An early health technology assessment of target product profiles for COVID-19 vaccines: data for supporting R&D for better vaccine and selecting the right vaccine for maximising public health impact

บทคัดย่อ

การระบาดของโรคติดเชื้อไวรัสโคโรนา 2019 (COVID-19) ทำให้มีผู้ติดเชื้อและเสียชีวิตทั่วโลก ทางออกที่ยั่งยืนของวิกฤตครั้งนี้ คือ การมีวัคซีนป้องกันการติดเชื้อ COVID-19 องค์การอนามัยโลกร่วมกับผู้เชี่ยวชาญด้านวัคซีนได้กำหนดเป้าหมายเกี่ยวกับคุณลักษณะของวัคซีน COVID-19 เช่น กลุ่มเป้าหมาย วิธีการให้วัคซีน ความปลอดภัยและประสิทธิผล เพื่อเป็นแนวทางให้ผู้พัฒนาและวิจัยวัคซีนรวมถึงผู้กำหนดนโยบายตัดสินใจใช้วัคซีนที่จะออกสู่ตลาดในอนาคต งานวิจัยนี้จึงมีวัตถุประสงค์เพื่อเตรียมรับมือกับคำถามเชิงนโยบายที่จะเกิดขึ้นในอนาคตอันใกล้ ได้แก่ (1) ประเมินผลกระทบด้านสาธารณสุขและต้นทุน-ประสิทธิผลของวัคซีน COVID-19 ในบริบทของประเทศไทย (2) หาคุณลักษณะที่สำคัญของวัคซีนที่ทำให้มีความคุ้มค่าในบริบทประเทศรายได้น้อยถึงปานกลางเพื่อให้ผู้พัฒนาวัคซีนใช้เป็นแนวทางในการวิจัยสำหรับประชากรกลุ่มนี้ (3) ให้ทราบราคาสูงสุดของวัคซีน COVID-19 ที่ทำให้วัคซีนยังมีความคุ้มค่าในบริบทประเทศไทย และ (4) จัดลำดับความสำคัญกลุ่มเป้าหมายของวัคซีนป้องกันโรค COVID-19

Background

Since the severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2) or COVID-19 was identified for the first time in China in December 2019 (1), the outbreak has spread and caused a global pandemic throughout the world. As of 13 April 2020, the outbreak of COVID-19 has resulted in 1,773,084 confirmed cases with 111,652 deaths across more than 200 different countries and territories (2). In Thailand, during the early phase of the outbreak, the majority of COVID-19 cases were imported from China, however, the first local case was detected in mid-January and has spread across the country (3). As of 14 April 2020, the outbreak has resulted in 2,613 confirmed cases with 41 deaths (4). The 30-39 years old age group has the highest proportion at 23.8% (623 cases). The overall case-fatality rate was estimated to be 1.6% (4).

To tackle the COVID-19 pandemic, the development of COVID-19 vaccine is a global priority for research and product development (5). More than 95 vaccine candidates are under development worldwide (6, 7). Most candidates are in pre-clinical development (>90%), less than 10 candidates in Phase I, and only one candidate in Phase 2 (7). Recently, World Health Organization (WHO) in collaboration with seven global experts (including Dr. Yot Teerawattananon) had developed the target product profiles (TPPs) for COVID-19 vaccines which was issued on 9th April 2020 (8). They obtained the first COVID-19 vaccine TPPs through deliberation and qualitative approach over the two-week timeline. The TPPs described the preferred profiles of COVID-19 vaccine characteristics including indication for use, contraindication, safety, efficacy, dose regimen, route of administration, product stability and storage, duration of protection, and target populations. The TPPs are useful for a wide range of target audience including: 1) vaccine scientists and clinical researchers, 2) product developers and industry, and 3) governments and funding agencies which are likely to be the payers once the vaccine becomes available.

Since COVID-19 vaccine tends to be proposed for government reimbursement, many policy relevant information should be taken into account when informing coverage decision making. These include public health impact, appropriate vaccine price and value for money, government budget implication as well as implementation barriers. Currently, there is limited such information to make evidence-informed policy on COVID-19 vaccine across settings. In addition, for the early stage of the vaccine development, the TPPs can be used to inform R&D decision making in order to achieve desirable vaccines for future public reimbursement. Currently, an early health technologies assessment (HTA) is increasingly being used during early stages of health product development and called early HTA (9, 10).

Early HTA is used to inform research and development about the design and management of new medical technologies (11). It can be used to mitigate the risks, perceived by industry and the public sector, associated with market access, and healthcare decision making related to the coverage of medical products and the use of these products under

competing and uncertain conditions. For example, early HTA can be sued to explore the potential public health impact of the new medical technology with different market access strategies and the best possible price given regulatory constraints. Moreover, a value-of-information (VOI) analysis which quantifies the value (loss) of missing information in early economic models can be used for identifying the amount that clinical researchers, product developers and industry, and decision maker would be willing to pay for information prior to making decisions as well as uncertainty around those decisions (12, 13). The differences between early and mainstream HTA are illustrated in Table 1 (14).

Table 1 The differences between early and mainstream HTA

	Early HTA	Mainstream HTA
Objective	Assess (likely) safety, effectiveness and cost-effectiveness profiles of a new medical technology	Assess safety, effectiveness and cost effectiveness of a new medical technology
Decision support	Decision support for manufacturers and investors about design and management of a technology as well as regulatory and reimbursement strategy	Decision support for regulators, payers and patients about market clearance, payment and usage of a medical technology
Available evidence	Evidence from early bench and animal testing, early clinical experience and previous generations of the technology	Usually evidence from clinical studies performed with the new technology
Influence on technology performance	Potentially significant influence on (future) clinical performance of a new medical technology	Limited or no influence on clinical performance of a new medical technology

Source: Pietzsch and Pate-Cornell, 2008 (14)

In the early phase of the COVID-19 vaccine development, at least one of the companies in Thailand i.e. BioNet Asia is developing the vaccine[1]. To perform this early HTA, early-stage health economic model and value-of-information analysis are required to conduct aiming to determine policy decisions regarding the reimbursement and price negotiation of the vaccine. Given that there will be several profiles of COVID-19 vaccines available with different product characteristics, this study can be used to identify the most cost-effective (impactful) vaccine. The study findings will be useful for supporting R&D decision making, pre-clinical preliminary market assessments, identification of potential

[1] https://www.who.int/blueprint/priority-diseases/keyaction/Novel_Coronavirus_Landscape_nCoV_11April2020.PDF?ua=1

successful projects, development of future trial design, and assessment of future reimbursement and pricing in Thai context as well as other limited resource settings (15).

Study objectives

General objectives

1. To assess cost-effectiveness of the hypothetical COVID-19 vaccines that are in line with the current WHO's COVID-19 vaccine TPP
2. To assess public health impact of the hypothetical COVID-19 vaccines that are in line with the current WHO's COVID-19 vaccine TPP
3. To identify the relative importance of COVID-19 vaccine characteristics which may affect the vaccine's public health impact and its value for money in Thailand

Specific objectives

1. To estimate the future situation of COVID-19 infection in Thailand and then assess public health impact and cost-effectiveness of the hypothetical COVID-19 vaccines that are in line with the current WHO's COVID-19 vaccine TPP;
2. To identify the relative importance of COVID-19 vaccine characteristics, i.e. target populations, cost of vaccination, vaccine efficacy, immunisation strategies, and possible uptake rate, as well as risk behaviours that change post-vaccination, all of which may affect the vaccine's public health impact and its value for money in Thailand (if relevant, preferable TPPs for COVID-19 vaccines to maximise the probability that the vaccine being successful in implementation will be identified);
3. To determine the maximum price at which the hypothetical COVID-19 vaccine remains cost-effective in the Thai healthcare setting given different scenarios on COVID-19 infection and vaccine characteristics;
4. To conduct sub-group analysis prioritising target population(s) for COVID-19 vaccine if there is need for rationing the vaccine in Thailand.

Methodology

Early-stage health economic model

Cost-utility analysis using transmission dynamic model to estimate the costs and outcomes of the WHO's TPPs for COVID-19 vaccine combined with current intervention (i.e. existing prevention interventions combined with standard of care) will be performed compared to the current intervention without vaccination as shown in Table 2. The TPPs of the COVID-19 vaccine with different key characteristics will be obtained from the WHO's Working Group on Vaccine Target Product Profile for COVID-19. A series of targeted vaccine characteristic including protective efficacy (both reduction in transmissibility and disease severity), protective duration, target population, and administration and logistic condition will be considered under two criteria: preferred condition and minimal condition as indicated by WHO in Table 3. This study will assume

change of behaviours as a result of receiving the vaccine in terms of the decreasing rate of social distancing interventions, hand hygiene and wearing mask for all target populations from unchanged (preferred condition) to 20% (minimal condition). In addition, the percentage of change and their effects will be consulted with experts.

