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ORIGINAL RESEARCH ARTICLE

Cost-Utility Analysis of Universal Maternal Pertussis Immunisation in Thailand: A Comparison of Two Model Structures

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Abstract

Objectives This study aimed to assess the cost-effectiveness of introducing universal maternal pertussis immunisation under the national vaccine programme in Thailand.

Methods We conducted a cost-utility analysis from a societal perspective to compare maternal vaccination with (1) TdaP vaccine, (2) Td vaccine and aP vaccine, and (3) Td vaccine only. We constructed two decision-tree models with Markov elements, each following a different clinical pathway, to allow us to examine structural uncertainty. Costs were converted to 2021 Thai Baht (THB) and a discount rate of 3% was applied to health and cost outcomes, with sensitivity analysis at 0% and 6%. Parameter uncertainty was investigated through deterministic and probabilistic sensitivity analysis, with expected value of perfect information analysis.

Results Maternal pertussis vaccination would avert 27 cases and up to one death per year. The incremental cost-effectiveness ratio (ICER) for adding aP to the maternal immunisation schedule is 2,184,025 THB/QALY and the ICER for replacing maternal Td vaccination with TdaP is 3,198,101 THB/QALY. Maternal pertussis vaccination only becomes favourable in the probabilistic sensitivity analysis at cost-effectiveness thresholds above 6,000,000 THB/QALY, far above the Thai threshold of 160,000 THB/QALY. If incidence is less than 397 cases per 100,000, maternal pertussis vaccination will not be cost-effective in Thailand, within the plausible range for vaccine effectiveness and probability of hospitalisation. Budget impact is dominated by vaccination costs, which represent 12% and 18% of the 2021 national vaccine programme budget for introducing aP vaccine or for switching Td with TdaP vaccine, respectively.

Conclusions We have found that maternal pertussis immunisation is not cost-effective in Thailand. Although there may be substantial under-reporting of pertussis cases, comparison with hospital data suggests that most under-reported cases are not hospitalised and therefore have negligible impact on our results. However, considerations such as affordability and local manufacturing may also be important for national immunisation programme decision-making.

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Key Points

Given current evidence, maternal pertussis vaccination is unlikely to be cost-effective in Thailand.

Comparison with hospital data suggests that under-reporting is expected to be among non-hospitalised cases, with minimal impact on costs or QALYs.

Two model structures gave similar results, suggesting limited impact of assumptions around clinical progression in the model.

Considerations such as affordability and local manufacturing may be more important for national immunisation programme decision-making.

1 Introduction

Pertussis (whooping cough) is a highly contagious disease of the respiratory tract caused by *Bordatella pertussis* [1]. Although there has been a considerable reduction in morbidity and mortality with the rise in vaccination over the past decades, it has been estimated that pertussis still causes around 24 million cases and 160,000 deaths in infants younger than 5 years globally [2]. In countries with high diphtheria-tetanus-pertussis (DTP) vaccine coverage, the greatest burden of disease occurs in infants aged less than 6 months, who are also mostly likely to suffer complications and death [3]. Maternal pertussis immunisation can significantly reduce the burden of pertussis in this group, through transfer of maternal antibodies across the placenta and protection against infection of the infant by the mother [4, 5]. Modelling studies have shown maternal vaccination to be more cost-effective than cocooning, in which close contacts of infants are vaccinated to prevent transmission [6].

In Thailand, DTP immunisation has greatly reduced the incidence of pertussis [7]. Reported cases and deaths are highest among infants aged less than 1 year [8]. Since 2015, the number of pertussis cases has risen, although it is unclear whether this is due to disease resurgence or enhanced surveillance [9]. As in other settings, incidence from passive surveillance of pertussis is likely to be underreported, with several studies suggesting high prevalence of pertussis among infants and adults with prolonged cough [10–12]. Although Thai medical associations recommend maternal pertussis immunisation, the vaccine is not yet provided free of charge through the national vaccination programme [13]. Other countries that have introduced maternal pertussis immunisation administer TdaP, a combination vaccine of tetanus, reduced-dose diphtheria, and acellular pertussis vaccine. Thailand is the first country to have licensed a monovalent acellular pertussis (aP) vaccine, manufactured in Thailand. Clinical trials have shown the aP vaccine to be safe and have non-inferior immunogenicity to TdaP [14–16]. However, all cost-effectiveness studies identified considered TdaP and not monovalent aP [6, 17–19].

Thailand is considering whether to include either TdaP or aP within the National List of Essential Vaccines, to be provided free of charge to all pregnant women. This study has been undertaken to understand the health and economic implications of introducing maternal pertussis vaccination in Thailand, by evaluating the cost-effectiveness, budget impact, and key sources of uncertainty.

2 Methods

We conducted a cost-utility analysis from a societal perspective, to compare maternal vaccination with (1) TdaP vaccine, (2) Td (tetanus and reduced dose diptheria) vaccine and aP vaccine delivered concurrently as two separate vaccines, and (3) Td vaccine (current practice in Thailand). In each case, we considered a single-dose regimen delivered to the pregnant woman at 27–36 weeks' gestation, during antenatal care visits, utilising existing maternal immunisation infrastructure in Thailand. Expected outcomes were expressed in terms of quality-adjusted life-years (QALY) to account for both life expectancy and quality of life. We follow a single cohort of pregnant women and neonates over a lifetime horizon. We additionally conducted budget impact analysis from the government perspective over a 5-year period. Methods adhered to the Thai methodological guidelines for conducting health technology assessment and reporting followed the Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) [20, 21].

2.1 Model Overview

After reviewing prior published economic evaluation studies on maternal pertussis immunisation, two researchers (SB and EW) each independently constructed a different decision-tree model with Markov elements, using Microsoft Excel with Plant-A-Tree add-in [22]. The use of two different models allowed analysis of structural uncertainty related to clinical progression, which is rare in the literature [23]. Health outcomes for branches of the model were identified through reviewing existing decision tree models for maternal pertussis vaccination [18, 19, 24, 25] and literature on clinical progression of the disease [26, 27]. For infants, the first model structure assumes that after hospitalisation, severe cases are admitted to intensive care (ICU), for which the outcomes may be alive without complications, alive with chronic respiratory symptoms, alive with chronic neurological complications, or death. In this model structure, deaths caused by pertussis only occur in the ICU branch for both mothers and infants. In the second model structure, hospitalised cases are treated separately by symptoms (pneumonia, encephalitis, other complications, no complications), with corresponding death rates for each branch and chronic outcomes only occurring among infants in the encephalitis branch (Fig. 1b). In both model structures, the outcomes for the mother for each branch are alive or dead only (i.e., no chronic

conditions). During a stakeholder consultation with clinicians, researchers, policymakers, and representatives from pharmaceutical companies, there was no clear consensus on which model structure best represented the clinical pathway in Thailand (see Online Supplementary Material (OSM) Resource 1). Model structure 1 was therefore taken as the base model structure, with structural uncertainty analysis conducted for the alternative model structure.

For infants, the decision tree models cover the first 0-3 months of life, under the assumption that all infants are protected by DTP1 vaccination by 3 months of age, since Thailand has maintained 99% DTP1 coverage for more than 10 years [28]. This assumption aligns with similar studies conducted in settings with high DTP primary series coverage [18, 29]. The decision tree for mothers has a time horizon of 5 years, based on duration of protection studies for adult pertussis vaccination [30]. We do not account for subsequent pregnancies in our model. The lifetime health and cost impacts for outcomes of the decision tree were calculated using Markov models with a 1-year cycle, in order to incorporate the impact of chronic conditions. The discount rate is set at 3% for health and cost outcomes, with one-way deterministic sensitivity analysis at 0% and 6%, in line with Thai methodological guidelines [20]. If the standard deviation or confidence interval was not available for a parameter, a standard error equivalent to the mean was used for analysis. The two models developed for this study are available upon request.

2.2 Measurement of Outcomes

Clinical parameters were identified through a review of international literature and national databases (Table 1). Pertussis incidence was taken from national surveillance data [8], but since pertussis incidence from surveillance data in Thailand is likely under-reported [9], we conducted one-way sensitivity analysis with the upper bound taken from the World Health Organization (WHO) global pertussis burden of disease study estimate for Thailand [2]. Given there is a factor of 50 difference between the WHO estimate and national surveillance data, we undertook a survey during a national stakeholder consultation to identify the appropriate pertussis incidence to use in the base analysis (OSM Resource 1). Probability of death was taken from the 2014 Thailand burden of disease [31] and deaths among cases of hospitalised pertussis were estimated from the national inpatient database, which includes records for all patients covered by the Universal Coverage Scheme, or around 72% of the Thai population [32]. Due to age classifications in the database, we assumed that proportion of deaths among infants aged 0–1 years was the same as for infants aged 0–3 months. For model 1, we were unable to obtain estimates for proportion of pertussis cases that are hospitalised, admitted to an intensive care unit (ICU), and result in long-term chronic sequelae from the inpatient database, so we averaged available data from Canada, New Zealand and the USA [19, 33, 34]. For model 2, proportion of cases with complications and associated death rates were derived from other economic evaluation studies [35–37].

