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Original Article/Research

An empirical study looking at the potential impact of increasing cost-effectiveness threshold on reimbursement decisions in Thailand

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ABSTRACT

Background: There has been lots of debate regarding an appropriate value of cost-effectiveness threshold (CET). To our knowledge, Thailand is the only country which has explicit CET and has increased the CET. Therefore, Thailand is in a unique position to help answer the question of what happened when CET was increased. The study objectives were to explore the impact of increasing CET on the submitted medicine price by industry and the decision to be included in the National List of Essential Medicine in Thailand.

Methods: Retrospective secondary data analyses were conducted using data from economic evaluation reports being reviewed by the National Drug Subcommittee. In total, 55 reports were included in the analysis, which represented 295 observations as each report could have more than one medicine for different indication and/or target population. The intervention of interest was the change in CET policy from 100,000 THB/QALY in 2008 to 120,000 THB/QALY in 2010 to 160,000 THB/QALY in 2013.

Results: There is no evidence suggesting the increase in CET affected the submitted medicine prices (price change=19%, p-value=0.457) or increased the likelihood of a positive reimbursement decision (OR=1.596, p-value=0.532). There were other factors which may influence medicine prices and reimbursement decision.

Conclusions: The change in the CET did not significantly affect health resource allocation. The findings do not support whether the current CET value in Thailand should be increased. Future research should continue to monitor the submission and re-analyse the current work as more data become available using both quantitative and qualitative approaches.

Introduction

Public healthcare payers around the world are progressively using economic evidence to inform decision-making (such as whether to include a medicine in healthcare benefit package) to achieve universal health coverage.[1] These decisions are based on an incremental cost-effectiveness ratio (ICER), which represents additional cost per an additional unit of health gain, frequently expressed as quality-adjusted life year (QALY) gained or disability-adjusted life year (DALY) averted.[2,3] ICER compares costs occurred and health benefits yielded from a new health intervention as compared to the standard care available or next best alternative. The intervention is considered cost-effective

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(representing good value for money), if the ICER is less than the maximum financial investment that a public payer will commit to generate a unit of health gain, which is known as a cost-effectiveness threshold (CET).[2] When properly used (i.e. reflect health opportunity cost), CET enhances health maximization, and ensures consistent decision making across different types of health interventions and disease areas.[4] Empirical evidence has evaluated both the pros and cons of either implicit or explicit CETs in making reimbursement decisions and value-based pricing in many settings.[5–8]

Thailand's public healthcare system included three health insurance schemes: the social security scheme (for employed individuals); the Civil Servant Medical Benefit Scheme (for civil servants in the government); and the universal coverage schemes which covers the remaining of population around 75%. Reimbursement for medicines under UCS will be made possible only if the medicines are listed in the NLEM, and NLEM relies on cost-effectiveness evidence.

During the past decades, although there has been a debate around an optimal CET and a significant development of methodological choices for estimating or adjusting CET,[2,9–13] to our knowledge, no country has changed their existing explicit CET except Thailand.[14] Thailand is the only country that has an explicit CET and has revised its CET twice. Through the deliberation among the National List of Essential Medicine (NLEM) Subcommittee members, the first CET was issued at THB100,000 (approximately USD3,000) per QALY gained in 2008, then increased to THB120,000 (USD3,500) per QALY in 2010, and increased again in 2013 to THB160,000 (USD4,600) per QALY gained. The increase of CET was based on the request from stakeholders which was submitted to the NLEM Subcommittee to discuss. We are conducting a separate qualitative study to explore the true history of the cost-effectiveness threshold (CET) in Thailand, including its initial development and the reasons for its two increases. This upcoming research aims to provide a detailed and accurate account of the historical evolution of CET and its changes over time in Thailand. Increasing the CET would theoretically allow more medicines to be included in the NLEM, which is the only pharmaceutical reimbursement list in Thailand. Similar to other countries using cost-effectiveness evidence to inform policy for universal health coverage,[5,8,15,16] there has been pressure to increase the CET in Thailand again. This movement could mean improved access to medicines for affected populations (opportunity for medicines with higher prices to be enlisted in NLEM) and greater equity by providing drugs that would otherwise only be available to those who can pay privately. However, resources are finite, and increasing the CET means that resources will be displaced from elsewhere to accommodate the less efficient technologies.[4] These issues (e.g. to increase or not to increase the CET) have been discussed extensively elsewhere[4,10] and are beyond the scope of this paper.