At present, the licensed specific treatments for the COVID-19 have not been available, but a number of potential treatments are currently investigated in the clinical trials (16, 17). The potential therapeutic options for the COVID-19 treatment can be grouped into 1) Antiviral agents e.g. remdesivir, chloroquine or hydroxychloroquine, lopinavir/ritonavir and other HIV protease inhibitors and 2) Immune-based therapy e.g. convalescent plasma, interleukin-6 inhibitors and interleukin-1 inhibitors. The clinical data to date of the potential therapeutic options is shown in Appendix. Nonetheless, the trials will be completed in different time, for instance, trials for remdesivir are expected the completion in May (18, 19) or September (20) in 2020.

As all countries are employing some forms of intervention to contain and mitigate the effects of COVID-19, we will exclude the counterfactual scenario of 'no intervention', as a comparator. Age-specific reported cases and deaths representing the incidence of COVID-19 infection in Thailand combined with other local epidemiological, clinical, and economic data will be applied to inform and validate the model. The tested model should reproduce the COVID-19 situation in the Thai context before being used to simulate the impact of introducing the vaccine within the national immunisation programme and compare with the current situation of no vaccine with three different baseline scenarios on the proportion of population who already had natural immunity. Both costs and consequences in terms of Quality Adjusted Life Years (QALYs) will be quantified from health system's perspective with a 3% discounting rate per year both costs and health outcome.

Willingness to pay at 160,000 Thai baht (USD 5,110) will be used as a threshold in Thailand to estimate the value for money of the vaccine (21). The timeframe for vaccination campaign will be one year but the costs and consequences would be counted with lifetime horizon. The list of input parameters is detailed in Table 4. These input parameters will affect the vaccine costs, related-healthcare costs, safety outcome and health outcomes post-vaccination (Figure 1) (22). Then, the ICERs will be carried out based on the difference of vaccine characteristics.

Table 2 Effectiveness of current prevention interventions for COVID-19

Author, year	Intervention	Method	Result
Milne and Xie, 2020 (23)	Social distancing interventions: school closure, workplace non-attendance, increased case isolation, and community contact reduction	Simulation model	Social distancing intervention can flatten the epidemic curve, reduce the maximum daily case numbers, and lengthen outbreak duration.
Koo et al, 2020 (24)	The combined intervention, in which quarantine, school closure, and workplace distancing	Simulation model	The combined intervention reduced the estimated median number of infections by 99·3% when R0 was 1·5, by 93·0% when R0 was 2·0, and by 78·2% when R0 was 2·5.
Greenhalgh et al, 2020 (25)	N95 respirators and surgical masks	Meta-analysis of RCTs	N95 respirators and surgical masks show not statistically significant differences in prevention laboratory-microbial infection. Meta-analysis indicated protective effect of N95 respirators against laboratory-confirmed bacterial colonisation (RR = 0.58, 95% CI 0.43 to 0.78).
MacIntyre et al, 2015 (26)	Surgical masks and cloth masks	RCTs	The rate of infection is higher in the cloth mask arm compared with the medical mask arm (relative risk (RR)=13.00, 95% CI 1.69 to 100.07).
World Health Organization, 2017 (27)	Hand hygiene	Systematic review	Hand hygiene can prevent microbial transmission and infections.

Table 3 Target Product Profiles (TPPs) for COVID-19 vaccine developed by WHO and to be used as a base-case in this study

Vaccine characteristic	**Preferred condition (base case analysis)**	**Minimal condition (scenario analysis)**
Target population	The whole population in all age group *Note: Recognise that herd immunity (and transmission blocking) will depend on broad immunisation, likely including children.*	Special considerations for the elderly and other population at risk.
Safety/ Reactogenicity	At least comparable to WHO-recommended routine vaccines, providing a highly favourable risk-benefit profile, ideally with only mild, transient adverse events related to vaccination and no serious AEs related to vaccination, including in individuals with compromised immune function.	Safety and reactogenicity whereby vaccine benefit clearly outweighs safety risks. Safety profile demonstrated primarily mild, transient health effects and rare serious AEs related to vaccination.
Vaccine efficacy 1) Transmissibility reduction 2) Severity reduction	1) 70% efficacy on preventing transmission of SARS-CoV-2 in healthy adults. 2) 70% efficacy on preventing severe cases COVID-19 in healthy adults.	1) 50% efficacy on preventing transmission of SARS-CoV-2 in healthy adults. 2) 50% efficacy on preventing severe cases COVID-19 in healthy adults.
Dose regimen	Primary series: Single-dose regimen preferred Booster doses: every 1 year or at time of new outbreak.	Primary series: 2 doses, and with preference for short interval between doses. Booster doses: every 1 year or at time of new outbreak.
Duration of protection	Confers protection of at least 1 year after primary series and can be maintained by booster doses.	Confers protection of at least 6 months after primary series and can be maintained by booster doses.
Uptake rate	80% whole population in all age groups.	80% elderly and other population at risk.
Administration	Non-parenteral is preferred for ease of rapid administration and other logistical issues.	Other routes: syringe/needle or other adjunct equipment.
Storage condition	Room temperature with shelf life of at least 12 months.	At least 2-week stability at 2-8°C or storage -20°C with shelf life of at least 12 months.

Source: Adapted from the Working Group on Vaccine Target Product Profile, 2020 (8)

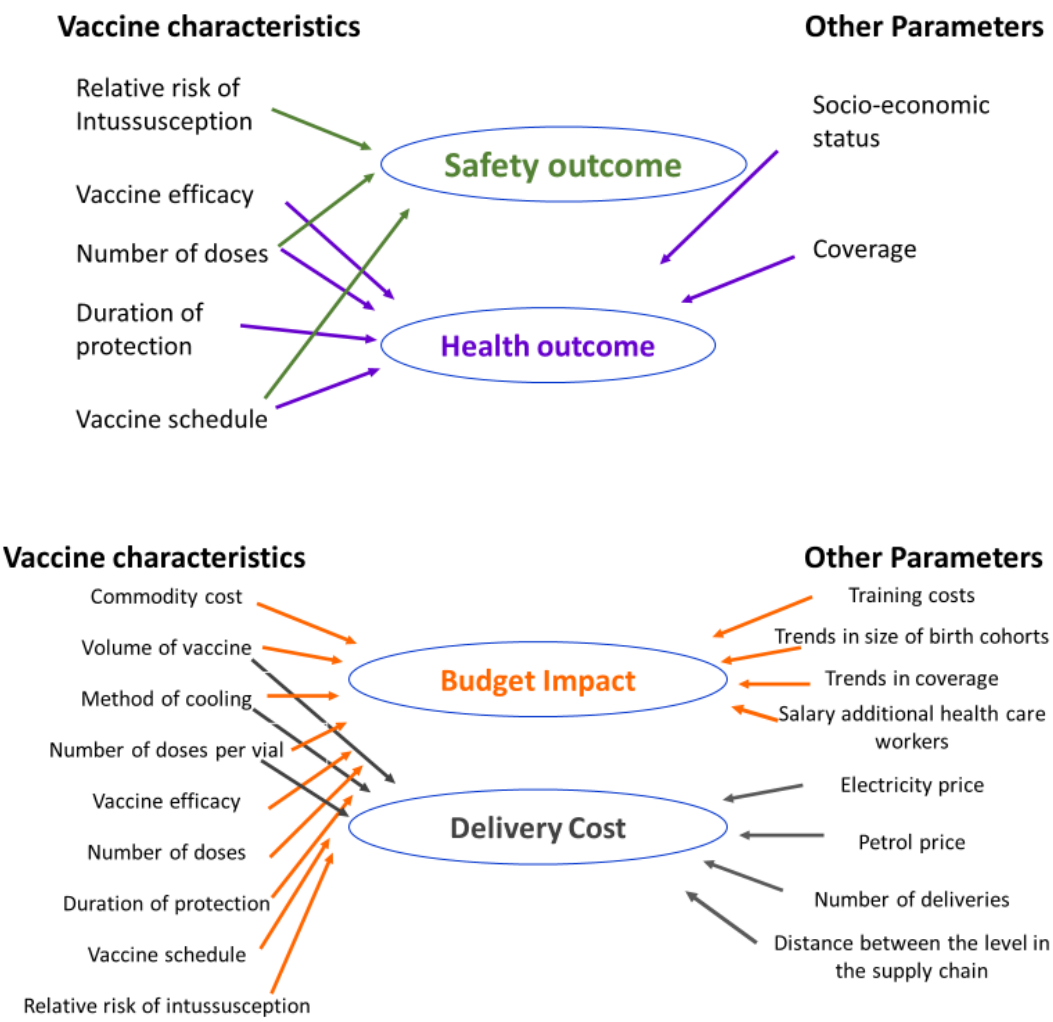

Figure 1 Parameters influencing health outcomes and vaccination costs

- **Transmission Dynamic Model**

An age-structured dynamic epidemiological model will be developed to estimate age-specific incidence and outcomes of COVID-19 infection under different condition of the vaccination programme. (Figure 2) This transmission model will be based on a SEIR structure where the entire population will be divided into four main compartments representing different stages of disease; susceptible (S) representing those who have not been infected or fully vulnerable to infection; exposed (E) representing those who have been infected but not yet progressed to become infectious; infected (I) representing those who are infectious; and recovered (R) representing people who have transient immunity after recovered from infection or effectively vaccinated. For those who are infectious, three sub compartments representing level of severity among the infected cases; no symptoms, mild symptoms, and hospitalised are classified. Among those with hospitalisation, patients will be divided into three categories; non-ICU, ICU and ventilator treated. Age-specific number of daily reported cases and deaths will be used and fitted