Vaccine coverage was estimated to be the same as for maternal Td vaccination. For both infants and mothers, the model assumes that vaccine benefit comes from protection against infection without additional protection against severe disease or death.

For vaccine effectiveness in infants, we identified two recent systematic reviews of the effectiveness of maternal pertussis vaccination [50, 51]. Neither systematic review had conducted a meta-analysis. Upon reviewing the characteristics of studies included in these reviews, we identified three observational studies that aligned with our study population and intervention (infants aged 0–3 months, aP-containing vaccine administered to mother at 28–38 weeks' gestation). Two of the studies [52, 53] were assessed to be at serious risk of bias by one of the systematic reviews due to use of the screening method [50]. For this reason, we therefore selected a single study (a case control study from Australia [43]) for the vaccine effectiveness estimate instead of conducting a meta-analysis of the studies identified in the systematic reviews [54]. However, since the confidence intervals for this study are very large and the effectiveness estimates for infection much lower than other studies, we used values from the most recent screening study as the upper bound of vaccine effectiveness in the sensitivity analysis [52].

Our literature review did not identify any studies reporting vaccine effectiveness among pregnant women. We identified one meta-analysis on pertussis vaccine effectiveness and duration of protection across infants, adolescents, and adults [8], and one randomised controlled trial (RCT) on vaccine efficacy in adults [55]. Efficacy estimates from the RCT were much higher than vaccine effectiveness studies and only included 2.5 years' follow-up, whereas most studies suggest that duration of protection from vaccination in adolescents and adults lasts beyond 4 years [8]. In the meta-analysis, vaccine effectiveness estimates for adults (≥ 20 years) came from a single study, with very wide confidence intervals [56]. We therefore used the meta-analysis vaccine effectiveness estimates per year after vaccination from adolescents, based on six effectiveness studies with low heterogeneity.

All efficacy and effectiveness studies identified were for TdaP vaccine. The only studies identified on aP vaccine only reported immunogenicity data. It has been shown that there is non-inferiority of aP compared with

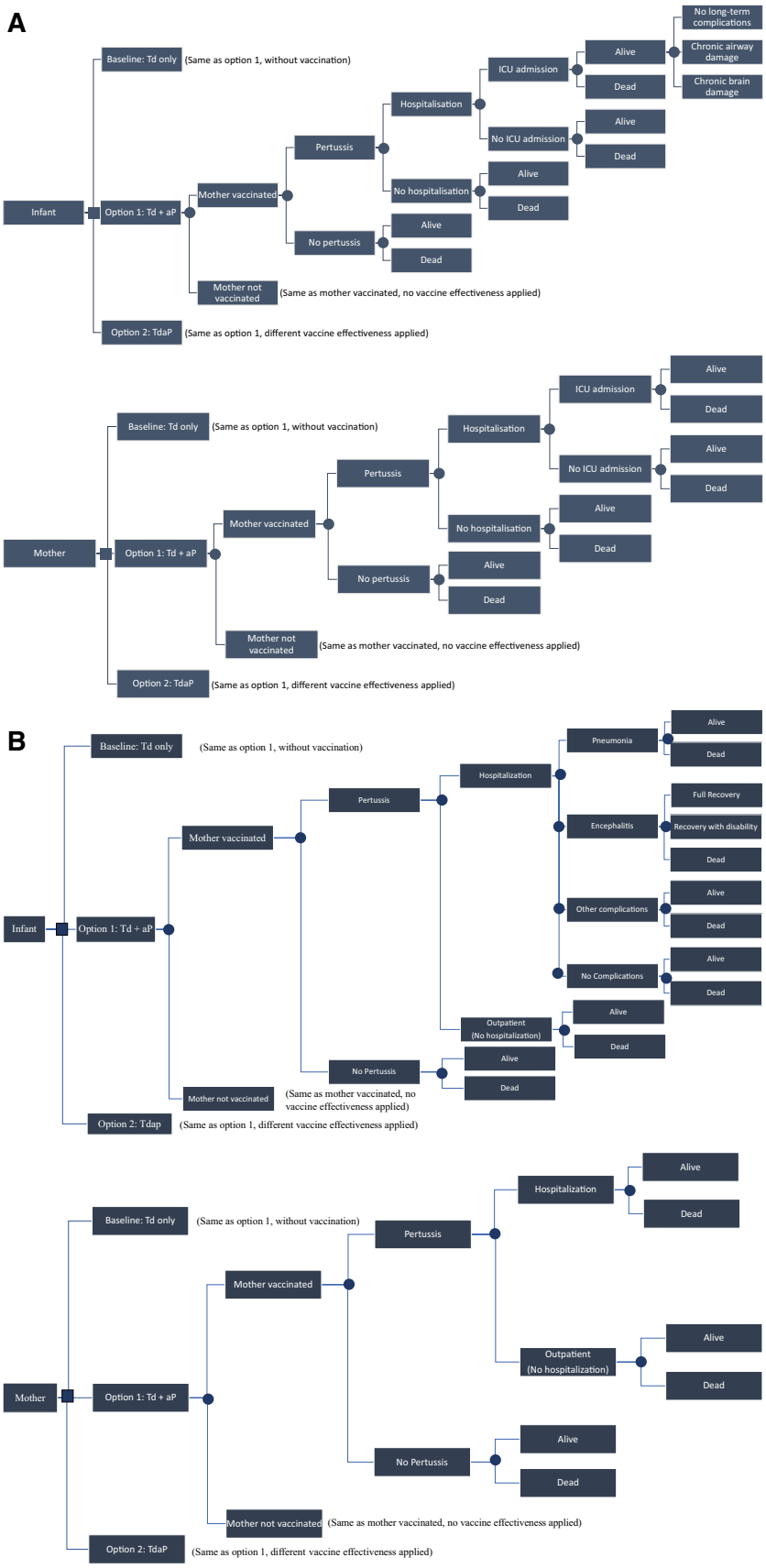

Fig. 1 Decision tree model structure for model 1 (base model) (**A**) and model 2 (structural uncertainty analysis) (**B**)

Table 1 Parameters used in models 1 and 2

Parameter	Mean	Standard error	Distribution	References
Clinical parameters				
Incidence of pertussis, 0–3 months	0.000378	0.000378	Beta	[8]
Incidence of pertussis, adults	0.000002	0.000002	Beta	[8]
Proportion of pertussis cases hospitalised, 0–3 months	0.656	0.190	Beta	[19, 33, 34]
Proportion of pertussis cases hospitalised, 18–45 years (female)	0.030	0.030	Beta	[34]
Relative risk of death from chronic brain damage	6.00	6.00		[38]
Probability of death (all causes), 0 years	0.009485	0.000116	Beta	[31]
Probability of death (all causes), 26 years (female)	0.000765	0.000018	Beta	[31]
Average age of childbirth in Thailand	25.100	0.019	Normal	[32]
Average duration of pertussis short-term respiratory complications, infants (weeks)	4.271	0.505	Gamma	[39]
Average duration of pertussis pneumonia, adults (days)	14.28	4.60	Gamma	[32]
Average length of hospital stay for pertussis, infant (days)	17.43	7.28	Gamma	[32]
Clinical parameters in model 1 only				
Proportion of pertussis hospitalisations admitted to ICU, 0–3 months	0.1	0.1	Beta	[33]
Proportion of pertussis hospitalisations admitted to ICU, 18–45 years (female)	0.1	0.1	Beta	Assumption
Incidence of chronic respiratory damage among ICU admissions, 0–3 months	0.033	0.033	Beta	[33]
Incidence of chronic airway damage among ICU admissions, 0–3 months	0.033	0.033	Beta	[33]
Probability of death among pertussis ICU admissions, 0–3 months	0.317	0.014	Beta	[32]
Probability of death among pertussis ICU admissions, 18–45 years (female)	0.933	0.029	Beta	[32]
Relative risk of death from chronic airway damage	1.00	1.00		[38]
Average length of hospital stay for pertussis, mother (days)	7.33	6.11	Gamma	[32]
Clinical parameters in model 2 only				
Proportion of pertussis hospitalisations with pneumonia, 0–3 months	0.23	0.005	Beta	[40]
Proportion of pertussis hospitalisations with encephalitis, 0–3 months	0.005	0.002	Beta	[40, 41]
Proportion of pertussis hospitalisations with other complications, 0–3 months	0.68	0.006	Beta	[40]
Probability of death from pertussis with pneumonia, 0–3 months	0.125	0.058	Beta	[35]
Probability of death from pertussis with encephalitis, 0–3 months	0.33	0.33	Beta	[35, 36]
Probability of death from pertussis with other complications, 0–3 months	0.01	0.001	Beta	Assumption
Probability of recovery with disability from pertussis with encephalitis, 0–3 months	0.33	0.142	Beta	[34, 35, 37]
Vaccine efficacy parameters				
Coverage of maternal vaccination	0.770	0.0005	Beta	[42]
aP vaccine effectiveness against pertussis infection, 0–3 months	0.690	0.194	Beta	[43]
aP vaccine effectiveness against pertussis infection 1st year after vaccination, adults	0.720	0.026	Beta	[30]
aP vaccine effectiveness against pertussis infection 2nd year after vaccination, adults	0.640	0.028	Beta	[30]
aP vaccine effectiveness against pertussis infection 3rd year after vaccination, adults	0.320	0.061	Beta	[30]
aP vaccine effectiveness against pertussis infection 4th year after vaccination, adults	0.420	0.112	Beta	[30]
aP vaccine effectiveness against pertussis infection 5th year after vaccination, adults	0.120	0.105	Beta	[30]
TdaP vaccine effectiveness against pertussis infection, 0–3 months	0.690	0.194	Beta	[43]
TdaP vaccine effectiveness against pertussis infection 1st year after vaccination, adults	0.720	0.026	Beta	[30]
TdaP vaccine effectiveness against pertussis infection 2nd year after vaccination, adults	0.640	0.028	Beta	[30]
TdaP vaccine effectiveness against pertussis infection 3rd year after vaccination, adults	0.320	0.061	Beta	[30]
TdaP vaccine effectiveness against pertussis infection 4th year after vaccination, adults	0.420	0.112	Beta	[30]
TdaP vaccine effectiveness against pertussis infection 5th year after vaccination, adults	0.120	0.105	Beta	[30]
Utility parameters				
Utility for pertussis short-term respiratory complications, infants	0.580	0.029	Beta	[44]
Utility for pertussis long-term neurological complications, infants	0.770	0.021	Beta	[44]