From a policy perspective, there are other pressing issues to consider, which have been discussed to a lesser extent in the literature. The explicit CET in Thailand has been used as the basis for price negotiations with manufacturers. To what extent could an increase in CET influence medicine prices for the public sector? This question applies not only to countries considering a change in CET, but also to those considering whether publishing an explicit CET is appropriate. Currently, there has been limited study on the impact (effect) of a change of CET on the decision-making process i.e. reimbursement decisions. Policy literature emphasizes the difference between formal institutions, representing the set of written rules that govern behaviors, and informal institutions reflecting social values and cultural norms.[17,18] Studies from the United Kingdom (UK) seem to suggest that NICE recommendations follow a much higher implicit threshold than the published CET, and this threshold may depend on other factors such as rare disease status.[15] If the CET is either ignored or used in a different way than envisaged by the decision-makers, the question on whether to change the CET may be perhaps premature, with greater insight needed into how policy institution's function and the role of decision within that environment. No prior study has been conducted to investigate the impact of changing a CET on stakeholders' behavior and funding decisions. The situation in Thailand provides a unique opportunity with an empirical dataset for evaluating such effects.

This information is not only valuable for discussions around whether to change the CET in Thailand, but also for other settings considering whether to introduce an explicit CET or to change the CET in use. This study examines the immediate impact of increasing the CET on the new medicine prices submitted by pharmaceutical companies, and the impact on decisions to include or exclude new medicines in the NLEM of the Thai government.

Methods

The conceptual framework and study protocol are published elsewhere.[14] Briefly, the framework is based on hypotheses of what could happen if a CET were to be increased. A higher CET may affect the medicine prices submitted by pharmaceutical companies, the likelihood that medicines will be included in the NLEM, and the budget impact of reimbursable medicines. Longer-term impacts, such as access to medicines and overall population health, are included in the conceptual framework but are outside the scope of the present study. Specifically, with higher CET, medicines with higher ICERs may be considered cost-effective, and subsequently included in the NLEM.

Retrospective data were obtained from economic evaluations reports reviewed by the NLEM subcommittee between 2008 to 2020. The NLEM subcommittee is the body with authority to make recommendations to the Thai Ministry of Public Health on which medicines to include under the NLEM. Reports that did not pass the appraisal from the Health Economics Working Group, and thus were not considered by the NLEM Subcommittee, were excluded. Since some medicines were nominated to the NLEM subcommittee for more than one medical indication, our unit of analysis is the unique combination of a medicine and its medical indication and/or target population (children or adults). Given that one report may cover more than one medicine and one medicine may be used for different indication and/or target population, the analysis included 55 reports based on 201 medicines with a total number of 295 observations. Fifty-two observations were considered by the NLEM subcommittee when the CET was at THB100,000, 101 observations considered when the CET at THB120,000, and 142 observations considered when the CET was at THB160,000. Therefore, the observations when CET was at THB100,000 and THB120,000 were combined into one group with 153 observations to enhance power of the analysis.

Study design

In this analysis, we considered the effect of changes in the CET on: (1) yearly medicine prices submitted by the manufacturer; and (2) reimbursement decisions. A straightforward pre-post approach was considered originally,[14] but two sources of biases cannot be addressed by a pre-post approach. Firstly, the policy of increasing the CET may not be exogeneous: there could be other factors affecting the policy decision that also affect the outcome variables. Secondly, the time of submission could not be controlled explicitly due to missing information (e.g. year of submission). Therefore, a difference-in-difference (DID) approach was employed, which is a quasi-experimental method that compares the changes in outcomes between an intervention group and a control group.[19,20] DID can remove the effect from factors that have same effect on the intervention group and the control group over time. We divided all the medicines into two groups based on their ICERs. In our analysis, we set the control group as all medicines that we hypothesized would never be considered as cost-effective, even if committee members use a higher implicit CET for their decisions than the published CET value. In the baseline analysis, we set this "not cost-effective" ICER as THB300,000/QALY. The intervention group included the medicines with ICER from THB0 to THB300,000/QALY, and the medicines that are cost-effective regardless of the CET value (i.e. positive incremental

QALYs and negative incremental cost). The control group included the medicines with ICER above THB300,000/QALY, and the medicines that are not cost-effective regardless of CET value (i.e. negative incremental QALYs and positive incremental cost). Fig 1 illustrates the estimation of potential impact of CET.