to estimate the transmission rate of COVID-19 for each of the two. Interactions between age groups will be accounted by using a matrix of contact patterns to account for the fact that the probability of one infected person infecting one particular susceptible person will depend on their respective age groups and the degree of contact between them. Data will be obtained from publicly available resources including literature, reports, and information from online sources. Three main scenarios varying the initial conditions of the percentage of population who already had natural immunity to COVID-19 at 0%, 30% and 60% will be examined to reflect the uncertainties of the COVID-19 current situation and the amount of population exposed to the infection at the time of vaccine introduction. The case incidence and deaths will be estimated by solving a set of ordinary differential equations (ODE) performing in R. Outputs from this dynamic model will be further examined in an economic analysis.

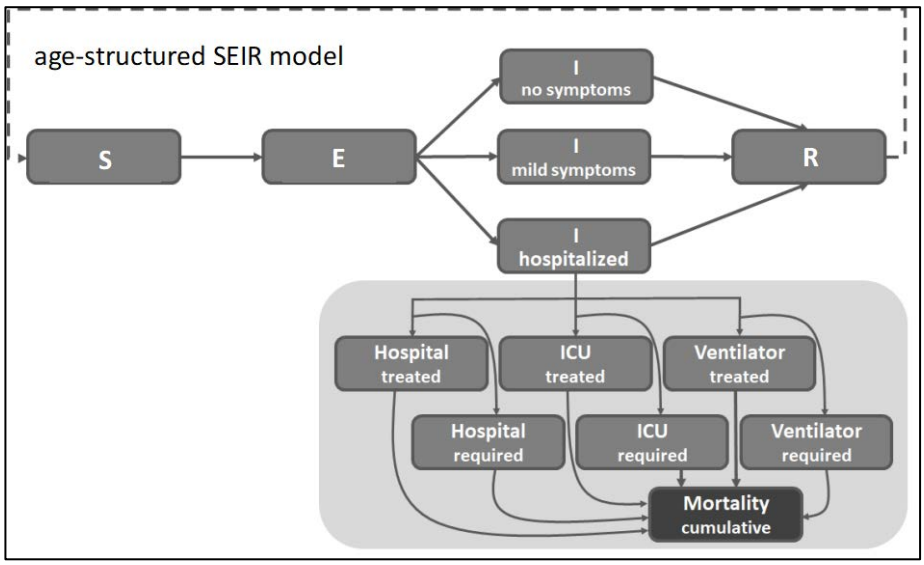

Figure 2 Transmission dynamic model structure (SEIR)

Source: Adopted from CoMo Model developed by CoMo consortium. Available from https://comomodel.net/

- **Cost-utility analysis**

The estimated number of COVID-19 cases including all subgroups of severity level and deaths based on different condition of the vaccination program and target population will be fed into the economic evaluation. Cost and utility parameters will be incorporated to estimate the total costs and health gains from each vaccination option.

Based on healthcare system's perspective, direct medical costs incurred by COVID-19 due to either no symptoms, mild symptoms, or hospitalised with all treatment conditions will be estimated. The overall cost includes the costs of vaccination programme, adverse events, laboratory test, outpatient visit and hospitalisation. In the absence of actual cost data COVID-19 vaccine, our analysis will utilise cost data from 1) Influenza, as the best-case scenario, and 2) Ebola, as the worst-case scenario, which will also be estimated

based on published literature. For other prevention interventions, there are several non-pharmaceutical interventions being currently employed, however, our analysis will only focus on those which incur cost to the healthcare systems. Hence, our existing prevention interventions combined with standard of care will include: (i) the use of personal protective equipment (PPE) including N95 masks, (ii) disinfection and hand hygiene, (iii) surveillance measures such as screening and testing, and (iv) hospitalisation care such as potential therapeutic options, ICU beds and ventilators. Data will be obtained from literature review, hospital survey or administrative data of Ministry of Public Health, and expert opinion (if appropriated).

The health-related quality of life values (utility) of the four health states; mild symptoms, hospitalised treated, ICU treated and ventilator treated among children and adults who suffered from illness will be quantified. Data will be obtained from a literature review or primary data collection. All costs and cost-utility ratios will be adjusted and reported based in year 2020. Results presented in term of an incremental cost-effectiveness ratio (ICER) which will be calculated.

- **Uncertainty analysis**

Using the cost-effectiveness model, deterministic sensitivity analyses will be conducted to understand which parameters have the largest impact on the model results. A set of parameter inputs from both transmission dynamic and economic model will be included. The most influential parameters will be displayed in the form of a tornado diagram and ranked in order of their influence. For each of the most influential parameters, deterministic targets (minimum acceptable targets, acceptable targets and ideal targets) will be identified in order for the vaccine to be considered cost-effective compared to existing prevention interventions combined with standard of care. Any identified target values that are considered infeasible (e.g. negative costs) will be ignored, this step must be repeated iteratively in order to refine TPPs until they are populated with realistic model inputs only. Only significant parameters identified from deterministic sensitivity analysis will be used in the threshold analysis to quantify the maximum costs of the vaccine to the given ceiling threshold of 160,000 THB (USD 5,110) per QALY gained (21). If deemed of interest, multiway sensitivity analyses of different scenarios could be conducted for parameters of interest where variables are expected to be correlated (e.g. risk of infection in vaccinated individuals and severity of infection in vaccinated individuals).

Following the deterministic analysis, a probabilistic sensitivity analysis (PSA) will be conducted using a second order Monte Carlo simulation to assess the probability of each TPP being cost-effective with a given set of characteristics and vaccine price (28). Probability distributions will be defined as follows: 1) beta-distribution is assigned where parameter values ranged from zero to one, such as transition probabilities and utility parameters; 2) gamma-distribution is specified when parameter values were above zero and positively skewed by costs variables; and 3) a log-normal distribution is

used for odd ratio or relative risk derived from meta-analysis. Iterative reviews of the probabilistic analysis can be performed to identify TPPs with a target probability of cost-effectiveness compared to existing prevention interventions combined with standard of care. The target probability being cost-effectiveness should be set to the given ceiling threshold. The PSA will simulate for 1,000 iterations to yield a range of plausible values for lifetime costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs). The results will be depicted in graphs where the probability of the TPP for COVID-19 vaccine being cost-effective against different costs are plotted (29). Similarly, a cost-effectiveness acceptability curve (CEAC) could be produced and depicted in graphical format, if deemed of relevance for this analysis.

- **Value-of-information analysis**

Subsequently, value-of-information (VOI) analyses will be conducted to further inform researchers, manufacturers and policy makers about the consequences of making a wrong decision regarding funding a COVID-19 vaccine. The VOI analyses will be performed through the expected value of perfect information (EVPI) and expected value of partial perfect information (EVPPI) approach (12, 13). These analyses will provide an understanding of the potential value that could be attained by reducing the uncertainty in the model and prioritising parameters which would reduce the risks of incorrect decision making. These concepts were demonstrated in the Thai context for a potential HIV vaccine by Leelahavarong et al. 2011 (29).

The overall expected value of perfect information (EVPI) is the difference between the expected net benefit of the optimal strategy given perfect information (12, 13), which can be written as:

$$E_{\theta}[\max_t NB(t,\theta)]$$

and the expected net benefit of strategy that would be adopted given current imperfect information, which can be presented as:

$$\max_t[E_{\theta}NB(t,\theta)]$$

The formula can be shown as follows:

$$EVPI = E_{\theta}[\max_t NB(t,\theta)] - \max_t[E_{\theta}NB(t,\theta)]$$

where θ is the set of parameters for the model, which were assigned prior probability distributions; t is the set of possible decisions or strategies; and NB (t, θ) is the function of net benefit for decision t and parameters θ. To quantify the value of receiving further information on the chosen parameters, partial EVPI is the difference between the expected value of a decision made with perfect information about a particular vector of the parameters (θ) and the current optimal decision. With perfect information, θi is the

known vector of the parameters of interest θ; then the expected net benefit of a decision made would now be found by averaging over the uncertainty in θ that remains once we know θi and then by selecting the optimal treatment that provides maximum expected net benefit, and can be written as:

$$\max_t[E_{\theta|\theta t}NB(t, \theta)]$$

At this stage, we do not have perfect information on θi, so the expected value of any decision made with perfect information about θi is found by averaging the uncertain ranges of the parameters θi and can be presented as:

$$E_{\theta i}[\max_t E_{\theta|\theta t}NB(t \mid \theta)]$$

The additional value of collecting perfect information on a subset θt of uncertain model parameters is therefore given by the following equation:

$$E_{\theta i}[\max_t E_{\theta|\theta t}NB(t \mid \theta)] - \max_t[E_{\theta|\theta t}NB(t, \theta)]$$

The analysis of partial EVPI will use the Thai ceiling threshold at 160,000 THB (USD 5,110) per QALY gained (21).