Table 1 (continued)

Parameter	Mean	Standard error	Distribution	References
Utility for pertussis short-term pneumonia, adults	0.820	0.035	Beta	[44]
Utility parameters for model 1 only				
Utility for pertussis long-term respiratory complications, infants	0.820	0.018	Beta	[44]
Utility parameters for model 2 only				
Utility for pertussis with short-term encephalitis, infants	0.51	0.029	Beta	[44]
Utility for pertussis without complications, infants	0.6	0.029	Beta	Assumption
Utility for pertussis with other complications, infants	0.58	0.029	Beta	Assumption
Utility for pertussis outpatient, infants	0.7	0.021	Beta	Assumption
Utility for pertussis outpatient, adults	0.85	0.031	Beta	Assumption
Length of stay in hospital without complications, infants (days)	16	4.07	Gamma	[32]
Length of stay in hospital with pertussis pneumonia, infants (days)	36	13.73	Gamma	[32]
Length of stay in hospital with pertussis encephalitis, infants (days)	11	3.60	Gamma	[32]
Length of stay in hospital with pertussis other complications, infants (days)	15	1.38	Gamma	[32]
Length of stay in hospital with pertussis, adults (days)	6	0.28	Gamma	[32]
Number of outpatient visits per pertussis episode, infants and adults	2	2	Gamma	[45]
Vaccine cost parameters (THB 2021)				
Td vaccine, price per dose	21.33			[46]
aP vaccine, price per dose	350			Manufacturer
TdaP vaccine, price per dose	550			Manufacturer
Td vaccine, wastage rate	0.41	0.13	Beta	[47]
aP vaccine, wastage rate	0.05	0.05	Beta	[47]
TdaP vaccine, wastage rate	0.05	0.05	Beta	[47]
Administration and service delivery cost per dose, maternal vaccination (includes syringe and safety box)	6.38	6.38	Gamma	[48]
Direct medical cost parameters (THB 2021)				
Chronic neurological damage, per year, aged 0–14 years	1814.61	37.60	Gamma	[38]
Chronic neurological damage, per year, aged 15–59 years	4988.52	61.43	Gamma	[38]
Chronic neurological damage, per year, aged ≥ 60 years	1325.05	77.69	Gamma	[38]
Direct medical cost parameters for model 1 only				
Hospitalised pertussis, per episode, aged 0 years	36,153	18,963	Gamma	[32]
Hospitalised pertussis, per episode, aged 18–45 years (female)	10,861	12,921	Gamma	[32]
Chronic respiratory damage, per year, aged 0–14 years	1533.91	1417.78	Gamma	[38]
Chronic respiratory damage, per year, aged 15–59 years	3611.10	62.61	Gamma	[38]
Chronic respiratory damage, per year, aged ≥ 60 years	3971.61	31.30	Gamma	[38]
Direct medical cost parameters for model 2 only				
Hospitalised pertussis, per episode, aged 18–45 years (female)	12,159.42	496.03	Gamma	[32]
Outpatient pertussis, infants and adults	312.81	312.81	Gamma	[32]
Hospitalised pertussis without complications, per episode, aged 0 years	27,716.75	10,478.61	Gamma	[32]
Hospitalised pertussis with pneumonia, per episode, aged 0 years	81,050.47	28,434.78	Gamma	[32]
Hospitalised pertussis with encephalitis, per episode, aged 0 years	24,214.85	11,882.64	Gamma	[32]
Hospitalised pertussis with other complications, per episode, aged 0 years	28,608.00	3534.54	Gamma	[32]
Direct non-medical cost parameters (THB 2021)				
Cost of travel per day	62.75	62.75	Gamma	[48]
Cost of food per day	170.36	170.36	Gamma	[48]
Chronic neurological damage, per year	20,146.28	20,146.28	Gamma	[38]
Direct non-medical cost parameters in model 1 only				
Chronic respiratory damage, per year	8,189.16	8,189.16	Gamma	[38]
Indirect cost parameters (THB 2021)				
Indirect cost parameters for model 1 only				
GDP per capita, Thailand 2020	146,586.55	N/A	Gamma	[49]

Table 1 (continued)

Parameter	Mean	Standard error	Distribution	References
Indirect cost parameters for model 2 only				
Loss of income per day, adults	323.89	323.89	Gamma	[48]

aP acellular pertussis, *GDP* gross domestic product, *ICU* intensive care unit, *Td* tetanus and reduced-dose diptheria, *THB* Thai Baht

TdaP in phase 2/3 trials [14]. We therefore assume equal vaccine effectiveness between aP and TdaP. Adverse events following immunisation (AEFI) have not been included in either health or cost outcomes, on the basis that pertussis vaccines have shown no contraindications aside from rare anaphylactic reactions [1, 16]. Furthermore, we assume maternal pertussis vaccination does not cause any blunting of the primary immunisation series. A study in Thailand did not find any evidence to suggest that blunting takes place [57, 58].

2.3 Valuation of Outcomes

No health state valuations were identified in the Thai population and it was not possible to conduct a direct measure of health state utility for pertussis due to COVID-19. We therefore used utility scores from a study in the USA that covered long- and short-term health states for pertussis infection in adults and infants [44]. For model 2, we were unable to identify utility weights for pertussis with other complications from either the literature or database of utility values [59]. We therefore assumed that all acute complications in infants had the same utility weight as short-term respiratory complications in infants. Since the QALYs for the acute period of illness contributed to less than 0.2% of the total QALYs for the other complications branch of the decision tree, this assumption was considered unlikely to substantially affect results.

2.4 Measurement and Valuation of Resources and Costs

All costs were transformed to 2021 THB values, using the exchange rate from the Bank of Thailand [60] and consumer price index (CPI) from the Bureau of Trade and Economic Indices [61]. Data on direct medical costs and length of stay for hospitalised cases were taken from the Thai inpatient database [32] and direct non-medical costs were estimated from length of stay and the Thai standard cost list database [48]. Annual direct costs for chronic conditions were taken from a cost-effectiveness study on pneumococcal vaccination in Thailand [38]. Only model 2 includes outpatient costs, which were taken from the cost list database [48]. In both models, indirect costs assume that, for hospitalised infants, one caregiver does not work for the full duration of hospital stay.

2.5 Uncertainty Analysis

Parameter uncertainty was investigated through deterministic sensitivity analysis, in which one parameter is varied at a time to identify the parameters with the greatest impact on results, and through probabilistic sensitivity analysis, for which a Monte Carlo simulation was run 9,614 times, for 95% confidence that the median is between the 49th and 51st percentile [62]. The probabilistic sensitivity analysis was presented as cost-effectiveness acceptability curves.