The four elements for the DID analysis were: the pre-intervention period; the post-intervention period; the intervention group; and the control group. The focus of the study was the change in CET. The pre-intervention period was the period with CET being THB100,000 and THB120,000. The post-intervention period was the period with CET being THB160,000. For the intervention group, the first difference was the difference in prices between the drugs submitted during the post-intervention period and the drugs submitted during the pre-intervention period. The first difference for control group can be defined similarly. The second difference is the difference between the difference in prices from the intervention group and the difference in prices from the control group. Therefore, DID offers an approach for us to explore the impact of increasing CET (the change in CET).

This approach entails a number of assumptions. Firstly, as the CET increased from THB100,000 to THB120,000 and to THB160,000, we assumed that the change in CET affected the medicines with ICERs around the CET (i.e. the intervention group) more than those with ICERs much higher than the CET (i.e. the control group). The second assumption is that the time trend affected both the intervention group and control group similarly. The third assumption required is that the other potential events affected both intervention group and control group equally. To test the robustness of the results, we examined the effect of changing different ICER thresholds including THB200,000, THB300,000, THB400,000, THB500,000, and THB1,000,000.

Covariates

Independent and dependent variables

The two dependent variables are submitted medicine price and reimbursement decision. For the submitted price, different medicines have different units in the original data, e.g. THB per pill or THB per treatment course. To make the submitted price comparable across different medicines, we converted all submitted price to yearly cost (e.g. Reimbursement decision referred to whether the medicine was included in the NLEM (yes or no). The independent variable has 2 levels, whether: 1) medicines submitted at the period with CET being THB160,000; or 2) medicines submitted at the period with CET being THB100,000 or THB120,000.

Other covariates

We included in the analysis the covariates which we hypothesized could affect the yearly medicine price including the reimbursement decisions (based on a previous literature review which was published in the study protocol [14]). Potential covariates of medicines were categorized into the following groups: indication details; disease information; economic evidence; and others. Indication details consisted of treatment type (add-on therapy, monotherapy, or combination), treatment line (first-line or non first-line), and treatment plan (lifetime or not lifetime). Disease information comprised whether the medicine was for adults only or for all ages; whether the medicine was for communicable disease (CD), cancer, or non-cancer non-communicable disease (NCD); and whether the medicine was for a rare disease (<10,000 cases in Thailand) or ultra rare disease (<1,000 cases in Thailand). Economic evidence included the comparator (e.g. standard of care or placebo) used in the economic evaluation, incremental cost, and incremental QALY. Others consisted of medicine type (chemical or biologics), type of evidence supported (randomized control trials or RCT, non-RCT), whether the medicine had patent, and whether the medicine underwent price negotiation. Additional details of the variable can be found in the supplementary material and the protocol paper.[14]