Table 4 List of input parameters

Parameter Inputs	Sources
Epidemiology	
Population size (Overall and age group, Thailand)	Office of the National Economic and Social Development Council (30)
Birth and death rates of Thai population (age specific)	Office of the National Economic and Social Development Council (30)
Reported case data; age stratified daily new case and death reports	Department of disease control, Ministry of Health, Thailand (4) Source: https://covid19.th-stat.com/
Mixing contact patterns between age groups in Thailand	Thailand contact survey (31)
Ratio between the actual and reported cases (reporting fraction)	Literature review/Expert opinion
Clinical	
Probability of no symptoms COVID-19	Literature review/Surveillance data (1)
Probability of mild symptoms COVID-19 (self-treatment care)	Literature review/Surveillance data (1)
Probability of hospitalised COVID-19 (non-ICU, ICU and Ventilator)	Literature review/Surveillance data
Duration of infectiousness (days)	Literature review (32)
Recovery period (days)	Literature review/Local data
Probability of dying from COVID-19 (no symptoms, mild symptoms and hospitalized with non-ICU, ICU and ventilator)	Literature review/Local data (33, 34)
Vaccine efficacy	Assumption
Vaccine duration	Assumption
Economic Evaluation	
Cost of vaccine	Assumption with different scenarios e.g. with and without mechanisms on tiered pricing, pool procurement, compulsory purchase (eminent domain) and advance market commitment.
Cost of vaccine administration (including logistics)	Assumption
Cost of adverse events management per case	Assumption

Table 4 List of input parameters

Parameter Inputs	Sources
Cost per COVID-19 infection with no symptom per case	Literature review/Data collection
Cost per COVID-19 infection with mild symptom per case	Literature review/Data collection
Cost per non-ICU hospitalised COVID-19 infection per case	Literature review/Data collection
Cost per ICU hospitalised COVID-19 infection per case	Literature review/Data collection
Cost per hospitalised COVID-19 infection ventilator treated per case	
~~Cost of productivity loss~~	Literature review/Data collection
Cost of diagnosis (screening and testing)	Literature review/Data collection
Cost of PPE and N95 masks	Literature review/Data collection
Cost of hand hygiene/disinfection	Literature review/Data collection
Utility value of patients with mild symptom due to COVID-19 infection	Literature review/Data collection
Utility value of patients with non-ICU hospitalised COVID-19 infection	Literature review/Data collection
Utility value of patients with ICU hospitalised COVID-19 infection	Literature review/Data collection
Utility value of patients with hospitalised COVID-19 infection ventilator treated	Literature review/Data collection
Utility value of vaccinated target population and no infection	Literature review

Expected deliverables

- Evidence-informed Target Product Profiles for COVID-19 vaccine for R&D with the focus on preferable COVID-19 vaccine for low- and middle income settings;
- Estimated health impact, costs, value for money and intermediate-term government budget impact of different types of COVID-19 vaccines in comparison to other public health measures for prevention and control of COVID-19 outbreak under the Thai healthcare setting;
- Price information for negotiation with companies to increase access to COVID-19 vaccine that the Thai government as well as other limited resource settings willing to include COVID-19 vaccine into its response policy for COVID-19

Research team

1. Yot Teerawattananon[1,2,3], Ph.D.
2. Wanrudee Isaranuwatchai[1], Ph.D.
3. Pattara Leelahavarong[1], Ph.D.
4. Wang Yi[3], Ph.D.
5. Nantasit Luangasanatip[4], Ph.D.
6. Christopher Matthew Neil Painter[1], M.Sc
7. Sarayuth Khuntha[1], B.Sc.
8. Juthamas Prawjaeng[1], Pharm.D.
9. Wirichada Pan-Ngum[4], Ph.D.
10. Pritaporn Kingkaew[1], Ph.D.
11. Hannah Clapham[3], Ph.D.
12. Minah Park[3], Ph.D.

[1]Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
[2] National Health Foundation, Thailand
[3] Saw Swee Hock School of Public Health (SSHSPH), National University of Singapore (NUS), Singapore
[4]Mathematical and Economic Modelling (MAEMOD), Mahidol Oxford Tropical Medicine Research Unit (MORU), Faculty of Tropical Medicine, Mahidol University, Thailand

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England). 2020;395(10223):497-506.
2. World Health Organization. Coronavirus disease (COVID-2019) situation report - 84 [cited 2020 April 15]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.
3. Pongpirul WA, Pongpirul K, Ratnarathon AC, Prasithsirikul W. Journey of a Thai Taxi Driver and Novel Coronavirus. The New England journal of medicine. 2020;382(11):1067-8.
4. Department of Disease Control, Ministry of Public Health, Thailand. Covid-19 Infected Situation Reports [cited 2020 April 15]. Available from: https://covid19.th-stat.com/.
5. WHO R&D Blueprint. A coordinated Global Research Roadmap: 2019 novel Coronavirus Global research and innovation forum: towards a research roadmap Geneva: World Health Organisation (WHO) 2020.
6. BioWorld™. Biopharma products in development for COVID-19: Cortellis™; 2020 [Available from: https://www.bioworld.com/COVID19products#vac.
7. Vaccine Centre at the London School of Hygiene & Tropical Medicine. COVID-19 vaccine development pipeline 2020 [Available from: https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/.
8. World Health Organization. WHO Target Product Profiles for COVID-19 Vaccines 2020 [cited 2020 April 23]. Available from: https://www.who.int/blueprint/priority-diseases/key-action/WHO_Target_Product_Profiles_for_COVID-19_web.pdf?ua=1.
9. Ijzerman MJ, Steuten LM. Early assessment of medical technologies to inform product development and market access: a review of methods and applications. Applied health economics and health policy. 2011;9(5):331-47.
10. IJzerman M, Koffijberg H, Fenwick E, Krahn M. Emerging Use of Early Health Technology Assessment in Medical Product Development: A Scoping Review of the Literature. PharmacoEconomics. 2017;35(7):727-40.
11. Sculpher M, Drummond M, Buxton M. The iterative use of economic evaluation as part of the process of health technology assessment. Journal of health services research & policy. 1997;2(1):26-30.
12. York Health Economics Consortium. Expected Value of Perfect Information (EVPI) [Available from: https://yhec.co.uk/glossary/expected-value-of-perfect-information-evpi/
13. York Health Economics Consortium. Expected Value of Partially Perfect Information (EVPPI) [Available from: https://yhec.co.uk/glossary/expected-value-of-partially-perfect-information-evppi/.
14. Pietzsch JB, Pate-Cornell ME. Early technology assessment of new medical devices. International journal of technology assessment in health care. 2008;24(1):36-44.
15. Hartz S, John J. Contribution of economic evaluation to decision making in early phases of product development: a methodological and empirical review. International journal of technology assessment in health care. 2008;24(4):465-72.
16. U.S. National Library of Medicine. ClinicalTrials.gov [cited 2020 May 1]. Available from: https://www.clinicaltrials.gov/ct2/results?cond=covid-