For the one-way deterministic sensitivity analysis, the upper and lower bounds were set at the 95% confidence intervals, except for parameters where the standard deviation was not available, in which case the upper and lower bounds were set as ± 20% of the mean, and for the following parameters: for hospitalisation rate, the maximum and minimum values identified from the literature were used (since the mean for hospitalisation rate was calculated as an average of data from other countries, for which the standard error was not available) (see Sect. 2.2); for vaccine effectiveness in infants the upper bound was set as the mean value from another study (since it was higher than the upper 95% confidence interval from the selected study) (see Sect. 2.2); for infant pertussis incidence the upper bound applied the estimation from the WHO burden of disease study (since it was in excess of the 95% confidence interval from national surveillance data) (see Sect. 2.2); and for vaccine price, in which the upper and lower bounds were either set at ± 20% of the price or at the reference price from competing manufacturers, whichever was more extreme (OSM Resource 2).

Structural uncertainty in terms of clinical pathway was assessed by comparing results with the alternative model structure outlined in Sect. 2.1. In the model comparison, care was taken to align the population, intervention, comparator, outcomes, study type, and time horizon, as well as parameters used [63].

Since this study is assessing a national level immunisation programme, we have not considered differences among sub-groups or differential distribution of impacts.

2.6 Expected Value of Perfect Information (EVPI)

We conducted expected value of perfect information (EVPI) analysis to understand whether data limitations in our analysis warrant the collection of additional information before a policy decision can be made. EVPI analysis estimates the monetary value of further data collection at a given cost-effectiveness threshold [64]. We considered both full EVPI, which considers all parameters simultaneously, as well as partial EVPI at the individual parameter level. Unlike deterministic sensitivity analysis, EVPI is based on probabilistic analysis and hence accounts for uncertainty distribution [64]. We estimated EVPI using an effective population equivalent to the number of pregnant women over a period of 5 years, using an outcome discount rate of 3%, under the assumption that the decision to introduce a vaccine and the available vaccine products would remain constant for the next 5 years. We ran the simulation 1000 times for full EVPI, applying the Thai cost-effectiveness threshold of 160,000 THB/QALY. For partial EVPI, we ran 50 cycles of the inner and outer loop at the cost-effectiveness threshold with maximum EVPI, in order to identify the parameters with the highest expected value of perfect information. For these parameters (pertussis incidence among infants, probability of hospital admission in infants, probability of ICU admission in infants, and vaccine effectiveness in infants), we repeated the analysis with 500 cycles for the inner and outer loops at the Thai cost-effectiveness threshold of 160,000 THB.

2.7 Model Validation

Face validation through a series of stakeholder consultation meetings was conducted to verify model structure and input parameters (OSM Resource 1). External validation was undertaken by comparing the results of model 1 and model 2, which showed good comparability, and by comparing estimated number of hospitalisations from each model with those observed in the inpatient database (Table 2). External validation suggests that both model 1 and model 2 may slightly underestimate the burden of pertussis.

2.8 Budget Impact Analysis

The budget impact analysis estimated the 5-year financial impact of a maternal pertussis vaccination programme, from a government payer perspective. There is no discounting of costs or health outcomes. We estimated number of pregnant women from annual number of hospital deliveries and number of infants from population estimates of the National Statistical Office of Thailand [32, 65]. The budget impact analysis used the same data for vaccine coverage, probability of infection and disease progression, and costs for vaccination and treatment as the cost-effectiveness analysis.

3 Results

3.1 Base Case

Table 3 presents the base-case analysis. The marginal health benefit for maternal pertussis vaccination is negligible, averting 27 cases and up to one death per year. This results in a very high ICER for both options, at 2,184,025 THB/QALY for adding aP vaccine to the existing Td vaccination programme and 3,198,101 THB/QALY for replacing the existing Td vaccine with TdaP. Since we assume aP and TdaP vaccines have the same efficacy, TdaP vaccine has a less favourable ICER due to its higher price. Less than 1% of incremental QALYs gained came from the mother.

3.2 Uncertainty Analysis

Results from the probabilistic sensitivity analysis Monte Carlo simulation are presented in Fig. 2. At the current vaccine price, both aP and TdaP are very unlikely to be cost-effective. This is also shown by the cost-effectiveness acceptability curves, which show that the current practice of providing Td only is an optimal choice (with probability to be cost-effective of more than 50%) at thresholds below 6,000,000 THB/QALY, almost 40 times greater than the Thai threshold (Fig. 3).

Table 2 Model validation against the Thai inpatient database, which covers around 70% of the Thai population

	Model estimates		Inpatient database: whooping cough or pneumonia due to *B. pertussis*	
	Model 1	Model 2	1° diagnosis	1° or 2° diagnosis
Cases per year	54	54	NA	NA
Hospitalisations per year	31	31	9	37
Deaths per year	1	1	0	2

Table 3 Health outcomes and incremental cost-effectiveness ratio for maternal pertussis vaccination (probabilistic analysis)

	Comparator: Td only	Option 1: Td + aP	Option 2: TdaP
Number of cases	54.2	26.6[a]	26.8[a]
Number of cases averted	–	27.6[a]	27.4[a]
Number of deaths	1.0	0.5	0.5
Number of deaths averted	–	0.5	0.5
Incremental QALY	–	0.00012895	0.00012968
Incremental cost (THB, provider perspective)	–	283	416
Incremental cost (THB, societal perspective)	–	282	415
ICER (THB/QALY gained, societal perspective)	–	2,184,025	3,198,101

aP acellular pertussis, *ICER* incremental cost-effectiveness ratio, *QALY* quality-adjusted life-years, *Td* tetanus and reduced dose diptheria, *THB* Thai Baht

[a]Difference in cases averted reflects a high level of parameter uncertainty in the probabilistic sensitivity analysis

In the one-way deterministic sensitivity analysis, infant pertussis incidence was the only parameter for which maternal pertussis immunisation became cost-effective (Fig. 4). With infant pertussis incidence at 0.02, adding aP vaccine to the maternal immunisation programme has an ICER of -8,080 THB/QALY (cost saving) and replacing Td vaccination with TdaP has an ICER of 11,330 THB/QALY.

We undertook threshold analysis for infant pertussis incidence, since this was the only parameter that influenced the most cost-effective intervention in the one-way deterministic sensitivity analysis, and for vaccine price. Adding aP vaccine to the existing vaccination programme becomes cost-effective when pertussis incidence is greater than a threshold of 397 cases per 100,000 infants (equivalent to 497 cases in Thailand per year) or aP vaccine price