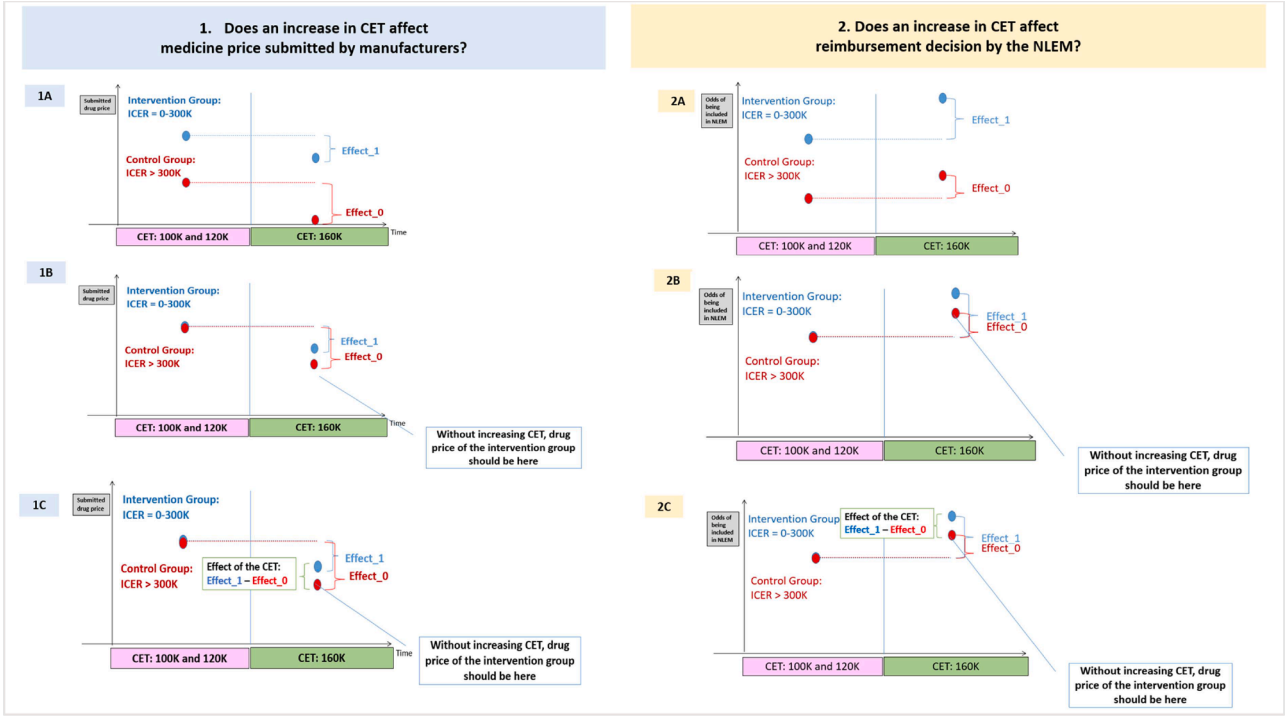

Fig 1. Pictures illustrating the difference-to-difference approach to capture the potential impact of cost-effectiveness threshold.
Note. Fig 1A illustrated the change in medicine price over time (from the period when CET = 100K and 120K to the period when CET = 160K). Fig 1B represents the price of medicine would be if there was no increase in CET (red dot). Fig 1C shows how the difference in Effect_1 and Effect_0 would represent the impact of CET. Figs 2A to 2B aim to capture the impact of increasing CET on reimbursement decision.

Statistical analysis

Multivariable linear regression analysis was used for the log of yearly medicine cost as the cost data were highly skewed. Another multivariable logistic regression model was used for reimbursement decision. The associated regression equations are presented below.

For yearly medicine cost:

$$logCost_i = \alpha_0 + \alpha_1 * Treatment_i + \alpha_2 * HighCET_i + \alpha_3 * Treatment_i * HighCET_i + \alpha_4 * X_i + \epsilon_i$$

For reimbursement decision:

$$logit(p(IncludeDrug_i = 1)) = \beta_0 + \beta_1 * Treatment_i + \beta_2 * HighCET_i + \beta_3 * Treatment_i * HighCET_i + \beta_4 * Z_i$$

$Treatment_i$ was 1 for medicines in the intervention group (medicines with ICER less than THB300,000) and 0 for medicines in the control group (medicines with ICER above THB300,000/QALY). $HighCET_i$ (or time trend) was 1 for medicines submitted at the period with CET being THB160,000 and 0 for medicines submitted at the period with CET being THB100,000 or THB120,000. α_3 and β_3 were the coefficients of interest, measuring the difference-in-differences estimates. X_i and Z_i represented the covariates.

The definition for each specific element for the reimbursement decision equation are as followed (and for the yearly medicine cost followed similar definition):

β_0 represents the probability of reimbursement for drugs in the control group during the pre-intervention period.
β_1 indicates the difference of reimbursement probabilities between drugs in the intervention group and control group.
$\beta_0 + \beta_1$ refers to the probability of reimbursement for drugs in the intervention group during the pre-intervention period.
β_2 represents the difference in probabilities of reimbursement (trend) between the pre-intervention period and post-intervention period.
$\beta_0 + \beta_2$ refers to the probability of reimbursement for drugs in the control group during the post-intervention period.
$\beta_0 + \beta_1 + \beta_2$ indicates the probability of reimbursement for drugs in the intervention group during the post-intervention period without the change in CET.
β_3 is the coefficient of interest – impact of change in CET.
$\beta_0 + \beta_1 + \beta_2 + \beta_3$ represents the probability of reimbursement for drugs in the intervention group during the post-intervention period with the change in CET.

The statistical analysis was conducted using Stata Statistical Software: Release 17 (College Station, TX: StataCorp LP).

Results

Table 1 reports the descriptive results of the 295 observations to explain the characteristics of the medicine submission reviewed by the NLEM subcommittee for public reimbursement in Thailand over the past 13 years. Cancer medicines became more common during the period when CET was set at 160K (40% compared to 18% in the period when CET was 100K or 120K). Medicines for rare diseases were more common when CET was at 100K or 120K (42% compared to 11% when CET was at 160K), whereas medicines for ultra rare diseases became more common (35% from 16%) in the period when CET was 160K. The majority of medicines had ICERs > THB300,000.

