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Addressing Pertussis Outbreaks in the Deep South of Thailand, 2024: a Comparative Cost-effectiveness Study of Various Vaccination Coverage Strategies

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Abstract

Pertussis outbreaks continue to challenge public health efforts in the Deep South of Thailand. Low vaccination coverage is among many key contributory factors. The objective of this study is to explore policy alternatives aiming to expand vaccination coverage in Thailand's Deep South. We applied a compartmental model alongside rapid cost-effectiveness analysis to examine how different vaccination strategies impact pertussis cases and associated costs. Four vaccination scenarios with varying coverage levels (ranging from 62% to 91% within a 120-day timeframe) were compared against a scenario with the baseline vaccine coverage (61%). With a reproduction number (R_0) of five, the model predicted a remarkable decrease in pertussis cases and fatalities as the vaccination coverage increases. All scenarios yielded cost-saving outcomes, with the scenario of an increase of 10% coverage being the most cost-effective relative to the status quo. However, in high epidemic states (R_0=6), the scenario of an increase of 30% coverage was the most optimal for cost-saving in deaths prevention. These results highlight the need for expedite vaccine roll-out and the integration of non-pharmaceutical interventions for pertussis control. Further studies that explore various aspects of the model while incorporating more intricate parameters are recommended.

Keywords: pertussis, vaccine coverage, vaccine-effectiveness, cost-effectiveness

Introduction

Pertussis is a highly contagious respiratory disease caused by *Bordetella pertussis* (*B. pertussis*).[1,2] It usually begins with common-cold-like symptoms, but the coughing can last for weeks or months and symptoms may include typical symptoms such as paroxysmal cough, inspiratory whooping, post-pertussis vomiting, or apnea in children aged less than one year.[3] Its common transmission route is by person-to-person direct contact through respiratory droplets or contact with airborne droplets.[4] People of all ages can be infected but children less than one year are the most vulnerable and are prone to complications.[3–5]

Pertussis is a vaccine-preventable disease. In Thailand, the Expanded Program on Immunization schedules five doses of diphtheria and tetanus toxoids, whole-cell pertussis (DTwP) vaccine at 2, 4, 6, 18 months, and 4–6 years of age, and Tetanus toxoid and lower dose of diphtheria and acellular pertussis vaccines (Tdap) is recommended for children aged over seven years and adults and pregnant women with 27–36 weeks gestational age.[6–8] Vaccine effectiveness (VE) after five doses ranged from 98% in the first 12 months to 71% by five years.[9] The VE of three doses of diphtheria-tetanus-pertussis vaccines (DTP) was 83.5% (95% confidence interval (CI) 79.1–87.8%) between 6–11 months following the last dose of immunization.[10] Immunity against pertussis will last about 5–7 years.[6] Children who have a history of vaccination will get milder symptoms when infected.[6]

In the latter half of 2023, the incidence of pertussis cases in Thailand continued to rise and exceeded the 5-year median. The majority of cases (307/323) were found in the Deep South of Thailand (three southernmost provinces, namely, Narathiwat, Pattani,

and Yala).[11] Many outbreak clusters occurred in these provinces in late 2023. For example, two clusters of pertussis occurred in Pattani with over 30 cases involved in both clusters combined.[12–14] The age range of the cases varied from 18 days to 53 years. Both clusters occurred among household and community contacts. The age-appropriate DTP vaccine coverage in the outbreak villages ranged from 43.0% to 70.5%.

The low DTP vaccine coverage remains a major problem of pertussis outbreaks in the Deep South of Thailand. This region has experienced pertussis outbreaks and continues to exhibit low rates of pertussis vaccine adoption. Data from the Health Data Center, Ministry of Public Health (MOPH), Thailand showed that the vaccine coverage of first dose, third dose, and fifth dose DTP in these provinces in 2023 ranged between 70–81%, 37–66%, and 34–70%, respectively. These figures were lower than the national target vaccine coverage (90%).[15]

The Division of Epidemiology and the Division of Communicable Diseases of the Department of Disease Control (DDC) of the MOPH are the main responsible authorities for halting the increasing trend of pertussis. One of the key action points is to expedite the vaccination rate for people in Thailand's Deep South region. Thus, it is imperative to assess the outcomes of vaccine programs in different coverage scenarios through both the public health and economic lens. Therefore, the objective of this study is to assess a scenario-based prediction of the number of cases and deaths by pertussis and cost-effectiveness in different vaccine coverage scenarios.