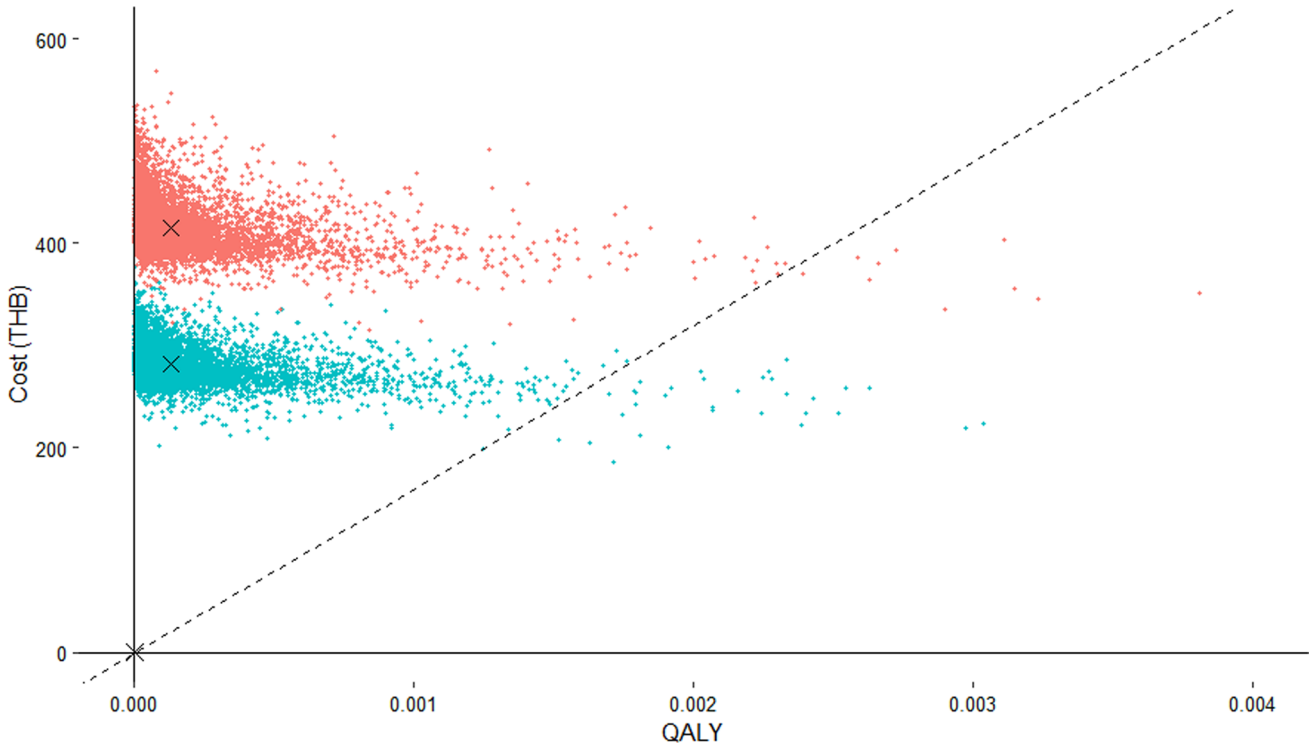

Fig. 2 Incremental cost-effectiveness ratio (ICER) plane showing results from the probabilistic sensitivity analysis. Each dot represents a single run of the Monte Carlo simulation. Blue dots represent Td + aP and red dots represent TdaP. The crosses show the results from the deterministic analysis as a reference and the black dashed line represents the Thai cost-effectiveness threshold of 160,000 THB/QALY

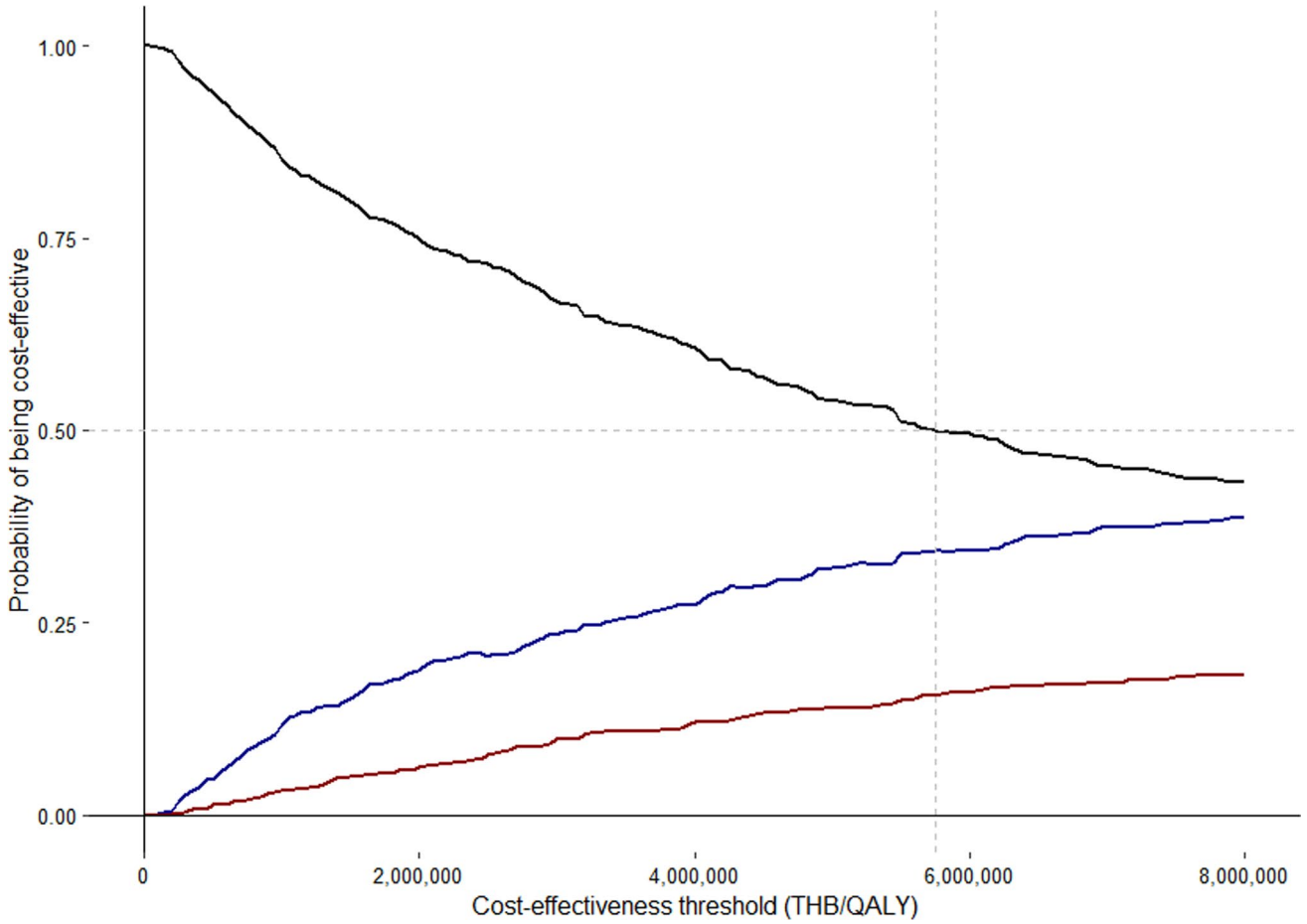

Fig. 3 Cost-effectiveness acceptability curves showing the probability of each option (Td—black, Td + aP—blue, TdaP—red) being the most cost-effective option at different cost-effectiveness thresholds

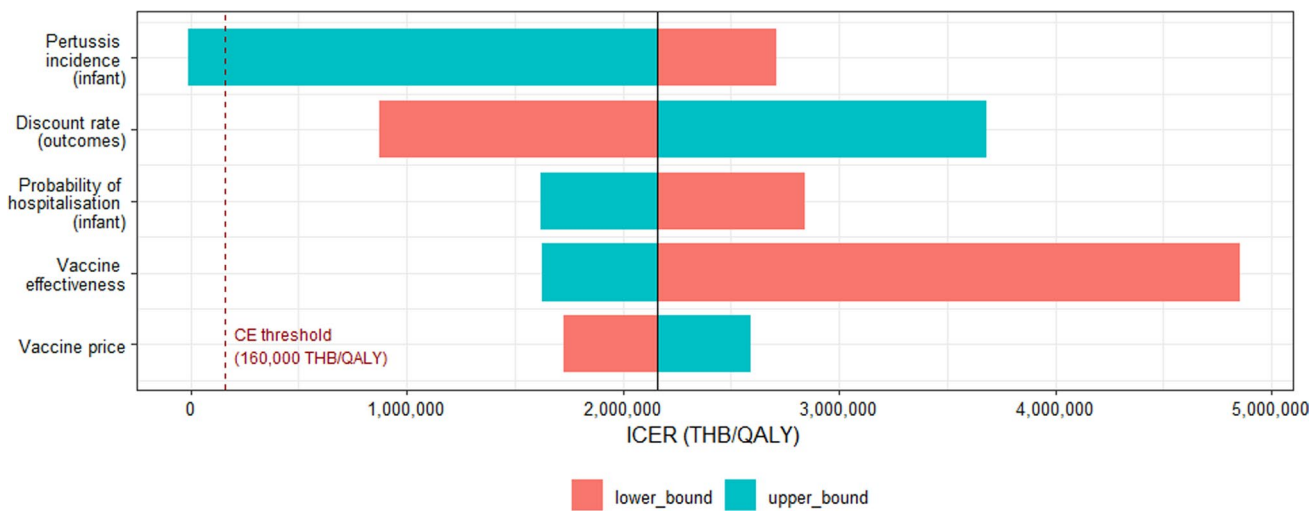

Fig. 4 Tornado diagram for one-way deterministic sensitivity analysis, showing the parameters for which the one-way deterministic sensitivity analysis showed the greatest decrease in ICER

is below a threshold of 27.77 THB per dose. Replacing Td vaccine with TdaP becomes cost-effective when TdaP price per dose is less than 62.55 THB. Since the upper bound for pertussis incidence in our sensitivity analysis has poor agreement with the number of pertussis hospitalisations in Thailand, we undertook a final threshold analysis of the lowest probability of hospitalisation for which the upper bound pertussis incidence is still cost-effective, on the premise that there may be significant under-reporting of non-hospitalised cases. We found that probability of hospitalisation would need to be above 0.13 for this scenario to remain cost-effective for option 1 (Td + aP), equivalent to 327 infant hospitalisations per year. This is more than eight times greater than the number of cases in the inpatient database (Table 2).

In this study, we only considered structural uncertainty in the clinical pathway, by comparing the results from two model structures. Table 4 compares the results from both models. The incremental cost and QALYs were very similar between the two model structures.