Positive reimbursement decision (Accept) is in yellow and negative reimbursement decision (Reject) is in red in Fig 2 showing the impact of ICER on reimbursement decisions (with only positive ICERs included). [15] As ICER increased, more negative reimbursement decisions occurred with exceptions.

Table 2 presents the DID results on the impact of CET and other covariates on the percentage change in yearly medicine prices and the odds of medicine being included in NLEM. The table highlighted key findings and the full results can be found in Supplementary 1.

Table 1
Descriptive characteristics of observations included in the analysis

Variables	CET=100K and 120K	CET=160K
Number of observations	153	142
Medicine type***		
Chemical	84 (55%)	111 (78%)
Biologics	69 (45%)	29 (20%)
No data	0 (0%)	2 (2%)
Cancer medicines***	27 (18%)	57 (40%)
Non-cancer NCD medicines	84 (55%)	88 (62%)
Medicines for all-age diseases (compared to medicines only for adults)***	78 (51%)	7 (5%)
Comparator type***		
Standard care or current practice	43 (28%)	82 (58%)
Placebo	24 (16%)	0 (0%)
Palliative care	34 (22%)	6 (4%)
Best supportive care	20 (13%)	17 (12%)
Others	32 (21%)	37 (26%)
Treatment type***		
Monotherapy	89 (58%)	67 (47%)
Combination	38 (25%)	70 (49)
Add-on therapy	26 (17%)	5 (4%)
Treatment line		
First-line treatment	79 (52%)	58 (40%)
Non first-line treatment	74 (48%)	84 (60%)
Rare disease status***		
Rare disease medicines	64 (42%)	16 (11%)
Ultra rare disease medicines	25 (16%)	49 (35%)
Medicines with patent	56 (37%)	38 (27%)
Medicines underwent price negotiation	51 (33%)	38 (27%)
Incremental QALYs (mean ± SD)***,+	3.3 ± 4.7	1.6 ± 3.2
Incremental Cost (median (IQR))*,+	658,988 (1,089,844)	232,338 (609,536)
Number of observations with:		
	15 (10%)	8 (6%)
• ICER < THB100,000/QALY	12 (8%)	10 (7%)
• THB100,000 < ICER < THB160,000/QALY	43 (28%)	8 (6%)
• THB160,000 < ICER < THB300,000/QALY	75 (49%)	98 (69%)
• ICER > THB300,000/QALY	5 (3%)	10 (7%)
• Positive incremental QALY and negative incremental cost (dominant choices)	3 (2%)	8 (6%)
• negative incremental QALY and positive incremental cost (dominated choices)		
Number of observations included in the NLEM**	53 (35%)	29 (20%)

Note. SD = standard deviation; IQR = interquartile range; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; NLEM = National List of Essential Medicine
Significant difference between the two groups: * p<0.05, ** p<0.01, *** p<0.001
+ Analyses were based on 271 observations only

Impact of increasing CET on submitted yearly medicine price

The increase in CET did not significantly affected the submitted medicine prices by the industry to the NLEM subcommittee. The base case results are presented in Table 2. The coefficient for time trend indicated a 60.5% reduction (95% CI = (-80.0%, -22.0%)) in the submitted medicine prices over time. Sensitivity analysis using different cutoffs are presented in Supplementary 2, showing that conclusions were robust that no evidence was found that increasing CET affected the submitted medicine prices.

Covariates that showed a significant association with the higher submitted medicine price include: i) non first-line medicine (compared to first-line); ii) biologics compared to chemical compound medicines; iii) medicines with evidence from RCTs; iv) medicines for all ages compared to medicines targeting adults only; v) medicines for non-rare diseases (compared to medicines for rare disease); and vi) medicines

