule for outcomes-based MEAs, a condition for contingent CDF-coverage, and a means to provide Thai-specific evidence. An MEA or CDF can be used to 'kick-start' rapid access, minimize government spend and the CED can be used to bolster the Thai evidence base and provide the payer with a means of egress at the point of data maturity

#### Case Examples:



- Japan provides early access to advanced treatment (including cancer, rare disease) which are not listed yet
- In Korea, CED is available as a form of RSA, but has seen limited use
- German CED is for non-drug interventions such as medical device

Source: Lewis et al., 2015; Medicare's Coverage With Evidence Development: A Policy-Making Tool in Evolution. *J Oncol Pract.* 2007;3(6):296-301. <sup>31,32</sup>; Lee et al., 2021, <sup>23</sup>

The participants supported CED. Especially when combined with something like the CDF, this was seen as being able to provide earlier access, sharing risk between payer and manufacturer and providing a seamless transition to full reimbursement as more data becomes available.

- Noted that evidence development could be supported by advanced centres such as Chulabhorn Royal Academy. This would have the added benefit of developing Thailand's data-collection infrastructure

- Participants noted that only Thai data would be acceptable for reimbursement decisions that are not based on large, global phase III trials. There is little interest in referring to international data to make Thai reimbursement decisions in the CED setting

In combination with measures such as MEAs and CDF, CED provides an attractive means to deliver rapid access while reducing risk to the governmental payer. Major considerations are around data collection infrastructure. Discussions around implementation will be key, including criteria for patient access, infrastructure for continuous data collection and analysis, and mechanisms for evaluation. Expected benefits of adopting CED include development of Thai evidence collection infrastructure, expansion of the Thai-specific evidence base for multiple diseases and therapies, and Thailand's growth as a leader in such methodology and evaluation regionally and globally. Participants were fully aware of the challenges associated with this approach, but were optimistic and enthusiastic nonetheless.

### 3.4 Flexible ICER thresholds

#### Brief Description of flexible/ variable ICER threshold



- For limited number of cancer drug or rare disease drugs, South Korea applies flexible ICER threshold up to 2 GDP per capita, relative to 1 GDP per capita for normal treatments

- The acceptable threshold (ICER) for most new drugs is often below 25,000,000 KRW (USD 21,968, which is equivalent to Korea's per capita GDP) per QALY. This threshold value was created based on per capita GDP in Korea at the time in 2016

- Currently, for a limited number of anticancer drugs and orphan drugs, a flexible ICER threshold of up to 50,000,000 KRW (USD 43,936; two times GDP) per QALY has been used



- NICE in the UK has explicitly used a willingness to pay threshold ranging from £30,000 to £50,000 per QALY for life-threatening conditions



- Australia does not have an explicit threshold but accepted new medications which have thresholds ranging from AUD45,000 to AUD60,000 per QALY



- In Canada, CADTH, does not use the ICER or WTP as a binary threshold but considers a 'soft WTP' as one piece of information as part of a contextual decision-making process. As such, drugs with a wide range of ICERs are considered for reimbursement and ultimately go to provincial authorities where they are subject to measures such as MEAs and pricing controls



- The U.S. uses a wide range of thresholds from U.S. \$50,000/QALY to \$150,000/QALY depending on individual preferences or disease severity

Source: Yoo, Seung-Lai, et al., 2019<sup>33</sup>

Flexible ICER threshold is seen as an interesting solution, but it would require evidence to support. It is intuitively appealing, but there is no existing evidence in the Thai context that would inform how ICER thresholds should change for different therapeutic area.