3.3 Expected Value of Perfect Information (EVPI) Analysis

At the Thai cost-effectiveness threshold of 160,000 THB/QALY, the full EVPI is equivalent to 2,409,099 THB. At the cost-effectiveness threshold of 160,000 THB/QALY, the partial EVPI of each parameter was zero, in agreement with the cost-effectiveness acceptability curves that there is a dominant strategy (Td only). This suggests that additional data collection will have no additional value for the policy recommendation.

Table 4 A comparison of model results using two different decision tree structures to reflect uncertainty in the clinical pathway for hospitalised pertussis in Thailand

	Model 1 (base model)		Model 2 (alternative clinical pathway)	
	aP	TdaP	aP	TdaP
Incremental cost (THB, societal perspective)	282	415	280	421
Incremental QALY	0.000129	0.000130	0.000128	0.000126
ICER (THB/QALY gained)	2,184,025	3,198,101	2,189,497	3,333,448

Table 5 Estimated additional vaccination budget required per year

Vaccines	Additional vaccination budget per year, THB (% routine vaccination programme budget, 2021 [66])
Option 1: Td + aP	206,719,251 (12.2%)
Option 2a: TdaP (Pertagen)	302,631,289 (17.8%)
Option 2b: TdaP (Boostrix)	206,336,284 (12.1%)

3.4 Budget Impact Analysis

It is estimated that the Thai government would have to allocate an additional budget of 1,030,598,553 THB for option 1 (Td + aP) and 1,510,158,748 THB for option 2 (TdaP), over a 5-year period. Treatment costs saved by vaccination are negligible, at around 3,000,000 THB (< 0.2%), compared to the additional cost of vaccination. The additional vaccination budget required per year is shown in Table 5.

In a scenario analysis, we considered the additional budget required for an alternative policy option. In this analysis, Td and aP were administered for the first pregnancy, but aP only for subsequent pregnancies. The reduction in 5-year budget impact was negligible at around 20,000,000 THB, or around 2% of total budget, due to the relatively low cost of the Td vaccine.

4 Discussion

To our knowledge, this is the first study evaluating cost-effectiveness of maternal pertussis vaccination to consider both aP and TdaP vaccines. Maternal pertussis vaccination was unlikely to be cost-effective at the current cost-effectiveness threshold in Thailand of 160,000 THB/QALY. Both delivering aP vaccine at the same time as Td vaccination, as well as replacing Td with TdaP for vaccinating pregnant women, were very cost-ineffective, at over 2 million THB/QALY gained. More than 99% of QALYs gained from vaccination were from health gains in infants, suggesting that, in settings with reduced capacity or resources for modelling, researchers may wish to focus on infant health outcomes only.

Unique to this study, we conducted model comparison with the same policy question and parameters, but different model structure, in order to address structural uncertainty related to clinical progression. There was good concordance between the results of the two models, which is likely due to the very low number of deaths and chronic conditions from pertussis infection, even in the scenario with highest pertussis incidence, and the very high vaccination costs in relation to treatment costs at the population level, both of which would be expected to minimise the effect of differences in clinical progression of the disease after hospitalisation. Although this suggests a minor

impact of decision tree model structure on results, model differences may be more significant in settings with higher burden of disease or treatment costs.

The partial EVPI analysis did not show any additional benefit of collecting further information. The deterministic sensitivity analysis showed that only uncertainty around pertussis incidence in infants could alter whether maternal pertussis immunisation is cost-effective. In the base case, we used incidence data from national epidemiological surveillance, since this was favoured by national experts in the expert elicitation exercise (OSM Resource 1). However, surveillance data is expected to substantially underestimate the incidence of pertussis [9, 67]. This is corroborated by studies in infants with prolonged cough or severe pneumonia in Thailand [12, 68]. Other cost-effectiveness studies also identified incidence as a major driver of ICER [18, 29] and it is common for studies to use an adjustment factor to account for under-reporting [6]. We therefore conducted sensitivity analysis using the WHO global pertussis burden of disease study estimated incidence in Thailand, of 2000 cases per 100,000, using an equation based on DTP vaccine coverage [2, 67]. Whilst the sensitivity analysis initially seemed to suggest that maternal immunisation may be cost-effective with higher pertussis incidence, comparison with hospitalised pertussis cases in Thailand suggests that, if the true incidence is indeed closer to 2000 cases per 100,000, the majority of under-reported cases are not hospitalised, in which case even with substantial under-reporting of pertussis cases, maternal immunisation would remain cost ineffective. However, we should recognise a limitation of using hospitalisation data to validate our model. We considered a variety of ICD-10 TM codes in our analysis, to account for unclassified bacterial pneumonia and whooping cough, thus the range of potential number of hospitalisations per year was too broad to suggest which incidence is most likely to be representative of the true rate.

Our study assumes that vaccination protects against infection but does not affect the severity of infection. A number of studies suggest that the pertussis vaccine is more protective against severe disease [43, 50, 51, 69], but this may be due to greater specificity in case definition [30]. If vaccination does have a greater protective effect against hospitalisation and death, this would have slightly underestimated the cost-effectiveness. We also made the assumption that TdaP and aP vaccines do not differ in effectiveness. Only non-inferiority immunogenicity data are available for aP vaccine [14], and further research is required to demonstrate non-inferiority in phase 3 studies.

Our study has three limitations related to structural uncertainty that we were not able to capture through our model comparison. Firstly, we only considered policy options in which the same vaccine is given to all pregnant women, and not policy options to only deliver aP in subsequent pregnancies. This decision was taken in light of evidence of waning of Td antibodies within 1 year of vaccination [70, 71], however the scenario analysis for the budget impact analysis suggests that cost savings for this alternative policy option would be minimal due to the low price of Td vaccine. Furthermore, although we adhered to the Thai cost-effectiveness guidelines, uncertainty analysis showed that the discount rate applied for outcomes had a significant impact on results. Lastly, we chose to use a static model. A comparison of maternal pertussis vaccination cost-effectiveness studies in LMICs found that static models may overestimate cost-effectiveness in countries with DTP coverage over 90%, since there is no incorporation of herd effects [17]. However, another review concluded that static models are adequate to evaluate maternal pertussis vaccination [6]. It is likely that any overestimation resulting from the use of a static model is minor, as the ICER from the base case in our study is comparable to other cost-effectiveness studies, including those using static and those using dynamic models, when converted to 2021 THB [18, 19, 25, 29, 72, 73]. Although most other studies conclude that maternal pertussis vaccination is cost-effective, this is due to a higher cost-effectiveness threshold in other countries.

5 Conclusion

Maternal pertussis vaccination is one of a set of expensive vaccines that were proposed in 2021 for introduction in Thailand, alongside PCV vaccination and a second dose of IPV. Although we did not find maternal pertussis immunisation to be cost-effective, the final policy decision may be based on other considerations such as affordability, potential impact on local manufacturing capacity, or preventing outbreaks in border areas with high migration. The only available aP vaccine is manufactured in Thailand, and one of the TdaP vaccines is manufactured in Thailand with some components from Indonesia. It was therefore argued during the stakeholder consultation that there may be a considerable benefit to the economy in procuring the new vaccine, as well as potentially broader benefits for vaccine security through growing the vaccine manufacturing sector in Thailand and generating revenue for local research and development of new vaccines. However, given the vaccine is not cost-effective, it may be a better use of resources to focus on other locally manufactured vaccine products.

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Declarations

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Data availability The two models developed for this study are available upon request.

Code availability Not applicable.