Methods

Study Design

We used the susceptible-infectious-recovered model combined with cost-effectiveness analysis.[16] Our study encompassed around two million residents of all ages in the provinces of Thailand's Deep South, as mentioned above. At the time of our investigation, the overall coverage for primary vaccination (3-dose DTP) across all ages in this region was 61%, with an average vaccination rate of about 50 individuals per day. Under the status quo, the projected vaccine coverage over the next 120 days would increase by merely one percent.

Our focus on the 3-dose primary vaccination stemmed from the necessity for infants to receive three doses of the DTP vaccine to establish robust pertussis immunity. Thus, we aimed to complete the 3-dose primary vaccination to enhance immunity, with effectiveness typically ranging between 80–99% after completion.[17] However, the vaccine campaign in this study targeted all age groups, assuming that anyone with an incomplete DTP vaccination regimen could be vaccinated. Our target vaccination period spanned 120 days, aligning with the recommended interval for completing primary vaccinations, as per the Expanded Program on Immunization schedule administered.[8]

To assess vaccine coverage policy options, we categorized policies into four scenarios: Scenario 1—maintaining the current vaccination rate, leading to 62% coverage in 120 days, Scenario 2—raising coverage to 70% (a 10% increase) in the same period, Scenario 3—reaching 80% coverage (a 20% increase) within 120 days, and Scenario 4—achieving 90% coverage (a 30% increase) within the timeframe. Notably, the baseline complete 3-dose vaccine coverage at the start of the analysis was 61%. Table 1 summarizes these scenarios.

Figure 1 shows epidemic dynamics using a stock and flow diagram, with transitions between stocks governed by differential equations. Populations in each stock were determined by integrating functions over the flows. The transition from susceptible to infectious primarily depended on the basic reproductive number (R_0). Susceptible individuals were divided into those with incomplete and complete 3-dose vaccinations. Incomplete vaccination individuals either completed their vaccinations or stayed in the incomplete group. The rate of transition to the vaccination strand was governed by the frequency at which individuals were scheduled for immunization, reflecting the average vaccination rate in the population and the target vaccination period of 120 days. For model simplicity, the complete vaccinated population also incorporated those who already received booster doses.

Table 1. Summary of policy scenarios for primary vaccination for the Deep South of Thailand (all ages)

Scenario	Percentage increase of vaccination coverage by day 120	Vaccination rate (shots per day)	Overall complete vaccination coverage by day 120 (all ages)
1	0.7%	50	62% (61+0.7%)
2	10%	682	71% (61+10%)
3	20%	1,365	81% (61+20%)
4	30%	2,047	91% (61+30%)