- The participants acknowledged that all QALYs are not equal – a QALY is not always a QALY, disease severity was mentioned as an important consideration and one that would potentially change ICER thresholds

- However, it is unclear exactly how ICER thresholds should be changed for different levels of disease severity or other considerations (e.g. equity concerns). This would require valuation with the Thai public, and possibly additional economic/ theoretical studies in the Thai context to be convincing

The Canadian approach wherein the WTP threshold is not seen as a hard binary was explicitly noted as being interesting. However participants noted that Thai decision-makers are much more comfortable with viewing the WTP threshold as a hard binary cut-off decision rule. Further, Thai decision-makers do not currently have recourse to mechanisms such as MEAs to achieve reimbursement of drugs with ICERs that are above conventional WTP thresholds. It is unclear whether the culture of viewing WTP thresholds as a hard binary is amenable to change.

### 3.5 End-of-Life Criteria



#### Brief Description of EoL

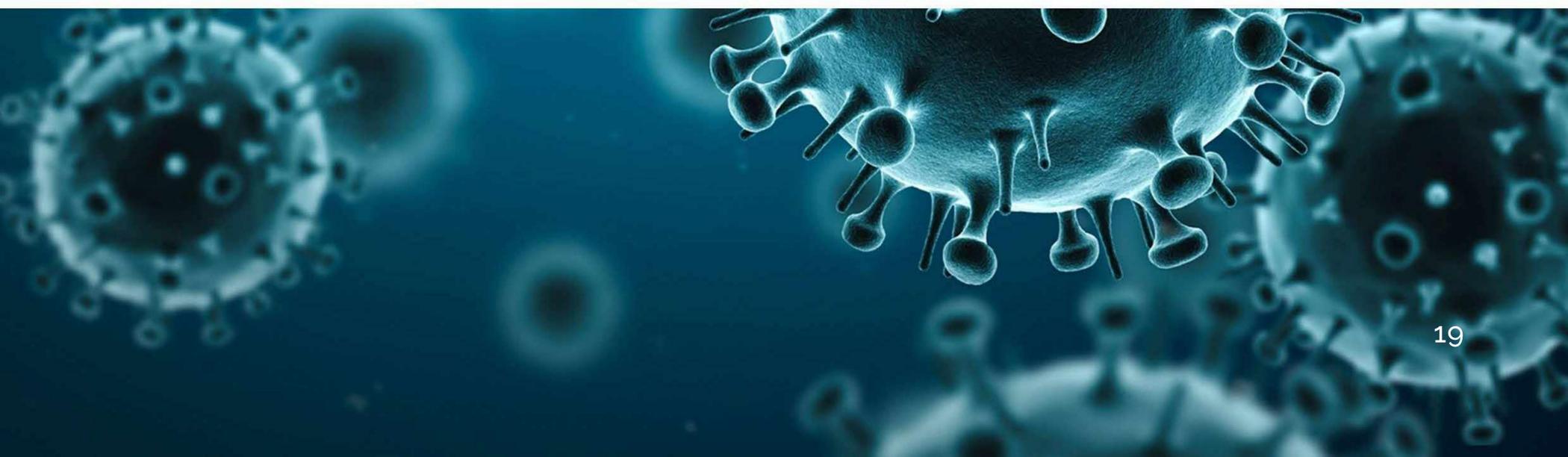
- NICE uses an end-of-life (EoL) criterion, allows treatments with an ICER over the regular threshold £20 000-£30 000 per QALY to be recommended
- Under this criterion, up to a maximum of 1.7 times the regular threshold, up to a maximum of £50,000 per QALY is allowed
- EoL criteria: drugs indicated for patients with a short life expectancy (<24 months) and should extend life by at least 3 months compared to current standard of care
- The assumption underlying the higher ICER threshold for EoL technologies is that society values time at the end of life more highly and is willing to pay more

Source: Josien et al., 2020 <sup>34</sup>

This was the least enthusiastically received solution.

- Participants noted that extension of life and minimizing clinical burden at end-of-life are considerations for Thai people
- However, there were concerns regarding how exactly EoL is defined and how the threshold should shift for drugs meeting EoL criteria
- The participants have shown limited enthusiasm and interest. To support implementation, it would require convincing Thai data showing how society values QALYs and WTP at end of life

Among all solutions, this was noted as being of least interest. Elements of severity of disease, raising the ICER threshold and other components of the EoL mechanism were seen to be captured by various other solutions (e.g. MEA, CDF, flexible ICER) with more generality, applicability and attractiveness.