19&term=&type=Intr&rslt=&age_v=&gndr=&intr=Drug+&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort=.
17. World Health Organization. Q&A on coronaviruses (COVID-19) [cited 2020 May 1]. Available from: https://www.who.int/news-room/q-a-detail/q-a-coronaviruses#:~:text=treatment.
18. U.S. National Library of Medicine. Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-5734™) in Participants With Severe Coronavirus Disease (COVID-19) [cited 2020 May 1]. Available from: https://clinicaltrials.gov/ct2/show/NCT04292899?intr=Remdesivir&draw=3&rank=6.
19. U.S. National Library of Medicine. Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-5734™) in Participants With Moderate Coronavirus Disease (COVID-19) Compared to Standard of Care Treatment [cited 2020 May 1]. Available from: https://clinicaltrials.gov/ct2/show/NCT04292730?intr=Remdesivir&draw=3&rank=7.
20. U.S. National Library of Medicine. The Efficacy of Different Anti-viral Drugs in COVID 19 Infected Patients [cited 2020 May 1]. Available from: https://clinicaltrials.gov/ct2/show/NCT04321616?intr=Remdesivir&draw=3&rank=10.
21. The Subcommittee for Development of National List of Essential Medicines. Meeting on The threshold at which an intervention becomes cost-effective. Meeting of the Subcommittee for Development of the National List of Essential Medicine 1/2016, Jainad Narendhorn meeting room. In: Health MoP, editor. Nonthaburi, Thailand2016.
22. Rattanavipapong W, Kapoor R, Teerawattananon Y, Luttjeboer J, Botwright S, Archer RA, et al. Comparing 3 Approaches for Making Vaccine Adoption Decisions in Thailand. International Journal of Health Policy and Management. 2020.
23. Milne GJ, Xie S. The Effectiveness of Social Distancing in Mitigating COVID-19 Spread: a modelling analysis. medRxiv. 2020:2020.03.20.20040055.
24. Koo JR, Cook AR, Park M, Sun Y, Sun H, Lim JT, et al. Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study. Lancet Infect Dis.
25. Trish Greenhalgh, Xin Hui Chan, Kamlesh Khunti, Quentin Durand-Moreau, Sebastian Straube, Declan Devane, et al. What is the efficacy of standard face masks compared to respirator masks in preventing COVID-type respiratory illnesses in primary care staff? 2020 [cited 2020 April 15]. Available from: https://www.cebm.net/covid-19/what-is-the-efficacy-of-standard-face-masks-compared-to-respirator-masks-in-preventing-covid-type-respiratory-illnesses-in-primary-care-staff/.
26. MacIntyre CR, Seale H, Dung TC, Hien NT, Nga PT, Chughtai AA, et al. A cluster randomised trial of cloth masks compared with medical masks in healthcare workers. BMJ Open. 2015;5(4):e006577.
27. World Health Organization. Evidence of hand hygiene as the building block for infection prevention and control. Geneva; 2017.
28. Briggs A, Sculpher M, Claxton K. Decision modelling for health economic evaluation. Oxford: Oxford University Press; 2006.
29. Leelahavarong P, Teerawattananon Y, Werayingyong P, Akaleephan C, Premsri N, Namwat C, et al. Is a HIV vaccine a viable option and at what price? An economic evaluation of adding HIV vaccination into existing prevention programs in Thailand. BMC Public Health. 2011;11(1):534.

30. Office of the National Economic and Social Development Council. [Available from: https://www.nesdc.go.th/nesdb_en/main.php?filename=index.
31. Prem K, Cook AR, Jit M. Projecting social contact matrices in 152 countries using contact surveys and demographic data. PLOS Computational Biology. 2017;13(9):e1005697.
32. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. The New England journal of medicine. 2020;382(13):1199-207.
33. Riou J, Counotte M, Hauser A, Althaus CL. Adjusted Age-Specific Case Fatality Ratio During the COVID-19 Epidemic in Hubei, China, January and Febuary 2020. medRxiv. 2020.
34. Russell TW, Hellewell J, Jarvis CI, van Zandvoort K, Abbott S, Ratnayake R, et al. Estimating the infection and case fatality ratio for coronavirus disease (COVID-19) using age-adjusted data from the outbreak on the Diamond Princess cruise ship, February 2020. Eurosurveillance. 2020;25(12):2000256.
35. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. The New England journal of medicine. 2020.
36. Chen J, LIU D, LIU L, LIU P, XU Q, XIA L, et al. A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19). Journal of Zhejiang University (Medical Science). 2020;49(1):0-.
37. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. The New England journal of medicine. 2020.
38. Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. JAMA. 2020.
39. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet (London, England). 2020;395(10229):1033-4.
40. Luo P, Liu Y, Qiu L, Liu X, Liu D, Li J. Tocilizumab treatment in COVID-19: A single center experience. J Med Virol. 2020.
41. Michot JM, Albiges L, Chaput N, Saada V, Pommeret F, Griscelli F, et al. Tocilizumab, an anti-IL6 receptor antibody, to treat Covid-19-related respiratory failure: a case report. Ann Oncol. 2020.
42. Zhang X, Song K, Tong F, Fei M, Guo H, Lu Z, et al. First case of COVID-19 in a patient with multiple myeloma successfully treated with tocilizumab. Blood Adv. 2020;4(7):1307-10.
43. National Institutes of Health. Therapeutic Options for COVID-19 Currently Under Investigation 2020 [cited 2020 May 1]. Available from: https://covid19treatmentguidelines.nih.gov/therapeutic-options-under-investigation/.

Appendix

The clinical data of the potential therapeutic options for the COVID-19

Drug name	Study design	Clinical data to Date
1. Antiviral agents		
1.1 Remdesivir	A multicenter, multinational cohort	53 patients with severe COVID-19 and hypoxia received compassionate-use remdesivir for up to 10 days and had a median of 18 days of follow-up; 68 percent (36 of 53 patients) had clinical improvement in terms of decreasing requirement for oxygen support- 57 percent of patients (17 of 30 patients) who were mechanically ventilated at baseline were extubated. 47 percent of patients (25 of 53 patients) were discharged and 13 percent (7 of 53 patients) died (35).
1.2 Chloroquine or hydroxychloroquine	A prospective randomized trial	30 adults with mild COVID-19 were randomized 1:1 to HCQ plus conventional treatment group and conventional treatment group, the proportion of patients with nasopharyngeal viral clearance at day 7 was not different with hydroxychloroquine (400 mg daily for 5 days) compared with standard of care, and one patient in the hydroxychloroquine group progressed to severe disease; interferon and other antiviral agents were used in both arms, which could be confounding factors (36).
1.3 lopinavir-ritonavir	A randomized trial	199 patients with severe COVID-19 received the addition of lopinavir-ritonavir (400/100 mg) twice daily for 14 days to standard care did not decrease the time to clinical improvement compared with standard care alone. There was a trend towards decreased mortality with lopinavir-ritonavir (19 versus 25 percent), and the numerical difference in mortality was greater among those who were randomized within 12 days of symptom onset, but neither difference was statistically significant (37).

Drug name	Study design	Clinical data to Date
2. Immune-based therapy		
2.1 convalescent plasma	case series	Five patients with severe COVID-19 and acute respiratory distress syndrome (ARDS), patients were given two transfusions (400 mL total) of convalescent plasma, along with antiviral therapy and steroids. The transfusions were administered between 10 and 22 days after admission. Symptoms improved in all patients in terms of decreasing nasopharyngeal viral load, decreased disease severity score, and improved oxygenation by 12 days after transfusion and no AEs were reported (38).
2.2 Interleukin-6 inhibitor (tocilizumab)	Case report	good outcomes with tocilizumab in terms of improvements in oxygenation, systemic inflammation, and hypoxic respiratory failure (1, 39-42), but systematic evaluation of the clinical impact of tocilizumab on COVID-19 has not yet been published.

Source: Derived from the National Institutes of Health (NIH): Therapeutic Options for COVID-19 Currently Under Investigation, 2020 (43).

Name: Yot Teerawattananon
Title: Mr
Office Mailing Address: Health Intervention and Technology Assessment Program
6 th Floor, 6 th Building, Department of Health, Ministry of Public Health,
Tiwanon Rd., Muang, Nonthaburi 11000, Thailand
Email: yot.t@hitap.net
Contact No: 02-590-4549

Academic Position:

- Founding Leader, Health Intervention and Technology Assessment Program

Academic qualifications:

- Ph.D. Health Economics, University of East Anglia, the UK, 2006
- Postgraduate Diploma in Health Sciences, University of East Anglia, the UK, 2003
- Doctor of Medicine, Chulalongkorn University, Thailand, 1997

Professional experience:

- Founding Leader of the HITAP, January 2007-present
- Senior Researcher, International Health Policy Program (IHPP), May 2001-Dec 2006
- Research Fellow, Senior Research Scholar Program in Health Financing and Health Economics, Health Systems Research Institute, January 2000-April 2001
- Hospital Director, Pong Hospital, Phayao Province, June1998-January 2000
- Medical Staff, ChiangKhum Hospital, Phayao Province, March 1997-June1998

Publication:

- Isaranuwatchai W, Teerawattananon Y, Archer RA, Luz A, Sharma M, Rattanavipapong W, et al. Prevention of non-communicable disease: best buys, wasted buys, and contestable buys. BMJ. 2020;368:m141. doi: 10.1136/bmj.m141.
- Teerawattananon Y, Dabak SV, Khoe LC, Bayani DBS, Isaranuwatchai W. To include or not include: renal dialysis policy in the era of universal health coverage. BMJ. 2020 Jan 28;368:m82. doi: 10.1136/bmj.m82.
- Yue M, Dickens BL, Yoong JS, I-Cheng Chen M, Teerawattananon Y, Cook AR. Cost-Effectiveness Analysis for Influenza Vaccination Coverage and Timing in Tropical and Subtropical Climate Settings: A Modeling Study.Value Health. 2019;22(12):1345-1354. doi: 10.1016/j.jval.2019.07.001.
- Suwanthawornkul T, Praditsitthikorn N, Kulpeng W, Haasis MA, Guerrero AM, Teerawattananon Y. Incorporating economies of scale in the cost estimation in economic evaluation of PCV and HPV vaccination programmes in the Philippines: a game changer? Cost Eff Resour Alloc. 2018;16:7. doi: 10.1186/s12962-018-0087-x.