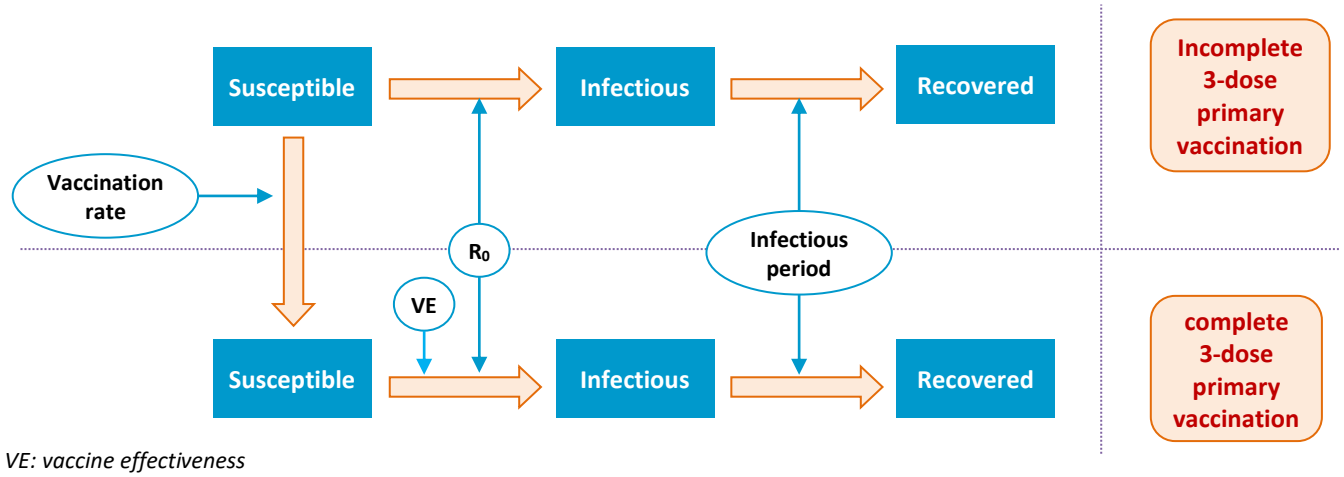

Figure 1. Model framework

Model Parameters and Assumptions

We used Vensim® software to execute the model, with the following assumptions serving as the basis for our calculations.[18]

First, we assumed homogeneous mixing within each vaccination group; all susceptible individuals had an equal chance of contact with infectees.

Second, we assumed a 50% cross-contact rate between infectious individuals, regardless of vaccination status, meaning susceptible persons had an equal chance of contact with both completely and incompletely vaccinated individuals.

Third, we set the start date of the model as 1 Feb 2024, and iterated over a one-year period (365 days) where the vaccination rate across model scenarios varied within the first 120 days. This notion was based on the hypothesis that the epidemic force, as determined by the R_0, continued throughout the year.

Fourth, due to difficulties in determining the active infectious population at the outbreak's onset, we estimated the initial pool as four times the new confirmed cases over three weeks in January 2024.[11] This was based on a 21-day (3-week) infectious duration. The rationale behind using a multiplier of four stems from the observation that the reported number of suspected pertussis cases in the preceding two months was four times higher than the number of confirmed cases.

Fifth, we accounted for vaccine impact by assuming a reduction in infection based on vaccine effectiveness (VE). Given a short period of analysis, we did not account for the waning of immunity.

Sixth, we assumed negligible birth and death rates within the population due to a relatively short time interval.

Seventh, we assumed that all model inputs remained constant over time. In this model, we set R_0=5. Evidence suggested that in countries with vaccination coverage of between 53–99%, the R_0 value ranges from 5–6.[19] We also conducted a sensitivity analysis to explore the results in a higher epidemic state (R_0=6).

Eighth, based on reported pertussis deaths in 2023 in Thailand, at the time of the study there was no fatality happening in completely vaccinated individuals.[11] Given that unvaccinated children were more susceptible to contract pertussis and tend to experience more severe disease, we assumed that the mortality rate among individuals completing 3-dose of primary vaccination was 10 times lower than among the unvaccinated population.[20]

Ninth, for vaccine and administration costs, we used the 3-dose DTP vaccine expense as the benchmark for primary infant immunization. We also identified the proportion of infections by age using data from the national surveillance reported in 2023.[11] Based on this proportion, we estimated the direct medical cost by age group, considering the varying rates of hospitalization across different age groups. Infants experience more severe infections and require hospitalization at a higher rate compared to children and adults.[21,22] For non-hospitalized infections, we assumed similar outpatient care costs across age groups.

Tenth, we excluded adverse events following immunization (AEFI) costs, given the pertussis vaccine's long history of minimal serious AEFI (2 out of 100,000 doses).[23,24] Additionally, there were no reports of serious AEFI among adults or pregnant individuals receiving the acellular pertussis vaccine or Tdap booster in 2023.[25]

Simplified key model formulas are presented in Table 2, while essential model parameters are listed in Table 3.