### 3.6. Elements of the Thai value flower– reflection of future values for Thailand

To conclude the session, participants were asked to assess several components of ISPOR's value framework as presented by Dr. Garrison.<sup>22</sup> A 2018 ISPOR task force developed an approach referred to as the 'value flower', with 10 potential additional values that new drugs can offer, as in Figure 2 above. The value flower "broadens the view of what constitutes value in healthcare" with elements that extend beyond traditional cost per QALY analysis. Methodological, conceptual and ethical limitations of the QALY as a generic measure of health have recently been comprehensively summarized in a systematic review by Rand and Kesselheim.<sup>35</sup>

The values seen as most important to participants during the workshop were:



Since all the above discussed HTA approaches are representing different dimension of values, for example, traditional CEA framework is representing QALY and net cost, and above-mentioned RSA or CDF incorporates severity of disease, it is interesting to see how the value is considered and expected in Thailand, and it's also worth to continuously explore this topic deeply in future. Extending the ICER and laying the foundations of an augmented CEA are active topics of research at present.<sup>36,37</sup>

## 4. Conclusion and calls for implementation

In general, participants showed more interest in tangible financial solutions (MEAs, CDF; CED maybe as an element of MEA/CDF) rather than theoretical or methodological solutions (flexible ICERs/variable WTP, EoL). These were seen as providing an acceptable split of risk between payer and manufacturer, while ensuring access – balancing the needs of all stakeholders. Importantly, all solutions have been proven to be feasible in other APAC and global settings.

**Implementation was noted as a central issue repeatedly.** While there's enthusiasm for several of these solutions, it will be imperative to bring all stakeholders in the Thai ecosystem to the table to bring these advancements to reality.

**The need for Thai-specific evidence for both reimbursement considerations and assessing Thai societal preferences was noted.** There were highlights on the need for Thai specific evidence for several solutions, such as CED, Thai societal preference and WTP for different diseases and disease severities, among others.

**Given Thailand's strong existing healthcare, HTA, clinical and academic infrastructure, implementation is possible. With political will and the correct conversations with the correct stakeholders, sustainable, win-win solutions are possible for all stakeholders in the Thai oncology ecosystem.**

In addition, there was strong emphasis on equity and sustainability of the system. Risk-sharing solutions that allow faster access without massively inflating budgets were seen as most attractive.

There was also an acknowledgement among all stakeholders that more severe diseases should likely have a higher WTP. A recent study also resonates with this concept, calling for more consideration of multiple/variable cost effectiveness threshold when QALYs are not equally valued from a societal perspective (e.g. QALYs accruing to people with severe disease compared with equivalent QALYs to other status).<sup>30,38</sup>

Stakeholders were hoping to avoid catastrophic healthcare spending for Thai patients using innovative tools to improve patient access. The set of solutions considered can address the concerns and values of Thai decision-makers, clinicians and researchers.

Remaining uncertainties included the following:



1. Concrete roadmap: timelines, evidence generation, set of stakeholders required for discussions



2. Evidence required to support uptake and implementation



3. How the recommendations from the multi-stakeholder discussion change HTA evaluation in practice, especially with respect to funding mechanisms, HITAP guidelines, ICER thresholds or others

## 5. Complementary – Oncologists workshop: oncologist role in Thailand HTA

### 5.1. Background

#### 5.1.1. Clinicians in priority-setting, reimbursement and HTA

To supplement the insights gained from the multi-stakeholder workshop detailed above, a smaller workshop was held with the clinical oncologists to understand the role of clinicians in the decision-making, prescription, priority-setting, and reimbursement processes, drivers of said processes and thoughts on the solutions vetted by the primarily policymaker and academic audience of the first workshop.