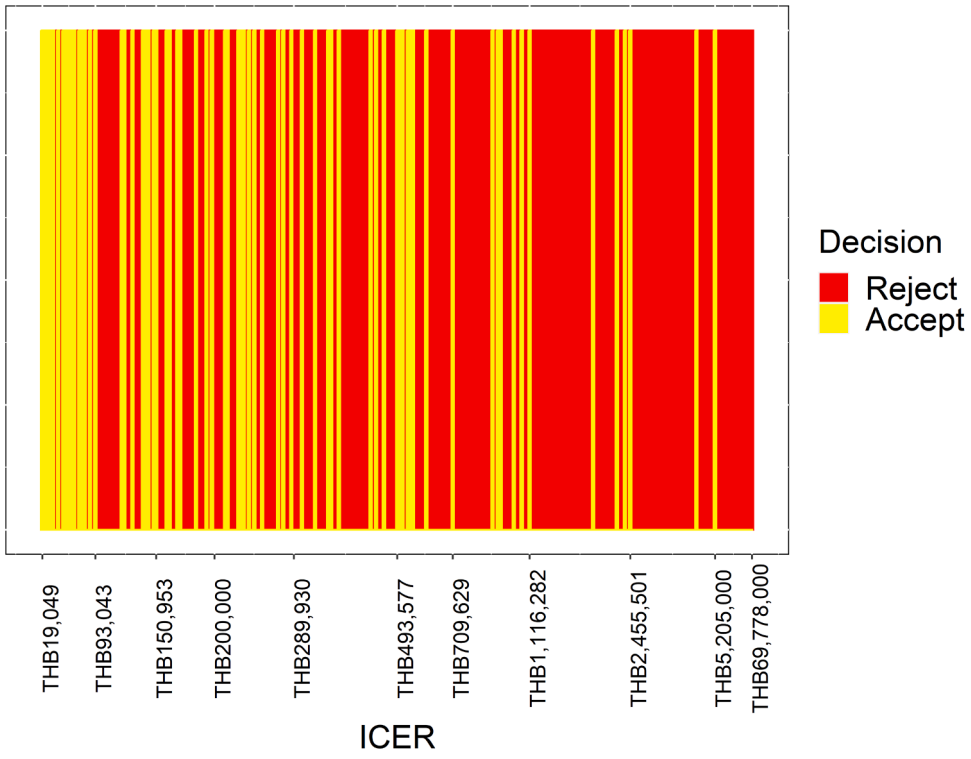

Fig 2. ICER values and associated reimbursement decision

Table 2
Regression results showing impact of increasing CET on the submitted medicine prices and the decisions to include medicines in the Thai NLEM

Objective 1: Medicine price submitted by the manufacturer (adjusted to yearly cost per medicine)			Objective 2: Reimbursement decision by the NLEM		
	% change in price	95% CI		Odds ratio	95% CI
Impact of CET[+]	19.6%	-19.6%, 142.9%	Impact of CET	1.596	0.170, 14.982
Time trend	-60.5% ***	-80.0%, -22.0%	Time trend	2.760	0.552, 13.794
Add-on therapy (vs monotherapy)	-58.5%	-87.9%, -29.7%	Add-on therapy (vs monotherapy)	0.404	0.029, 5.695
Combination therapy (vs monotherapy)	43.2%	-32.8%, 205.0%	Combination therapy (vs monotherapy)	0.976	0.229, 4.164
Non first-line (vs first-line)	114.0% **	16.6%, 292.7%	Non first-line (vs first-line)	1.216	0.312, 4.736
CDs vs NCDs	-4.7%	-56.0%, 106.9%	CDs vs NCDs	3.950	0.761, 20.504
Cancer vs other NCDs	117.7%	-21.5%, 503.8%	Cancer vs other NCDs	1.338	0.217, 8.238
Lifetime treatment (vs short-term)	-23.8%	-67.0%, 75.8%	Lifetime treatment (vs short-term)	0.444	0.084, 2.338
Chemical (vs biologics)	-77.0% ***	-86.6%, -60.5%	Chemical (vs biologics)	2.843	0.742, 10.896
With patent	-0.2%	-40.1%, 66.2%	With patent	3.647**	1.052, 12.651
With evidence from RCTs	135.1% **	8.0%, 411.4%	With evidence from RCTs	0.165*	0.023, 1.169
All ages (vs adults only)	126.8% **	5.0%, 390.4%	All ages (vs adults only)	6.272*	0.978, 40.215
Rare disease (vs non-rare disease)	-66.7%	-87.1%, -14.4%	Rare disease (vs non-rare disease)	7.169**	1.218, 42.177
Ultra rare disease (vs non-rare disease)	-40.9%	-83.2%, 107.3%	Ultra rare disease (vs non-rare disease)	1.888	0.257, 13.860
Incremental QALY	11.0% ***	2.8%, 19.7%	Incremental QALY	1.173	0.937, 1.468
Had price negotiation	21.5%	-34.6%, 125.7%	Had price negotiation	2.812**	1.036, 7.631
Constant	13.703***	11.959, 15.446	Constant	0.001***	0, 0.078