Table 2. Key model formula

Stock	Formula to present outflow of stock
Susceptible incomplete vaccination (dS/dt)	$-\beta S_1 I_1 - \beta S_1 I_2 - \nu S_1$
Susceptible complete vaccination	$-\beta(1-\mathrm{VE})S_2 I_2 - \beta(1-\mathrm{VE})S_2 I_1 + \nu S_1$
Infectious incomplete vaccination	$\beta S_1 I_1 + \beta S_1 I_2 - \gamma I_1$
Infectious complete vaccination	$\beta(1-\mathrm{VE})S_2 I_2 + \beta(1-\mathrm{VE})S_2 I_1 - \gamma I_2$
Recovered incomplete vaccination	γI_1
Recovered complete vaccination	γI_2

Incomplete vaccination: received less than three doses of pertussis vaccine or have never received the vaccine at all. Complete vaccination: completed at least three doses of vaccination regimen. β: basic reproduction number/ infectious period. S_1: susceptible to incomplete vaccination population. S_2: susceptible complete vaccination population. I_1: infectious incomplete vaccination population. I_2: infectious complete vaccination population. v: 1/vaccination period. VE: effectiveness of vaccine against infection. γ: 1/ duration of infection.

Table 3. Essential model parameters

Parameters	Approximate value	Remark or reference	Unit
Basic reproduction number	5	Kretzschmar et al.[19]	Dimensionless
Initial population	20.8 million	Bureau of Registration Administration, Department of Provincial Administration	Persons
Initial infectees	400	Model assumption	Persons
Baseline overall primary vaccination coverage	61.0%	Health Data Center, Office of Permanent Secretary, Ministry of Public Health	Dimensionless
Case fatality rate with incomplete vaccination	0.43%	Division of Communicable Diseases, Department of Disease Control	Dimensionless
Case fatality rate with complete vaccination	0.043%	Model assumption	Dimensionless
Intergroup cross-contact percentage	50.0%	Model assumption	Dimensionless
Infectious duration	21	Lauria et al.[4]	Days
Starting complete vaccinated percentage among infectees	13.0%	Division of Epidemiology, Department of Disease Control	Dimensionless
Vaccine effectiveness against infection among at least 3-dose vaccinees compared to incomplete (less than 3-dose) vaccination	83.5%	E Quinn et al.[10]	Dimensionless
Target vaccination duration	120	Model assumption	Days
Percentage of infants 0–3 months old among all infectees	10.0%	Division of Epidemiology, Department of Disease Control	Dimensionless
Percentage of infants 4–11 months old among all infectees	21.8%	Division of Epidemiology, Department of Disease Control	Dimensionless
Percentage of children 1–4 years old among all infectees	40.8%	Division of Epidemiology, Department of Disease Control	Dimensionless
Percentage of children 5–17 years old among all infectees	23.5%	Division of Epidemiology, Department of Disease Control	Dimensionless
Percentage of adults >18 years old among all infectees	3.9%	Division of Epidemiology, Department of Disease Control	Dimensionless
Percentage of hospitalized infants 0–3 months old among all infectees	65.6%	Botwright et al.[22]	Dimensionless
Percentage of hospitalized infants 4–11 months old among all infectees	28.1%	U.S. Centers for Disease Control and Prevention[21]	Dimensionless
Percentage of hospitalized children 1–4 years old among all infectees	10.3%	U.S. Centers for Disease Control and Prevention[21]	Dimensionless
Percentage of hospitalized children 5–7 years old among all infectees	2.7%	U.S. Centers for Disease Control and Prevention21	Dimensionless
Percentage of adults >18 years old among all infectees	3.0%	Botwright et al.[22]	Dimensionless

Table 3. Essential model parameters (cont.)

Parameters	Approximate value	Remark or reference	Unit
3-dose DTP vaccination cost	23.50	Division of Communicable Diseases, Department of Disease Control	Baht
3-dose vaccination administrative cost	19.14	Modified from Botwright et al.[22]	Baht
Treatment cost for hospitalized child, per episode	36,153.00	Modified from Botwright et al.[22]	Baht
Treatment cost for hospitalized adult, per episode	10,861.00	Modified from Botwright et al.[22]	Baht
Treatment cost for outpatient pertussis, children and adults per infection episode	312.81	Modified from Botwright et al.[22]	Baht

1 US$=36.11 Thai baht as of 15 Jul 2024

Interested Outcomes

We applied the health provider perspective, focusing on daily incident cases, cumulative cases, and cumulative deaths by day 365 for each scenario. The cost of interest included treatment and vaccination costs. We compared outcomes and costs incurred between policy alternatives (Scenarios 2–4) and the status quo (Scenario 1). The key outcome was cost savings (in Thai baht) per case or death averted.