Globally, clinicians and medical societies play a critical role in decisions about which treatments are considered for evaluation (priority setting) and in providing input to HTA/reimbursement processes for decision-making from the clinical perspective. However, decisions for coverage ultimately are made by therapeutic subcommittees within HTA subcommittee composed mostly of healthcare policymakers in most cases.

Clinicians are typically not involved with the details of implementing HTA mechanisms like MEAs or CDF or judging WTP thresholds for reimbursement. In certain systems at the level of reimbursement decisions, clinicians are only involved in signing off on recommendation of drugs for CDF recommendation or providing clinical expert input for CEA validation and aspects of the HTA clinical dossier.

In Thailand, medical oncologists advise the National Health Security Office (NHSO) and NLEM committee for priority-setting and guidelines. Clinicians provide expert clinical input throughout the HTA process, however participants noted they felt they lacked active roles and voices in the final decision-making process regarding reimbursement.

### 5.1.2. The evolving role of clinicians in APAC and global healthcare systems

Through literature searches and discussions with HTA stakeholders in APAC and globally we ascertained that there are existing frameworks and ongoing efforts to increase diversity of the decision-making process and participants, and observed how clinical stakeholders are increasingly engaged in final HTA decision making in several systems.

Taking the APAC region for closer observation, medical societies in some countries such as Cancer Disease Review Committee in South Korea, are providing patient centred insights. This includes medical need, treatment landscape as well as reimbursement criteria (subgroup for reimbursement) setting for HTA decision (but inevitably there are also concerns and criticism raised that in reality their inputs are more driven based on policy/ financial perspective).

From Jul 2021, the DREC subcommittee of the Korean HTA agency (HIRA) was requested to include at least one clinical expert recommended by relevant medical society (previously it was only demand basis, not mandatory); in Taiwan, medical societies/ clinical experts are involved in the decision-making committee for final deliberation, making voice from medical/ treatment need perspective for new drugs. Notably, these subcommittees are equivalent to Thailand's NLEM subcommittee. In Thai HTAs, medical oncologists were occasionally invited to clarify medicines in class and burden for the evaluation. Once the CEA was completed, clinicians will be invited again to be informed of results. However, the doctors did not provide any inputs for economic evaluation. On the other hand, as mentioned above, Korea and Taiwan use more interactive engagement model with oncologists and clinician, throughout the whole evaluation and decision-making process.

## 5.2. Objective of the Oncologists workshop

Following the HTA workshop with payers and academics in July 2021, the oncologists workshop as part of the series of activities, collects the input of the medical oncologist community.

-  Discussion of possible win-win solutions from previous workshop that were deemed most feasible and attractive by Thai policymakers, academics and patient organizations
-  To understand how availability of these solutions in Thailand might impact clinical practice and decision-making

## 5.3. Open discussion session

After an informative presentation of all relevant background and individual HTA mechanisms as well as the innovative values from the value flower for oncology consideration, the oncologists underwent some rounds of discussion based on the pre-set key questions as follows:

- 1 What are your thoughts about HTA currently in Thailand? And what is your involvement and experience during the HTA process?
- 2 What do you find is currently your greatest burden to recommending drugs that you wish to recommend or prescribe for use?
- 3 What is your current role in priority-setting and reimbursement considerations? What would you like it to be?
- 4 How much of a consideration is budget or cost-effectiveness vs. clinical effectiveness/international guidelines (e.g. NCCN)? What would you like it to be?
- 5 What are your opinions on the solutions outlined during the discussion above?
- 6 Policymakers have indicated that they are interested in the solutions we have outlined (MEAs, CDF, flexible ICERs, CED). If you know you have these tools available, does this change your decision-making and priority-setting in theory? If so, how?