Grant/Fundings Awarded:

- Thailand Research Fund's Senior Research Scholar (2012) (awarded to distinguished senior researchers, who have shown ability, integrity and excellence, and are well known in his/her research area, with the aim to provide support for the development of research teams lead by the TRF senior research scholars, and to build up long-term intellectual and training bases for the new generations of researchers in the country http://www.trf.or.th/)
- The ISPOR International Fellowship Award, International Society for Pharmacoeconomics and Outcome Research, 2008-2009

Name: Wanrudee Isaranuwatchai
Title: Ms
Office Mailing Address: Health Intervention and Technology Assessment Program
6 th Floor, 6 th Building, Department of Health, Ministry of Public Health,
Tiwanon Rd., Muang, Nonthaburi 11000, Thailand
Email: wanrudee.i@hitap.net
Contact No: 02-590-4549

Work Experience (Current)

- Mar 2020 – present: Program Leader (Director) and Senior Researcher, Health Intervention and Technology Assessment Program, Ministry of Public Health, Thailand
- Feb 2020 – present: Research Scientist, St. Michael's Hospital, Toronto, Canada
- Sept 2015 – present: Research Fellow, Institute for Clinical Evaluative Sciences, Toronto, Canada
- Aug 2014 – present:Assistant Professor, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

Academic and Training Background

- 2011 – 2012: Postdoctoral Fellow, Centre for Addiction and Mental Health, Toronto
- 2006 – 2012: PhD in Health Services Research (Health Economics), University of Toronto, Toronto
- 1999 – 2003: BSc in Health Sciences, University of Waterloo, Waterloo

Peer-Reviewed Publications (Selected)

- Isaranuwatchai, W., Teerawattananon, Y., Archer, R.A., Luz, A., Sharma, M., Rattanavipapong, W., Anothaisintawee, T., Bacon, R.L., Bhatia, T., Bump, J., Chalkidou, K., Elshaug, A.G., Kim, D.D., Reddiar, S.K., Nakamura, R., Neumann, P.J., Shichijo, A., Smith, P.C., & Culyer, A.J. Prevention of non-communicable disease: best buys, wasted buys, and contestable buys. BMJ. 2020 Jan 28;368:m141.
- Isaranuwatchai, W., de Oliveira, C., Mittmann, N., Evans, W.K., Peter, A., Truscott, R., & Chan, K.K.W. Impact of Smoking on Health System Costs Among Cancer Patients. British Medical Journal Open. 2019;9(6):e026022.
- Isaranuwatchai, W., Li, R., Glassman, A., Teerawattananon, Y., Culyer, A.J., & Chalkidou, K. Disease Control Priorities Third Edition: Time to Put a Theory of Change Into Practice; Comment on "Disease Control Priorities Third Edition Is Published: A Theory of Change Is Needed for Translating Evidence to Health Policy". International Journal of Health Policy and Management. 2019 Feb 1;8(2):132-5.

Research Funding (Selected)

- Oct 2019 – Sept 2022 Co-Investigator. The Epidemiology and Economic Burden of Hepatitis C Viral infection in the First Nations Population in Ontario. Canadian Institutes of Health Research (CIHR): Project Grant. (Co-PIs: Krahn, M. D., & Walker, J.; Co-Is: Allen, V.G., Feld, J.J., Isaranuwatchai, W., Mendlowitz, A.B., Mitsakakis, N., Murti, M., Sander, B.H., & Wong, W. W. L.). $650,250 CAD
- Apr 2019 – Mar 2026 Co-Investigator. Interventions research in homelessness, housing, and health. Canadian Institutes of Health Research (CIHR): Foundation Grant. (PI: Hwang, S.W.; Co-Is: Aubry, T. D., Dunn, J.R., Fabreau, G., Gaetz, S. A., Heineck, K. A., Isaranuwatchai, W., Nisenbaum, R., Palepu, A., Raine, L., Richter, T., Stergiopoulos, V., Thulien, N., & Watson, K.). $3,972,033CAD
- Chambers, A., Chen, C., Mozessohn, L., Rodin, D., Hodgson, D. & Lee, S.M.). $297,217

Name: Pattara Leelahavarong
Title: Ms
Office Mailing Address: Health Intervention and Technology Assessment Program
6 th Floor, 6 th Building, Department of Health, Ministry of Public Health,
Tiwanon Rd., Muang, Nonthaburi 11000, Thailand
Email: pattara.l@hitap.net
Contact No: 02-590-4549

Academic Position:

- Researcher, Health Intervention and Technology Assessment Program (2008-present)

Academic qualifications:

- Ph.D. Health Economics, University of Glasgow, the UK, 2018
- M.Sc. Pharmacy (Pharmaceutical Administration), Mahidol University, Thailand, 2009
- B.Sc. Pharmacy, Mahidol University, Thailand, 2004

Research interests:

- Health economics
- Health policy analysis
- Health prevention e.g. vaccine, health promotion intervention

Publication:

- Leelahavarong P, Doungthipsirikul S, Kumluang S, Poonchai A, Kittiratchakool N, Chinnacom D, et al. Health Technology Assessment in Thailand: Institutionalization and Contribution to Healthcare Decision Making: Review of Literature. Int J Technol Assess Health Care. 2019;35(6):467-473. doi: 10.1017/S0266462319000321.
- Leelahavarong P, Teerawattananon Y, Werayingyong P, Akaleephan C, Premsri N, Namwat C, et al. Is a HIV vaccine a viable option and at what price? An economic evaluation of adding HIV vaccination into existing prevention programs in Thailand. BMC public health. 2011;11:534.
- Kulpeng W, Leelahavarong P, Rattanavipapong W, Sornsrivichai V, Baggett HC, Meeyai A, Punpanich W, Teerawattananon Y. Cost-utility analysis of 10- and 13-valent pneumococcal conjugate vaccines: protection at what price in the Thai context? Vaccine. 2013;31(26):2839-47. doi: 10.1016/j.vaccine.2013.03.047

Research projects:

- Development of health promotion model for economic evaluation in Thailand: a case study of
- alcohol control interventions
- Systematic review and meta-analysis of intravitreal bevacizumab (avastin®) in macular diseases
- Asian collaborative research project to determine WTP/QALY
- Economic Evaluation of Neonatal Screening for Inborn Errors of Metabolism Using Tandem Mass Spectrometry in Thailand
- Cost-Utility and budget impact analysis of drug treatments in pulmonary arterial hypertension associated with congenital heart diseases in Thailand

Name: Wang Yi
Title: Dr
Office Mailing Address: 12 Science Drive 2, Tahir Foundation Building, #08-01G, Singapore 117549
Email: ephwyi@nus.edu.sg
Contact No: 65-86939601

Academic Position:

- Research Fellow, Health Intervention and Policy Evaluation Research (50%) & Singapore Population Health Improvement Centre (50%), Saw Swee Hock School of Public Health, National University of Singapore (07/2019-present)
- Post-doc Research Fellow, Centre for Health Services and Policy Research, Saw Swee Hock School of Public Health, National University of Singapore (07/2017-06/2019)
- Teaching Assistant, Department of Economics, National University of Singapore (08/2016-06/2017)

Academic qualifications:

- Ph.D. Economics, National University of Singapore, 2017, Dissertation: "Essays in Applied Economics, Household Behavior, and Environmental Economics"
- B.A. Science in Mathematics & Economics, Nanyang Technological University, 2012, with First class honours

Research interests:

- Health economics
- Labor economics and households' behaviors
- Environmental economics

Publication:

- Yue, M., Wang, Y., Low, C. K., Yoong, J. S. Y., & Cook, A. R. (2019). Optimal Design of Population-Level Financial Incentives of Influenza Vaccination for the Elderly. Value in Health.
- Salvo, A., & Wang, Y. (2017). Ethanol-blended gasoline policy and ozone pollution in Sao Paulo. Journal of the Association of Environmental and Resource Economists, 4(3), 731-794.