Results

Figure 2a shows pertussis incidence for each scenario over one year. During the initial 100 days, there were minimal differences observed among the scenarios. However, after day 120, distinct patterns emerged. By day 170, Scenario 1 showed a notable increase in daily incident cases compared to Scenario 4 (about a five-fold difference). Over one year, Scenario 1 saw a sharp rise in cases, while Scenarios 3 and 4 had incidences drop to nearly zero.

Figure 2b shows the cumulative incidence of pertussis cases for all scenarios. Likewise, a remarkable difference was observed after day 120. By day 170, Scenario 1 showed twice the cumulative incidence compared to Scenario 4 (5,265 versus 10,586 cases). This disparity was amplified gradually. By the end of the simulation, the cumulative incidence of Scenario 1 was approximately ten-fold higher than the incidence of Scenario 4.

Figure 2c presents cumulative deaths in the current epidemic force. Variations appeared after day 150. By day 250, cumulative deaths in Scenario 1 quadrupled those in Scenario 4. Over the whole one-year period, Scenario 1 experienced a 10-fold increase in cumulative deaths compared to Scenario 4, while Scenarios 2 and 3 varied between 40–90 deaths. Scenarios 3 and 4 had minimal differences in cumulative deaths.

Table 4 presents the total cost, case number, deaths, cost savings, amount saved per case, and amount saved per death of different vaccination scenarios in an

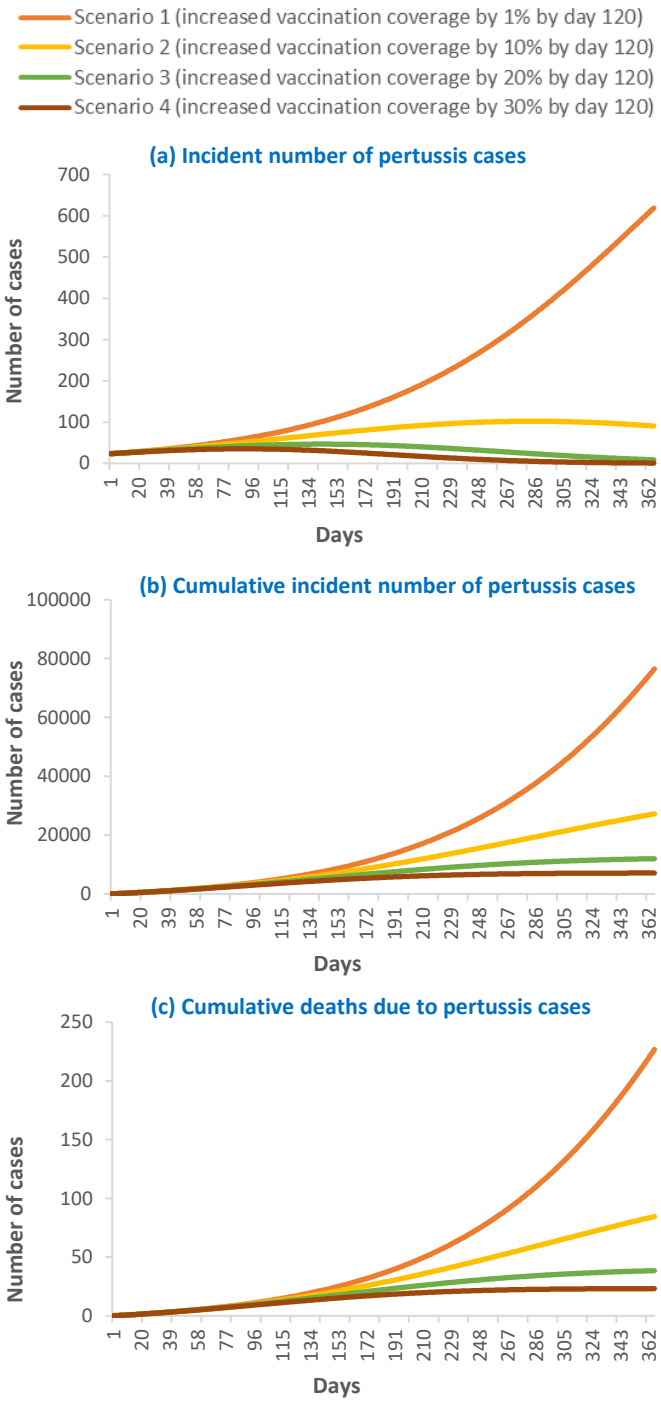

Figure 2. Incident number, cumulative incidence, and cumulative deaths of pertussis cases in Southern Thailand (R_0=5) in different vaccination scenarios