## 5.4. Discussion

Concerns specific to clinicians included gaps of understanding and involvement in HTA process in Thailand, lack of communication channels with broader stakeholders and limitation of oncologists' role in current HTA system. Clinicians noted that the largest barrier to access, prescribing and priority-setting for drugs (regardless of efficacy or recommendation by NCCN) is mainly the price/budget impact of new drugs, given the economic context of Thailand compared with countries like South Korea, Australia, or Singapore. It was noted that most proposed solutions existed in HICs with few analogues in LMICs. However, consensus reached was that Thailand is an outlier among LMICs and is formally an upper-middle-income country with a sophisticated HTA, clinical and academic infrastructure. There was enthusiasm at the prospect of being part of the discussion and having access to the drugs if all stakeholders could be brought to a centralized table and implementation of solutions could happen.

**The clinicians were eager to contribute and be part of the HTA modernization in Thailand and supported the initiative as a whole, echoing the sentiments of policymakers and academics.**

Compared with other HTA systems with interactive communication and decision-making involving multiple stakeholders, currently in Thailand clinicians are restricted to an advisory role. Their role provides priority setting based on unmet needs and insights on therapeutic benefit, but there is little interaction with other stakeholders like policymakers. As such clinicians are less aware of the HTA and decision-making process. However, they are open to be more involved in the process as much as possible, to contribute to better patient access to new treatments. The theme of having a more centralized, multi-stakeholder approach with clinician input was pervasive.

**“Enthusiasm and understanding of the mechanisms were clear, and the prospect of access to this class of assets was evident, however there was concern primarily around implementation – specifically, coordinating the various stakeholders in the ecosystem.”**

In terms of risk sharing, clinicians are familiar with patient access program (PAP) which aim to alleviate the financial burden of the individual patients. The prospect of more centrally-negotiated MEAs was seen as considerably more appealing. The bargaining power of a centrally driven negotiating bloc and the level of competition associated with such a mechanism was seen as more manageable, with more favorable outcomes and less administrative hassle than the current decentralized patchwork. PAPs are of limited help in terms of access, given the difficulties to meet the criteria and the increased administrative burden to the system. Simplifying such financial arrangements will be important to ensure patients have access.

Flexible ICERs were considered positive by the participants, as it seems like they incorporate other value dimensions in addition to cost and QALY. There was acknowledgement that this reflected the most central concern, which was price. Clinicians were especially attuned to the idea that decision-making should consider factors beyond a binary WTP threshold, and the idea of a Canadian-style 'soft ICER' seemed to make intuitive sense. They noted that being at the decision-making table for reimbursement decisions may help temper what was seen as a slightly more rigid, binary style of decision-making.

Major themes that emerged were:

- o Lack of a clear multi-stakeholder body where oncologists could interact with policymakers or be involved in the evaluation process, even though there is a great deal of enthusiasm
- o Prices need to be managed centrally with policymakers, e.g. using MEAs or CDF, because at point of prescription it becomes challenging for practicing oncologists to prescribe based on the financial realities of their patients
- o Use of MEAs alongside Thai trials/CED would be of interest
- o Oncologists would be interested to know concretely where they can play a role with policymakers and negotiators – e.g. conducting the trials needed for MEAs
- o The current HTA framework was not felt to be sufficient to secure clinician or patient access to innovative or curative oncology drugs, as emphasized in previous workshop

## 5.5. Conclusions

In summary, the participants were open and eager for engagement in the new drug evaluation process, given the lack of understanding and communication throughout the decision-making process.

The reality of high unmet need and low patient access in oncology area was pushing them to further contemplate how they can contribute beyond their current advisory role. In the context of increasing budget challenges in Thailand as in all other countries, balance between funding and disease burden need to have better centralized solutions, as well as more active leveraging of existing and innovative mechanisms, with more active multi-stakeholder interaction. Future improvement is promising, with increased focus on patient-centred value globally and regionally.



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## 7. Appendix

Appendix 1.