Grant/Fundings Awarded:

- Value of Haploidentical Hematopoietic Stem Cell Transplant after TCR-αβ and CD45+ Depletion following Reduced Intensity Conditioning in Adults with Hematological Malignancies, NCIS Seed Grant 2019, Co-Investigator
- Understanding Financial and Non-financial Barriers to Chronic Disease Management in Singapore: A Natural Experiment, Singapore MOE Tier 1 2018, Co-Investigator

Name: Nantasit Luangasanatip
Title: Dr
Office Mailing Address: 11/F Chamlong Harinsuta Build, 420/6 Rajvithi Road, Rajthevee, Bangkok, 10400, Thailand
Email: nantasit@tropmedres.ac
Contact No: +66-81620-2626

Academic Position:

- Research Fellow, Mathematical and Economic Modelling (MAEMOD), Mahidol Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand (10/2017- present)
- Assistant Research Fellow, London School of Hygiene and Tropical Medicine, Faculty of Epidemiology and Population health, London, UK (10/2016-09/2017)

Academic qualifications:

- Ph.D. Public Health (Health Economics), Queensland University of Technology (QUT), Brisbane, Australia, 2015
- M.Sc. in Economic Evaluation in Healthcare, City University, London, UK, 2009
- B.Sc. in Pharmacy, Chulalongkorn University, Bangkok, Thailand 2005

Research interests:

- Health Economics
- Transmission Dynamic model
- Evidence-synthesis
- Vaccine

Publication:

- Jit M, Ng Hui Lin D, Luangasanatip N, Atkins KE, Sandmann F, Robotham J, Pouwels KB. Quantifying the economic cost of antibiotic resistance and the impact of related interventions: Rapid methodological review, conceptual framework and recommendation for future studies. BMC Medicine 2020; 18:38.
- Luangasanatip N, Flasche S, Dance D, Bancroft G, Atkins T, Titball R, Jit M. The global impact and cost-effectiveness of a melioidosis vaccine. BMC Medicine. 2019;17:129.
- Luangasanatip N, Hongsuwan M, Lubell Y, Limmathurotsakul D, Srisamang P, Day NP, Graves N, Cooper BS. Cost-effectiveness of interventions to improve hand hygiene in healthcare workers in middle-income hospital settings: a model-based analysis. J Hosp Infect. 2018 Oct;100(2):165-175.
- van Kleef E, Luangasanatip N, Bonten MJ, Cooper BS. Why sensitive bacteria are resistant to hospital infection control. Wellcome Open Res. 2017 Mar 10;2:16.
- Luangasanatip N, Hongsuwan M, Limmathurotsakul D, Lubell Y, Lee AS, Harbarth S, Day NP, Graves N, Cooper BS. Comparative efficacy of hospital hand hygiene promotion interventions: a systematic review and network meta-analysis. BMJ. 2015;351:h3728.
- Luangasanatip N, Chaiyakunapruk N, Upakdee N, Wong P. Iron-chelating therapies in a transfusion-dependent thalassaemia population in Thailand: a cost-effectiveness study. Clin Drug Investig. 2011;31(7):493-505.

Name: Christopher Matthew Neil Painter
Title: Mr
Office Mailing Address: Health Intervention and Technology Assessment Program
6 th Floor, 6 th Building, Department of Health, Ministry of Public Health,
Tiwanon Rd., Muang, Nonthaburi 11000, Thailand
Email: chris.p@hitap.net
Contact No: 02-590-4549

Academic Position:

- Project Associate, Health Intervention and Technology Assessment Program, Thailand (10/2019 - present)
- Senior Health Economist, Costello Medical (10/2018-10/2019)
- Health Economist, Costello Medical (06/2017 – 10/2018)
- Health Economist Intern, Costello Medical (01/2017 – 06/2017)

Academic qualifications:

- M.Sc. in Economics, Merit, University of Manchester, UK, 2016
- B.Sc. in Economics, Second Class, Division One (2:1), University of Manchester, UK, 2015

Selected Publications:

- Title: Modelling the Long-Term Clinical Outcomes of the Novel Single-Tablet Regimen Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in the UK Publisher: British HIV Association (BHIVA) 25th Annual Conference – Bournemouth, UK
- Title: Vax-The-Nation: A Budget Impact Analysis of Costs Associated with Measles Outbreaks in the USA Through Increasing Measles, Mumps and Rubella Vaccination Uptake Publisher: International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 24th International Meeting 2019 – New Orleans, USA

Name: Sarayuth Khuntha
Title: Mr
Office Mailing Address: Health Intervention and Technology Assessment Program
6 th Floor, 6 th Building, Department of Health, Ministry of Public Health,
Tiwanon Rd., Muang, Nonthaburi 11000, Thailand
Email: Sarayuth.k@hitap.net
Contact No: 02-590-4549

Academic Position:

- Research Assistant, Health Intervention and Technology Assessment Program (10/2016-present)

Academic qualifications:

- B.Sc. European Public Health, Maastricht University, the Netherlands, 2016

Research interests:

- Health technology assessment
- Health research and policy analysis
- Infectious disease and economic evaluation modelling

Publication:

- Khampang R, Khuntha S, Hadnorntun P, et al Selecting topic areas for developing quality standards in a resource-limited setting BMJ Open Qual 2019;8:e000491. doi: 10.1136/bmjoq-2018-000491
- Dorji K, Phuntsho S, Pempa, Kumluang S, Khuntha S, Kulpeng W, et al. Towards the introduction of pneumococcal conjugate vaccines in Bhutan: A cost-utility analysis to determine the optimal policy option. Vaccine. 2018;36(13):1757-65. doi: 10.1016/j.vaccine.2018.02.048

Awarded:

- Winning the third place for excellence in oral presentation on economic evaluation at the 8th HTAsiaLink Annual Conference 2019
- Winning the first prize on health system research category for the oral presentation at the 7th HTAsiaLink Annual Conference 2018

Name: Juthamas Prawjaeng
Title: Miss
Office Mailing Address: Health Intervention and Technology Assessment Program
6 th Floor, 6 th Building, Department of Health, Ministry of Public Health,
Tiwanon Rd., Muang, Nonthaburi 11000, Thailand
Email: Juthamas.p@hitap.net
Contact No: 02-590-4549

Academic Position:

- Research Assistant, Health Intervention and Technology Assessment Program (5/ 2019-present)
- Pharmacist at community pharmacy (2017- 4/2019)

Academic qualifications:

- Pharm.D. in Pharmaceutical care, Naresuan University, Phitsanulok, Thailand 2017.

Research interests:

- Health technology assessment
- Behavioural economics
- Network meta-analysis

Publication:

- Chong HY, Lim YH, Prawjaeng J, Tassaneeyakul W, Mohamed Z, Chaiyakunapruk N. Cost-effectiveness analysis of HLA-B* 58: 01 genetic testing before initiation of allopurinol therapy to prevent allopurinol-induced Stevens–Johnson syndrome/toxic epidermal necrolysis in a Malaysian population. Pharmacogenetics and genomics. 2018;28(2):56-67.

Name: Wirichada (Pongtavornpinyo) Pan - ngum
Office Mailing Address: Mathematical and Economic Modelling Group (MAEMOD)
Mahidol-Oxford Tropical Medicine Research Unit (MORU), Faculty of Tropical Medicine,
Mahidol University, 420/6 Rajvithi Road, Ratchathewi District, Bangkok 10400 Thailand
E-mail: pan@tropmedres.ac
Tel: (00-66-2) 3549128, Fax: (00-66-2) 3549169 Mobile: (00-66-81) 8636537

Employment:

- 2020 - Present Associate Professor at Department of Tropical Medicine and Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
- 2019 – Present Head of the Mathematical And Economic MODelling (MAEMOD) at Mahidol-Oxford Tropical Medicine Research Unit (MORU), Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
- 2016 – Present Honorary Visiting Research Fellow, Nuffield Department of Medicine, University of Oxford, UK
- 2015 - Present Leading TDModNet, Tropical Disease Modelling Network (http://www.tdmod.net/)
- 2006 – 2009 Clinical data manager, SEA Influenza Clinical Research Network, Mahidol Oxford Tropical Medicine Research Unit (MORU) Mahidol University

Education and Qualifications:

- 2006 University of Liverpool, PhD in Tropical Medicine
- 1999 University of Oxford, MSc in Applied Statistics
- 1998 University of Warwick, BSc MORSE (Mathematics Operational Research, Statistics and Economics)
- 1995 A level's: Mathematics, Further Mathematics, and Economics

Research funding:

- PI: Mathematical and economic modelling for optimal strategies to screen and treat chronic hepatitis C virus patients using novel antiviral agents with cost-effectiveness and budget impact analyses in Thai setting (National Science and Technology Development Agency 2018)
- Co-PI: The effectiveness of vitamin A supplement to decrease severity of hand foot mouth disease in toddlers (National Research Council of Thailand 2019)
- Co-PI: Cost-effectiveness analysis of rotavirus vaccine in Thailand (The National List of Essential Medicines (NLEM) Thailand 2018)

Recent publications:

- Mahikul W, Kripattanapong S, Hanvoravongchai P, Meeyai A, Iamsirithaworn S, Auewarakul P, Pan-Ngum W: Contact Mixing Patterns and Population Movement among Migrant Workers in an Urban Setting in Thailand. Int J Environ Res Public Health 2020, 17(7).
- Khunthason S, Kaewkungwal J, Pan-Ngum W, Okascharoen C, Apidechkul T, Lawpoolsri S: The Factors associated with the unsuccessful tuberculosis treatment of hill tribe patients in Thailand. J Infect Dev Ctries 2020, 14(1):42-47.
- Kinyanjui T, Pan-Ngum W, Saralamba S, Taylor S, White L, Nokes DJ: Model evaluation of target product profiles of an infant vaccine against respiratory syncytial virus (RSV) in a developed country setting. Vaccine X 2020, 4:100055.
- Mahikul W, White LJ, Poovorawan K, Soonthornworasiri N, Sukontamarn P, Chanthavilay P, Medley GF, Pan-Ngum W: Modelling population dynamics and seasonal movement to assess and predict the burden of melioidosis. PLoS Negl Trop Dis 2019, 13(5):e0007380.