epidemic state (R_0=5) by day 365. Cumulative cases and cumulative deaths in all alternative vaccination policies decreased exponentially compared to the status quo. Scenario 4, which aimed for the highest vaccination target, bore the largest vaccination cost but at the same time experienced the smallest volume of cases and deaths. The total treatment costs decreased as the vaccination target grew (180, 79, and 47 million baht for Scenarios 2, 3, and 4 respectively).

Table 4. Summary of cases, deaths and costs incurred for various vaccination scenarios in current epidemic state (R_0=5) by day 365

Interested outcome	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Cumulative cases (n)	76,501	27,219	11,970	7,098
Cumulative deaths (n)	227	85	38	23
Vaccine and administration cost (million baht)	0.3	3.5	7.0	10.5
Treatment cost (million baht)	505	180	79	47
Grand cost (million baht)	506	183	86	57
Cost saving (million baht)	Ref	322	420	448
Cases averted (n)	Ref	49,281	64,530	69,403
Deaths averted (n)	Ref	142	188	204
Cost saved (in baht) per case averted	Ref	6,540	6,501	6,458
Cost saved (in million baht) per death averted	Ref	2.27	2.23	2.20

Scenario 1: baseline strategy. Scenario 2: 10% increase of vaccination coverage by day 120. Scenario 3: 20% increase of vaccination coverage by day 120. Scenario 4: 30% increase of vaccination coverage by day 120. Ref: reference range.

Scenario 2 showed the least cost-saving (322 million baht) compared to Scenarios 3 and 4 (420–448 million baht) when contrasting with Scenario 1. Scenario 4 projected the largest number of cases (69,403) and deaths (204) averted—approximately 10–40% safer than Scenario 2. Scenario 2 had the most cost-saving policy option (6,540 baht per case prevented and 2.27 million baht for a death prevented) compared with other options despite having a diminutive margin.

Similar to the 'R_0=5' assumption, all vaccination policy alternatives exhibited cost-saving outcomes compared to the baseline scenario in a high epidemic state (R_0=6). The volume of cases and deaths averted in all interested scenarios in a high epidemic state was about 6–8 times as large as that in the current epidemic state. The monetary saving for a case averted varied between 6,585–6,594 baht, which is very close to the saving in the current epidemic state. The distinct change in the high epidemic state was that Scenario 4 became the most cost-saving option for preventing deaths, with a cost of 2.19 million baht per death prevented, as shown in Table 5.

Table 5. Summary of cases, deaths and costs incurred for various vaccination scenarios in high epidemic state (R_0=6) by day 365

Interested outcome	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Cumulative cases (n)	548,714	254,722	85,106	33,513
Cumulative deaths (n)	1,644	726	240	95
Vaccine and administration cost (million baht)	0.3	3.5	7	10.5
Total treatment cost (million baht)	3,624	1,683	562	221
Grand cost (million baht)	3,625	1,686	569	232
Cost saving (million baht)	Ref	1,939	3,056	3,393
Cases averted (n)	Ref	293,992	463,608	515,201
Death averted (n)	Ref	918	1,404	1,550
Cost saved (in baht) per case averted	Ref	6,594	6,591	6,585
Cost saved (in million baht) per death averted	Ref	2.11	2.18	2.19

Scenario 1: baseline strategy. Scenario 2: 10% increase of vaccination coverage by day 120. Scenario 3: 20% increase of vaccination coverage by day 120. Scenario 4: 30% increase of vaccination coverage by day 120. Ref: reference range.

Discussion

Overall, our study elucidates the benefit of policies to expedite primary vaccination against pertussis amongst children in the Deep South region of Thailand, in terms of both case and death reduction and cost savings.