Table 5. List of workshop participants

Name	Organization
Prof. Chirayu Auewarakul, MD, PhD	Dean of Princess Srisavagavadha College of Medicine and Medical Oncologist; Acting Director of Centre of Learning and Research in Celebration of HRH Princess Chulabhorn's 60th Birthday Anniversary
Asst.Prof. Teerapat Ungtrakul, MD	Deputy Dean of Princess Srisavagavadha College of Medicine and Medical Oncologist
Asst.Prof. Wisut Lamlerthon, MD	Deputy Dean of Princess Srisavagavadha College of Medicine and Medical Oncologist
Asst.Prof. Nuttavut Kantathavorn, MD	Assistant Dean of Princess Srisavagavadha College of Medicine and gynecologic oncologist
Jomtana Siripaibun, MD	Director of Oncology Medical Center Chulabhorn Hospital
Manassamon Navipipat, MD	Hematologist, Oncology Medical Center Chulabhorn Hospital
Nawaporn Poonswan, MD	Deputy director, Petchabun Hospital
Wachara Eamratsameekool, MD	Director, Phanomphrai Hospital, Roi Et
Asst. Prof. Aumkhae Sookprasert, MD	Medical Oncology Unit, Department of Medicine, Faculty of Medicine, Khon Kaen University
Assoc. Prof. Cherdchai Nopmaneejumruslers, MD	Deputy Director, Faculty of Medicine Siriraj Hospital, Mahidol University; Chair of Rare disease working group Thailand
Jinda Rojanamatin, MD	Director Rajavithi hospital (Ex-director National cancer institute)
Nopporn Cheanklin, MD	Executive Director, Health System Research Institute
Assoc. Prof. Puree Anantachoti, PhD	Faculty of Pharmaceutical Sciences, Chulalongkorn University
Pattara Leelahavarong, PhD	Faculty of Medicine Siriraj Hospital, Mahidol University

Rapeesupa Wangcharoenrung, PhD	Deputy Director, Fiscal Policy Research Institute Foundation
Asst. Prof. Sitaporn Youngkong, PhD	Faculty of Pharmacy, Mahidol University
Miss Sirithip Kudtiyakarn	President, Thai Cancer Society
Suleeporn Sangrajrang, PhD	Deputy Director of National Cancer Institute
Ugrid Milintangkul, MD	Adviser of Thai Cancer Society
Assoc. Prof. Virote Sriuranpong, MD, PhD	Head of Department of Medicine and Head of Excellence Chulalongkorn Comprehensive Cancer Center, Faculty of Medicine, Chulalongkorn University & The King Chulalongkorn Memorial Hospital
Assoc. Prof. Wichai Vassanasiri, MD	President of Thai Breast Society; Breast surgeon, Department of Surgical Oncology, Phramongkutklao College of Medicine

Appendix 2.

Table 6. *Result of ranking from polling practice of workshop (n=21)*

Solutions	Feasibility <i>Average rating</i>	Attractiveness <i>Average rating</i>
Managed entry agreements/risk sharing agreements (MEA)	5.6	6
Cancer Drug Fund-type solutions	4.8	5.2
Coverage with evidence development	4.7	5.1
Flexible ICER threshold	4.3	4.8
End-of-Life criteria	3.9	4.5

*\*rating scale for each item ranges from 0 to 7*

Table 7 Oncologists workshop participant

Name	Organization
Asst. Prof. Aumkhae Sookprasert, MD	Medical Oncology Unit, Department of Medicine, Faculty of Medicine, Khon Kaen University
Asst. Prof. Chanyoot Bandidwattanawong, MD	Medical Oncology Unit, Department of Medicine, Faculty of Medicine Vajira Hospital
Assoc. Prof. Ekaphop Sirachainan, MD	Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University
Adjunct Assoc. Prof. Napa Parinyanitikul, MD	Medical Oncology Unit, Department of Medicine, Faculty of Medicine, Chulalongkorn University & The King Chulalongkorn Memorial Hospital
Parichat Phongthai, MD	Oncology unit, Khon Kaen Hospital
Assoc. Prof. Patrapim Sunpaweravong, MD	Medical Oncology Unit, Department of Medicine, Faculty of Medicine, Prince of Songkla University