Name: Pritaporn Kingkaew
Title: Ms
Office Mailing Address: Health Intervention and Technology Assessment Program
6 th Floor, 6 th Building, Department of Health, Ministry of Public Health,
Tiwanon Rd., Muang, Nonthaburi 11000, Thailand
Email: pritaporn.k@hitap.net
Contact No: 02-590-4549

Academic Position:

- Researcher, Health Intervention and Technology Assessment Program (2007-present)

Academic qualifications:

- Ph.D. Health Sciences (digital health), University of Leeds, the UK, 2018
- M.Sc. Health Economics, University of York, the UK, 2010
- B.Sc. Pharmacy, Srinakharinwirot University, Thailand, 2007

Publication:

- Kingkaew P, Glidewell L, Walwyn R, Fraser H, Wyatt JC. Identifying effective components for mobile health behaviour change interventions for smoking cessation and service uptake: protocol of a systematic review and planned meta-analysis. Syst Rev. 2017 Oct 6;6(1):193. doi: 10.1186/s13643-017-0591-7.
- Teerawattananon Y, Kingkaew P, Koopitakkajorn T, Youngkong S, Tritasavit N, Srisuwan P, et al. Development of a Health Screening Package Under the Universal Health Coverage: The Role of Health Technology Assessment. Health Econ. 2016 Feb;25 Suppl 1:162-78. doi: 10.1002/hec.3301.
- Kingkaew P, Werayingyong P, Aye SS, Tin N, Singh A, Myint P, et al. An ex-ante economic evaluation of the Maternal and Child Health Voucher Scheme as a decision-making tool in Myanmar. Health Policy Plan. 2016;31(4):482-92.
- Kingkaew P, Maleewong U, Ngarmukos C, Teerawattananon Y. Evidence to inform decision makers in Thailand: a cost-effectiveness analysis of screening and treatment strategies for postmenopausal osteoporosis. Value Health. 2012;15(1 Suppl):S20-8.

Research projects:

- Service availability and readiness assessment of cochlear implantation and rehabilitation services in Thailand
- A cost-utility analysis and budget impact analysis of treatment for relapsing-remitting multiple sclerosis
- Development of the health technology assessment guideline version 3
- Cost-effectiveness analysis of Rotavirus vaccine in Bhutan
- Optimising the development of effective mobile health behaviour change interventions: text messages to support smoking cessation in Thailand
- A cost-utility and budget impact analysis of the sunitinib risk-sharing scheme for the treatment of metastatic RCC and for advanced GIST after failure of imatinib
- Access to assistive technology for people with disability: quality of life and capability

Name: Hannah E. Clapham, PhD
Email: **Hannah.clapham@nus.edu.sg**
Contact No: **+6594225849**

Positions Held

Assistant Professor (Tenure-track)
Saw Swee Hock School of Public Health, National University of Singapore January 2020-present

Head of Mathematical Modelling Group
University of Oxford, based in: Oxford University Clinical Research Unit (OUCRU), Vietnam, April 2017- November 2019

Mathematical Epidemiologist
University of Oxford, based in: Oxford University Clinical Research Unit (OUCRU), Vietnam, April 2016- April 2017

Post-Doctoral Fellow
Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, November 2013 – April 2016

Education:

PhD "Modelling Dengue Infection Dynamics and the Impact of Control Measures"
Department of Infectious Disease Epidemiology, Imperial College London 2009-2013, Funded by MRC.

MSc Modern Epidemiology, Imperial College London 2008- 2009
Funded by MRC. Dissertation work undertaken in Bangalore, India

BA Mathematics, 2.1. Hertford College, University of Oxford 2004- 2007

Relevant grants awarded:

Co-I, NMRC Singapore, COVID-19 modelling in Singapore (March 2020-March 2021), SGD$950,600

PI: Japanese Encephalitis Vaccine Modelling as part of the BMGF-GAVI Vaccine Impact Modelling Consortium (VIMC) (March 2017-March 2022) USD$252, 500.

Relevant publications:

Rachael Pung, Calvin J Chiew, Barnaby E Young, Sarah Chin, Mark IC Chen, **Hannah E Clapham**, et al. …, Li Wei Ang, Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures, 2020/3/17, The Lancet

Turner, H.C., Thwaites, G.E., Clapham, H.E., Vaccine-preventable diseases in lower-middle-income countries, The Lancet Infectious Diseases, September 2018, 18 (9), 937-939

Name: Minah Park
Office Mailing Address: 12 Science Drive 2, Tahir Foundation Building, #09-01, Singapore 117549
Email: ephpm@nus.edu.sg
Phone +65-97328280

Work Experience:

- Post-doctoral Research Fellow. Saw Swee Hock School of Public Health, National University of Singapore, Singapore (01/2019-Present)
- Teaching Assistant. Infectious Disease Epidemiology (postgraduate course); and 'Epidemics' (EdX). The University of Hong Kong, HKSAR (09/2014-06/2016)
- Associate Researcher, Dengue Vaccine Initiative (DVI), International Vaccine Institute, Seoul, Korea (09/2012–11/2013)
- Research Associate, Global Asia Institute, National University of Singapore, Singapore (11/2011 – 08/2012)
- Research Assistant, School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong (07/2010–12/2010)
- Program Coordinator, Asan Medical Center (AMC), Seoul, Korea (10/2006 – 06/2009)
- Intern, Mount Nittany Medical Center, Pennsylvania, USA (05/2006 – 08/2006)

Academic qualifications:

- Ph.D. Infectious Disease Epidemiology. School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, 2018 (Thesis supervisors: Prof. Joseph Wu (Primary), Prof. Ben Cowling, and Prof. Mark Jit)
- MPH. Epidemiology, Global Health Track. Mailman School of Public Health, Columbia University, New York, NY, USA, 2011
- BS. Health Policy. College of Health and Human Development, The Pennsylvania State University, University Park, PA, USA, 2006

Selected publications:

- **Park M**, Cook AR, Lim JT, Sun Y, Dickens BL. A Systematic Review of COVID-19 Epidemiology Based on Current Evidence. *J Clin Med*. 2020 Mar 31;9(4). pii: E967.
- Koo JR, Cook AR, **Park M**, Sun Y, Sun H, Lim JT, Tam C, Dickens BL. Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study. *Lancet Infect Dis*. 2020 Mar 23. pii: S1473-3099(20)30162-6.
- **Park M**, Jit M, Wu JT. Cost-benefit analysis of vaccination: a comparative analysis of eight approaches for valuing changes to mortality and morbidity risks. *BMC Med*. 2018;16(1):139.
- Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, Cohen C,Gran JM, Schanzer D, Cowling BJ, Wu P, Kyncl J, Ang LW, **Park M**, et al; Global Seasonal Influenza-associated Mortality Collaborator Network. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. *Lancet*. 2018; 391(10127):1285-1300.
- **Park M**, Wu P, Goldstein E, Joo Kim W, Cowling BJ. Influenza-Associated Excess Mortality in South Korea. *Am J Prev Med*. 2016;50(4):e111-e119.
- Virlogeux V, **Park M**, Wu JT, Cowling BJ. Association between Severity of MERS-CoV Infection and Incubation Period. *Emerg Inf Dis*. 2016;22(3):526-8.
- Virlogeux V, Fang VJ, **Park M,** Wu JT, Cowling BJ. Comparison of incubation period distribution of human infections with MERS-CoV in South Korea and Saudi Arabia. *Sci Rep*. 2016;6:35839.
- Cowling BJ, **Park M *(joint first author)***, Fang VJ, Wu P, Leung GM, Wu JT. Preliminary epidemiological assessment of MERS-CoV outbreak in South Korea, May to June 2015. *Euro Surveill*. 2015;20(25):7-13