We found that all pertussis vaccination policies that aim to achieve 10–30% additional coverage within 120 days would result in cost-savings compared to the status quo vaccination rate. An increment of 10% in primary vaccination coverage resulted in the most cost-saving for both case and death aversion compared

with other vaccination strategies in existing epidemic states. Although our results suggest favorable outcomes for a 10% augmentation of pertussis vaccination coverage amongst children, this still needs enormous effort in achieving such a target as it means a 10-fold increase from the baseline daily vaccination rate (from 50 to 682 vaccinations per day).

Various strategies to enhance vaccine coverage include community engagement, implementing mobile vaccination units, and targeted messaging to ensure that the information reaches diverse subgroups.[26,27] The MOPH and related health sectors should consider implementing such measures soon. Political commitment to harness resources for rapid vaccine roll-out and steadfast assistance from various stakeholders and residents are indispensable.

Our findings concur with existing evidence despite subtle differences in research questions and design. Wu et al suggested that over the lifetime of 40 birth cohorts, China's immunization program could helped prevent 93% of pertussis cases and 97% of pertussis deaths.[28] Girard underpinned that in England and Wales, maintaining vaccination coverage at a level of at least 90% would ensure the largest cost savings.[29]

It is worth noting that given a higher epidemic force, enhanced vaccination coverage to over 90% (30% increment) likely becomes the most cost-saving option for death aversion. This observation is consistent with a prior study during the COVID-19 pandemic in Thailand, which demonstrated that focusing vaccination efforts in high-epidemic areas, such as Samut Sakhon, where the migrant population faced a higher reproduction number, would yield more cost-effective (cost-saving) outcomes compared to a general population vaccination approach.[30]

Our findings suggest that a reduction in cases and deaths would not be noticeable within the first 100–120 days. Thus, policymakers should not consider these vaccination policies as a silver bullet to immediately halt an outbreak. Other control measures, such as isolation of cases, postexposure antimicrobial prophylaxis adherence, and strengthening of the surveillance system, should be implemented alongside a vaccine roll-out.[31,32] Moreover, communication strategies to enhance vaccine acceptance amongst people in Thailand's Deep South should be established. During the outbreak, the DDC communicated to the public the guidelines to strengthen immunity against whooping cough in southern border provinces in December 2023 and January 2024.[33–35] These measures include a vaccine mop-up policy booster for those under the age of seven years, pregnant women, and for children's caregivers in epidemic areas.[36] According to personal negative beliefs about the benefits of vaccination and religious and local tradition concerns, DDC and the public health authority in the Deep South also communicate about the source of vaccines and the explanation of the advantages of vaccination according to the spirit of religion.[37–39]

This is one of the first studies in Thailand to investigate the cost-effectiveness of the pertussis vaccine using real-world evidence, and we consider this as a methodological strength. Nonetheless, some limitations remain. First, the model did not explore in detail the effect of various influential factors on the model results, such as varying epidemic force by age groups, differences in the likelihood of contacts by geographic areas and age structures, and the interaction of public health programs and non-pharmaceutical interventions that may alter the effective contact rate. Second, we did not account for uncertainties in the model parameter (except for R_0) due to a lack of empirical data from domestic sources. This point comes with a suggestion that if data are available, the stochastic model that considers data uncertainties should be performed. Last, the interpretation of various vaccine programs should be made with caution. This is because, in reality, numerous unpredictable factors may affect vaccine roll-out, such as budget constraints, logistic hurdles, and societal willingness, all of which hold substantial sway over the initial policy intention. Further studies that explore various aspects of vaccine operational programs should be conducted and interpreted alongside our study.

Conclusion

A 10% increase in pertussis vaccine coverage from baseline levels is the most cost-effective for averting cases and deaths during existing epidemic conditions. Achieving higher coverage will incur more cost-savings for preventing deaths if the epidemic escalates. Further research should explore other influential factors and parameter uncertainties. Other control measures, including non-pharmaceutical interventions, should complement vaccination strategies.

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Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization: C.M., C.K., R.S.; Data curation: C.M.; Formal analysis: C.M., R.S.; Methodology: C.M., R.S.; Writing—Original draft: C.M., C.K., T.C., R.S.; Writing—Review and editing: C.M., C.K., T.C., R.S. All authors have read and approved the final manuscript.

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