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References

1. World Health Organization. Pertussis vaccines: WHO position paper—August 2015. Geneva. 2015. https://www.who.int/publications/i/item/who-position-paper-pertussis-vaccines. Accessed 20 Jan 2022.
2. Yeung KHT, Duclos P, Nelson EAS, et al. An update of the global burden of pertussis in children younger than 5 years: a modelling study. Lancet Infect Dis. 2017;17:974–80. https://doi.org/10.1016/S1473-3099(17)30390-0.
3. Plotkin SA, Orenstein WA, Offit PA. *Plotkin's vaccines*. 7th ed. Philadelphia. 2017.
4. Leuridan E, Hens N, Peeters N, et al. Effect of a prepregnancy pertussis booster dose on maternal antibody titers in young infants. Pediatric Infect Dis J. 2011;30:608–10. https://doi.org/10.1097/INF.0b013e3182093814.
5. Munoz FM, Bond NH, Maccato M, et al. Safety and immunogenicity of tetanus diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants. JAMA. 2014;311:1760. https://doi.org/10.1001/jama.2014.3633.
6. Fernandes EG, Rodrigues CCM, Sartori AMC, et al. Economic evaluation of adolescents and adults' pertussis vaccination: A systematic review of current strategies. Hum Vaccin Immunother. 2019;15:14–27. https://doi.org/10.1080/21645515.2018.1509646/SUPPL_FILE/KHVI_A_1509646_SM6108.DOCX.
7. Blackwood JC, Cummings DAT, Broutin H, et al. Deciphering the impacts of vaccination and immunity on pertussis epidemiology in Thailand. Proc Natl Acad Sci USA. 2013;110:9595. https://doi.org/10.1073/PNAS.1220908110.
8. Department of Disease Control. หน้าแรก | กรมควบคุมโรค. 2022. https://ddc.moph.go.th/disease_detail.php?d=29. Accessed 31 Jan 2022.
9. Thisyakorn U, Tantawichien T, Thisyakorn C, et al. Pertussis in the Association of Southeast Asian Nations: epidemiology and challenges. Int J Infect Dis. 2019;87:75–83. https://doi.org/10.1016/J.IJID.2019.07.016.
10. Koh MT, Liu CS, Chiu CH, et al. Under-recognized pertussis in adults from Asian countries: a cross-sectional seroprevalence study in Malaysia, Taiwan and Thailand. Epidemiol Infect. 2016;144:1192–200. https://doi.org/10.1017/S0950268815002393.
11. Siriyakorn N, Leethong P, Tantawichien T, et al. Adult pertussis is unrecognized public health problem in Thailand. BMC Infect Dis. 2016;2016:16. https://doi.org/10.1186/S12879-016-1357-X.
12. Suntarattiwong P, Kanjanabura K, Laopipattana T, et al. Pertussis surveillance in a children hospital in Bangkok, Thailand. Int J Infect Dis. 2019;81:43–5. https://doi.org/10.1016/J.IJID.2019.01.031.
13. Infectious Disease Association of Thailand. 2022. https://www.idthai.org/. Accessed 11 Apr 2022.
14. Sricharoenchai S, Sirivichayakul C, Chokephaibulkit K, et al. A genetically inactivated two-component acellular pertussis vaccine, alone or combined with tetanus and reduced-dose diphtheria vaccines, in adolescents: a phase 2/3, randomised controlled non-inferiority trial. Lancet Infect Dis. 2018;18:58–67. https://doi.org/10.1016/S1473-3099(17)30612-6.
15. Pitisuttithum P, Chokephaibulkit K, Sirivichayakul C, et al. Antibody persistence after vaccination of adolescents with monovalent and combined acellular pertussis vaccines containing genetically inactivated pertussis toxin: a phase 2/3 randomised, controlled, non-inferiority trial. Lancet Infect Dis. 2018;18:1260–8. https://doi.org/10.1016/S1473-3099(18)30375-X.
16. Fortuna L, Chaithongwongwatthana S, Soonthornworasiri N, et al. Enhanced post-licensure safety surveillance of a new recombinant acellular pertussis vaccine licensed as a monovalent (aP, Pertagen®) and tetanus, reduced-dose diphtheria

combination (TdaP, Boostagen®) vaccine for immunization of adolescents and adults in Thailand. Vaccine. 2020;38:8194–9. https://doi.org/10.1016/J.VACCINE.2020.10.070.
17. Russell LB, Sobanjo-ter Meulen A, Toscano CM. Evaluating the cost-effectiveness of maternal pertussis immunization in low- and middle-income countries: a review of lessons learnt. Vaccine. 2021;39:121–4. https://doi.org/10.1016/J.VACCINE.2020.10.054.
18. Hoshi S, Seposo X, Okubo I, et al. Cost-effectiveness analysis of pertussis vaccination during pregnancy in Japan. Vaccine. 2018;36:5133–40. https://doi.org/10.1016/J.VACCINE.2018.07.026.
19. Abu-Raya B, Coyle D, Bettinger JA, et al. Pertussis vaccination in pregnancy in Canada: a cost-utility analysis. Can Med Assoc Open Access J. 2020;8:E651–8. https://doi.org/10.9778/CMAJO.20200060.
20. Guidelines for Health Technology Assessment in Thailand (Second Edition). J Med Assoc Thailand. 2014;97:5.
21. Husereau D, Drummond M, Augustovski F, et al. Consolidated health economic evaluation reporting standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. Pharmacoeconomics. 2022;40:601–9. https://doi.org/10.1007/S40273-021-01112-8/TABLES/1.
22. Adeagbo CU, Rattanavipapong W, Guinness L, et al. The development of the guide to economic analysis and research (GEAR) online resource for low- and middle-income countries' health economics practitioners: a commentary. Value Health. 2018;21:569–72. https://doi.org/10.1016/J.JVAL.2017.10.003.
23. Petrou S, Gray A. Economic evaluation using decision analytical modelling: design, conduct, analysis, and reporting. BMJ. 2011;2011:342. https://doi.org/10.1136/BMJ.D1766.
24. Sartori AMC, de Soárez PC, Fernandes EG, et al. Cost-effectiveness analysis of universal maternal immunization with tetanus-diphtheria-acellular pertussis (Tdap) vaccine in Brazil. Vaccine. 2016;34:1531–9. https://doi.org/10.1016/j.vaccine.2016.02.026.
25. Westra TA, de Vries R, Tamminga JJ, et al. Cost-effectiveness analysis of various pertussis vaccination strategies primarily aimed at protecting infants in the Netherlands. Clin Ther. 2010;32:1479–95. https://doi.org/10.1016/J.CLINTHERA.2010.07.017.
26. Kilgore PE, Salim AM, Zervos MJ, et al. Pertussis: microbiology, disease, treatment, and prevention. Clin Microbiol Rev. 2016;29:449. https://doi.org/10.1128/CMR.00083-15.
27. Kline JM, Lewis WD, Smith EA, et al. Pertussis: a reemerging infection. Am Fam Physician 2013;88:507–14. www.aafp.org/afp. Accessed 21 Jan 2022.
28. UNICEF/WHO. WHO immunization data portal. 2021. https://immunizationdata.who.int/pages/profiles/tha.html. Accessed 20 Jan 2022.
29. van Hoek AJ, Campbell H, Amirthalingam G, et al. Cost-effectiveness and programmatic benefits of maternal vaccination against pertussis in England. J Infect. 2016;73:28–37. https://doi.org/10.1016/J.JINF.2016.04.012.
30. Wilkinson K, Righolt CH, Elliott LJ, et al. Pertussis vaccine effectiveness and duration of protection—a systematic review and meta-analysis. Vaccine. 2021;39:3120–30. https://doi.org/10.1016/J.VACCINE.2021.04.032.
31. IHPP. Lifetable—2014 Burden of Disease (Thailand). Nonthaburi. 2014.
32. National Health Security Office. Inpatient database. Bangkok. 2021.
33. Pertussis. Starship clinical guidelines. 2014. https://starship.org.nz/guidelines/pertussis/. Accessed 7 Feb 2022.
34. Centers for Disease Control and Prevention. Pertussis: clinical complications|CDC. 2019. https://www.cdc.gov/pertussis/clinical/complications.html. Accessed 21 Jan 2022.
35. Koplan JP, Schoenbaum SC, Weinstein MC, et al. Pertussis vaccine—an analysis of benefits, risks and costs. N Engl J Med. 1979;301:906–11. https://doi.org/10.1056/NEJM197910253011703.
36. Thampi N, Gurol-Urganci I, Crowcroft NS, et al. Pertussis post-exposure prophylaxis among household contacts: a cost-utility analysis. PLoS ONE. 2015;10: e0119271. https://doi.org/10.1371/journal.pone.0119271.
37. Caro JJ, Getsios D, El-Hadi W, et al. Pertussis immunization of adolescents in the United States. Pediatric Infect Dis J. 2005;24:S75-82. https://doi.org/10.1097/01.inf.0000160918.72953.51.
38. Kulpeng W, Leelahavarong P, Rattanavipapong W, et al. Cost-utility analysis of 10- and 13-valent pneumococcal conjugate vaccines: protection at what price in the Thai context? Vaccine. 2013;31:2839–47. https://doi.org/10.1016/J.VACCINE.2013.03.047.
39. Narkeviciute I, Kavaliunaite E, Bernatoniene G, et al. Clinical presentation of pertussis in fully immunized children in Lithuania. BMC Infect Dis. 2005;5:40. https://doi.org/10.1186/1471-2334-5-40.
40. Bettinger JA, Halperin SA, de Serres G, et al. The effect of changing from whole-cell to acellular pertussis vaccine on the epidemiology of hospitalized children with pertussis in Canada. Pediatric Infect Dis J. 2007;26:31–5. https://doi.org/10.1097/01.inf.0000247055.81541.04.
41. Barger-Kamate B, Knoll MD, Kagucia EW, et al. Pertussis-associated pneumonia in infants and children from low- and middle-income countries participating in the PERCH study. Clin Infect Dis. 2016;63:S187–96. https://doi.org/10.1093/CID/CIW546.
42. National Statistics Office of Thailand. Thailand Multiple Indicator Cluster Survey 2019, Snapshots of Key Findings Report. Bangkok. 2020. https://mics-surveys-prod.s3.amazonaws.com/MICS6/East%20Asia%20and%20the%20Pacific/Thailand/2019/Snapshots/Thailand%202019%20MICS%20Statistical%20Snapshots_English.pdf. Accessed 20 Jan 2022.
43. Saul N, Wang K, Bag S, et al. Effectiveness of maternal pertussis vaccination in preventing infection and disease in infants: the NSW Public Health Network case-control study. Vaccine. 2018;36:1887–92. https://doi.org/10.1016/J.VACCINE.2018.02.047.
44. Lee GM, Salomon JA, LeBaron CW, et al. Health-state valuations for pertussis: methods for valuing short-term health states. Health Qual Life Outcomes. 2005;3:1–14. https://doi.org/10.1186/1477-7525-3-17/TABLES/6.
45. Mongkonchoo K, Yamana H, Aso S, et al. Prediction of outpatient visits and expenditure under the Universal Coverage Scheme in Bangkok using subscriber's attributes: a random forest analysis. Public Health in Practice. 2021;2: 100190. https://doi.org/10.1016/J.PUHIP.2021.100190.
46. FDA Thailand. Medicines Regulation Division. Drug—Vaccine_SPC-Name. 2022. https://www.fda.moph.go.th/sites/drug/SitePages/Vaccine_SPC-Name.aspx. Accessed 1 Mar 2022.
47. Yoocharoen P, Chuanark P, Kattiya U, et al. Impact of vaccine wastage rate on national vaccine management and immunization schedule: a case study of DTP, DTP-HB and DTP-HB-Hib vaccine. Dis Control J. 2021;47:230–45. https://doi.org/10.14456/DCJ.2021.21.