Note. 95% CI = 95% confidence interval, CET = cost-effectiveness threshold, CDs = communicable diseases, NCDs = non-communicable diseases, RCTs = randomized controlled trials, QALY = quality-adjusted life years
[+] The difference-in-differences estimate represented the impact of CET and the coefficient estimate was converted to percentage change in medicine price using the following equation: [exp(time trend + did estimate) -1] - [exp(time trend) - 1], whereas the equation of [exp(coefficient) -1] was used for the other covariates.
* $p<0.05$, ** $p<0.01$, *** $p<0.001$

with higher incremental QALYs.

Impact of increased CET on probability of medicines to be included in NLEM

The increasing CET did not significantly affected the chance of medicines being included in the NLEM. Conclusions are robust to different CET cut-offs to define the control/intervention groups (as shown in Supplementary 2).

Significant factors that increased likelihood of a medicine being listed in the NLEM include medicines with a patent, medicines with evidence from RCTs, medicines for all ages, medicines for rare diseases, and medicines underwent price negotiation.

Discussion

This study is the first study evaluating the impact of increasing the CET on pharmaceutical reimbursement policy and manufacturer drug

pricing for national level policy. We found no significant effect of increasing the CET on either the submitted medicine prices or the likelihood of a positive recommendation for medicine inclusion on the pharmaceutical reimbursement list in Thailand. Specifically, though not significant, the submitted medicine prices appeared to be lowered and the probability of being included in the pharmaceutical reimbursement list appeared to increase over time.

Although further studies, including qualitative research, are warranted, few assumptions may explain the findings. For instance, the increased CET alone may not be significant enough to make substantial impact to the industry's decisions on the submitted medicine prices and, subsequently, the probability of medicines to be included in the NLEM. Moreover, during this study period, there were three different NLEM subcommittees. Although there were overlapping members of the subcommittees, three persons with different background took the chairmanship. The three subcommittees' chairs and their members were committed to the use of health economic evaluation to inform their reimbursement decisions; however, they introduced different implementation policies and procedures. For example, only the first subcommittee (2007-2010) considered industry-funded health economic evaluation.[5] The third subcommittee (2013-2020) always consulted the three public health insurers on potential budget impact before making reimbursement decisions.

From our findings, the extent to which the CET has been institutionalised in NLEM decision-making was unclear. Generally, decision rules were only considered to be institutionalised if they change how collective decisions were made.[17,21] Although formal rules, such as a cost-effectiveness threshold, are introduced and changed by negotiation and formal agreement, shared values and how stakeholders structure decision problems to come to a decision are slower to change.[18] Studies from HTA agencies in Canada and European countries, for example, suggest that explicit criteria and weights are not institutionalised, as committee members apply and weight criteria in line with their own values for reimbursement decisions, as opposed to published criteria and weights.[22,23] For CET use in decision-making, both the concept of cost-effectiveness and the threshold value should align with existing rules governing how the NLEM makes decisions, with reinforcement through processes such as deliberation (e.g. ongoing discussion with economists involved in the process), enforcement (e.g. the subcommittee chair ensuring that the CET is discussed in making a recommendation), and transparency.[17,18,24] Both our analysis and experience of the process (since HTA was used for NLEM decisions) suggested that the concept of cost-effectiveness is institutionalised in NLEM decision-making. Our analysis has shown that more cost-effective medicines were more likely to be accepted, and introduction of the cost-effectiveness threshold in Thailand was not only internally driven by the committee, but also supported by ongoing research on the concept of economic evaluation by the HTA agency. However, the insignificant effect of increasing the CET on either the submitted medicine prices or the likelihood of a positive recommendation for medicine inclusion on the pharmaceutical reimbursement list could be that the CET was inconsistently applied after its introduction, and over time the application of the CET became the norm.

An alternative explanation could be that the use of cost-effectiveness is institutionalised, but decision-makers have a higher implicit threshold in mind than the published CET value. Studies have suggested in the past that this may be the case for NICE recommendations in the UK.[15] If the implicit threshold of the committee is above THB160,000, our analysis would not expect to find any difference in committee recommendations following a change in the threshold. However, we would argue that the most probable explanation was that our analysis could not fully account for inclusion of other criteria. The three subcommittees always made claims that they used economic evaluation to inform decisions, not making reimbursement decisions based on economic evidence solely. Our findings support this assertion. In Thailand, adherence to the CET is not mandatory and cost-effectiveness is not a gateway criterion unlike in some countries such as the UK. Instead, cost-effectiveness is considered alongside other relevant criteria, including equity and affordability, and the threshold itself is intended as a reference point to support subcommittee members to interpret findings from the cost-effectiveness analysis. Therefore, the change in threshold may well have influenced committee interpretation of the cost-effectiveness evidence, but, since other criteria play an important role in the recommendation, the influence of the CET change may not have been great enough to significantly affect our results.

A major concern with increasing an explicit cost-effectiveness threshold is that it may encourage manufacturers to sell products at higher prices. Our analysis suggests that this is not the case, as does a comparison between the US and the UK markets, which found that having a formal cost-effectiveness constraint does not greatly alter the structure of pharmaceutical pricing.[25] However, it has been argued that more generous insurance coverage schemes would be expected to lead to higher prices,[26] and our results should be interpreted with cautions for two reasons. Firstly, in our analysis, medicine prices were based on the prices submitted by manufacturers for economic evaluations, in which manufacturers are requested to quote the price at which they would sell the product if it were deemed reimbursable under the NLEM in Thailand. The data on selling prices were not available, in particular when drugs are not included (i.e. more than half of the nominated medicines were rejected by the NLEM subcommittee). Furthermore, we did not have access to the prices negotiated with manufacturers (as only about 30% of drugs underwent price negotiation), and since the decision for price negotiation is partly dependent on cost-effectiveness results, this may have affected our findings. The use of selling price allowed us to explore the impact of the change in CET on manufacturer's behavior (their submitted price) and using the selling price as an outcome could be considered for future research where data are available. Secondly, the results from Thailand may not be generalisable to other settings. Thailand's CET is very low relative to high-income markets such as the UK and Japan, and the vast majority of pharmaceuticals are procured from foreign manufacturers. Changes in the threshold may therefore not have been significant enough to influence industry pricing decisions, as Thailand does not constitute a high share of market value.

This present study also confirms that other social values influence reimbursement decisions of the NLEM subcommittee in Thailand. Medicines for rare and ultra-rare disease treatments seem to have privilege over medicine treating more prevalent conditions. This reflects that the NLEM subcommittee did not only aim for health maximization across the entire population when exercising their power. Instead, they may want to assure that all patients, including those with rare or ultra-rare conditions, get some chance at a meaningful health gain, even if this exceeds standards for what would be considered a cost-effective use of health resources. As such, in 2019, the Thai government initiated the rare disease drug fund that provide financial support for diagnosis and treatment of rare diseases only.[27]

There are other study limitations to be cautious of. First, due to the nature of the study design (observational study), the analysis was prone to the risk of confounding and various types of biases which we tried to adjust for using DID approach. Regardless, there might have been other confounders (known and unknown) which were not included in the analysis. Second, it is possible that the insignificant findings could be due to small sample size. Third, not all drugs were prescribed for a whole year course. Therefore, estimating the cost of treatment based on a yearly basis should be interpreted accordingly. With more data, future research could look into this subgroup. Lastly, this study was done in a single country. Our results may not be generalizable to other settings with different politics, economy and health infrastructures. However, our results on the behavioral responses to the changing CET of the pharmaceutical companies may be able to generalised to other middle-income countries with similar context given that all companies submitted their prices are trans-national pharmaceutical companies.

Efficiency evidence can support the path to universal health coverage by assisting in the resource allocation decisions. To do so, information on CET is crucial in ensuring that limited healthcare resources are being used efficiently. The current findings showed that the change in CET in Thailand did not significantly influence the likelihood of a positive benefit package listing recommendation or the medicine prices set by manufacturers for public payers. The findings from this paper shed light to the potential impact of increasing a CET and highlighted a need for further research into the role of CET in informing policy decisions (with a qualitative approach), to better guide CET policy in Thailand and globally.

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The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Ethics approval

Ethics approval was granted by the Institute for Human Research Protection at the Ministry of Public Health of Thailand.

Data availability

Details of the data used in the analysis can be made available upon request.

Ethical approval

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Patient consent

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CRediT authorship contribution statement

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Declaration of competing interest

All authors declare no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hlpt.2024.100927.

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