48. Health Intervention and Technology Assessment Program (HITAP). Standard Cost List for Health Technology Assessment. 2010. https://costingmenu.hitap.net/. Accessed 20 Jan 2022.
49. The World Bank. GDP per capita (constant LCU)—Thailand|Data. 2021. https://data.worldbank.org/indicator/NY.GDP.PCAP.KN?locations=TH. Accessed 20 Jan 2022.
50. Vygen-Bonnet S, Hellenbrand W, Garbe E, et al. Safety and effectiveness of acellular pertussis vaccination during pregnancy: a systematic review. BMC Infect Dis. 2020;20:1–22. https://doi.org/10.1186/S12879-020-4824-3/TABLES/3.
51. Kandeil W, van den Ende C, Bunge EM, et al. A systematic review of the burden of pertussis disease in infants and the effectiveness of maternal immunization against pertussis. Expert Rev Vaccines. 2020;19:621–38. https://doi.org/10.1080/14760584.2020.1791092/SUPPL_FILE/IERV_A_1791092_SM4935.DOCX.
52. Amirthalingam G, Campbell H, Ribeiro S, et al. Sustained effectiveness of the maternal pertussis immunization program in England 3 years following introduction. Clin Infect Dis. 2016;63:S236–43. https://doi.org/10.1093/CID/CIW559.
53. Amirthalingam G, Andrews N, Campbell H, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. Lancet. 2014;384:1521–8. https://doi.org/10.1016/S0140-6736(14)60686-3.
54. Saint S, Veenstra DL, Sullivan SD. The use of meta-analysis in cost-effectiveness analysis. Pharmacoeconomics. 1999;15:1–8. https://doi.org/10.2165/00019053-199915010-00001.
55. Ward JI, Cherry JD, Chang S-J, et al. Efficacy of an acellular pertussis vaccine among adolescents and adults. N Engl J Med. 2005;353:1555–63. https://doi.org/10.1056/NEJMOA050824/SUPPL_FILE/NEJM_WARD_1555SA1.PDF.
56. Bell CA, Russell ML, Drews SJ, et al. Acellular pertussis vaccine effectiveness and waning immunity in Alberta, Canada: 2010–2015, a Canadian Immunization Research Network (CIRN) study. Vaccine. 2019;37:4140–6. https://doi.org/10.1016/J.VACCINE.2019.05.067.
57. Wanlapakorn N, Maertens K, Thongmee T, et al. Levels of antibodies specific to diphtheria toxoid, tetanus toxoid, and Haemophilus influenzae type b in healthy children born to Tdap-vaccinated mothers. Vaccine. 2020;38:6914–21. https://doi.org/10.1016/J.VACCINE.2020.08.058.
58. Wanlapakorn N, Thongmee T, Vichaiwattana P, et al. Antibodies to Bordetella pertussis antigens in maternal and cord blood pairs: a Thai cohort study. PeerJ. 2017;2017:2017. https://doi.org/10.7717/PEERJ.4043/SUPP-1.
59. Center for the evaluation of value and risk in health. CEA Registry. 2022. https://cevr.tuftsmedicalcenter.org/databases/cea-registry. Accessed 11 Apr 2022.
60. Bank of Thailand. Bank of Thailand (Statistical Data) FM_FX_001_S3 rates of exchange of commercial banks in Bangkok Metropolis. 2002. https://www.bot.or.th/App/BTWS_STAT/statistics/ReportPage.aspx?reportID=123&language=eng. Accessed 28 Jan 2022.
61. Bureau of Trade and Economic Indices. Consumer Price Index (CPI). 2022. http://www.price.moc.go.th/price/cpi/index_new_e.asp. Accessed 31 Jan 2022.
62. Morgan MG, Henrion M. Uncertainty: a guide to dealing with uncertainty in quantitative risk and policy analysis. Cambridge Univ Press. 1990. https://doi.org/10.1017/CBO9780511840609.
63. den Boon S, Jit M, Brisson M, et al. Guidelines for multi-model comparisons of the impact of infectious disease interventions. BMC Med. 2019;17:1–13. https://doi.org/10.1186/S12916-019-1403-9/FIGURES/2.
64. Sculpher M, Claxton K. Establishing the cost-effectiveness of new pharmaceuticals under conditions of uncertainty–when is there sufficient evidence? Value Health. 2005;8:433–46. https://doi.org/10.1111/J.1524-4733.2005.00033.X.
65. National Statistical Office. 1 demography population and housing branch. 2021. http://statbbi.nso.go.th/staticreport/page/sector/en/01.aspx. Accessed 11 Apr 2022.
66. Kumdee C. Policy Brief No. 109: Recommendations on budget management to give thai people free and timely access to basic vaccines. Nonthaburi. 2021. https://www.hitap.net/documents/182272. Accessed 5 Sep 2022.
67. Crowcroft NS, Stein C, Duclos P, et al. How best to estimate the global burden of pertussis? Lancet Infect Dis. 2003;3:413–8. https://doi.org/10.1016/S1473-3099(03)00669-8.
68. O'Brien KL, Baggett HC, Brooks WA, et al. Causes of severe pneumonia requiring hospital admission in children without HIV infection from Africa and Asia: the PERCH multi-country case-control study. Lancet. 2019;394:757–79. https://doi.org/10.1016/S0140-6736(19)30721-4.
69. McNamara LA, Skoff T, Faulkner A, et al. Reduced severity of pertussis in persons with age-appropriate pertussis vaccination—United States, 2010–2012. Clin Infect Dis. 2017;65:811–8. https://doi.org/10.1093/CID/CIX421.
70. Halperin SA, Langley JM, Ye L, et al. A randomized controlled trial of the safety and immunogenicity of tetanus, diphtheria, and acellular pertussis vaccine immunization during pregnancy and subsequent infant immune response. Clin Infect Dis Tdap Vaccine During Pregnancy. 2018;2018:1063. https://doi.org/10.1093/cid/ciy244.
71. Raya BA, Srugo I, Kessel A, et al. The decline of pertussis-specific antibodies after tetanus, diphtheria, and acellular pertussis immunization in late pregnancy. Published Online First. 2015. https://doi.org/10.1093/infdis/jiv324.
72. Terranella A, Asay GRB, Messonnier ML, et al. Pregnancy dose tdap and postpartum cocooning to prevent infant pertussis: a decision analysis. Pediatrics. 2013;131:e1748–56. https://doi.org/10.1542/PEDS.2012-3144.
73. Atkins KE, Fitzpatrick MC, Galvani AP, et al. Cost-effectiveness of pertussis vaccination during pregnancy in the United States. Am J Epidemiol. 2016;183:1159–70. https://doi.org/10.1093/AJE/KWV347.