Journal Of Nursing Practice
https://thejnp.org/
ISSN: 2614-3488 (print); 2614-3496 (online) Vol.9 No.2. January 2026. Page.446-458

Cost-Effectiveness of Maternal Tetanus Toxoid and Tetanus Diphtheria in Developing Countries: Systematic Review

Ana Claudia da Costa Guterres[1*], Sri Annisa Jamarupada[2], Tiara Mudrika[3], Azizah Yuhani[4], Sulistyaningsih[5], Putri Listiani[6]
[1] *Universitas Nasional Timor Lorosa'e*
[2,3,4,5] *Universitas Aisyiyah Yogyakarta*
[6] *Universitas Gadjah Mada*
**Corresponding author: claudiaguterre5@gmail.com*

ABSTRACT

Background: Maternal and neonatal tetanus (MNT) remains a public health threat in low- and middle-income countries due to suboptimal coverage of complete-dose maternal immunization. Although TT and Td vaccines are clinically effective, their cost-effectiveness in different country contexts needs systematic assessment.

Purpose: To evaluate the cost-effectiveness of maternal tetanus toxoid (TT) and tetanus-diphtheria (Td) vaccination in developing countries, focusing on economic outcomes and contextual variations.

Methods: This systematic review followed PRISMA 2020 guidelines. Literature was searched in PubMed, Scopus, ScienceDirect, Wiley, and Crossref. Inclusion criteria comprised CEA/CUA studies on maternal TT/Td immunization in developing countries. Reporting quality was assessed using the CHEERS 2022 checklist.

Results: From 2,040 records, four studies met inclusion criteria. All reported maternal TT/Td vaccination as highly cost-effective, with ICERs ranging from USD 3.61 to 15,600 per DALY or life-year saved. Key uncertainties included vaccine effectiveness and distribution costs, while program efficiency varied by local health system conditions.

Conclusion: Complete-dose maternal TT/Td immunization is a highly cost-effective public health intervention in resource-limited settings. However, policy implementation must be adapted to local contexts and supported by robust sensitivity analysis and reliable primary data.

Keywords: cost-effectiveness, developing countries, maternal immunization, tetanus toxoid, tetanus-diphtheria

Received November 10, 2025; Revised December 12, 2025; Accepted January 3, 2026
DOI: https://doi.org/10.30994/jnp.v9i2.995

BACKGROUND

Maternal and neonatal tetanus (MNTE) is a serious public health problem in low- and middle-income countries (LMICs), primarily due to low maternal immunization coverage and unhygienic delivery practices. To address this, Maternal and Neonatal Tetanus Elimination (MNTE) strategies have been implemented in 59 countries, with encouraging results: by the end of 2022, 80% of countries had achieved elimination, with an 89% reduction in cases and 84% reduction in neonatal deaths since 2000 (Jones et al., 2024). However, the COVID-19 pandemic has disrupted this achievement, making the integration of MNTE into immunization recovery programs crucial for maintaining elimination targets. Although elimination has been achieved in many regions, MTE remains a persistent threat, particularly in areas with uneven immunization coverage, weak monitoring systems, and limited access to health services. This situation maintains a high risk of recurrence (Yusuf et al., 2022).

Administration of the tetanus toxoid (TT) or combined tetanus-diphtheria (Td) vaccine to pregnant women is a crucial public health intervention to prevent maternal and neonatal tetanus (MNT). The World Health Organization (WHO) recommends two doses during pregnancy to ensure optimal protection for both mother and infant; however, coverage remains suboptimal in many low and middle-income countries (LMICs). Zegeye et al. (2024) reported that only 26% of pregnant women received the recommended two doses, with even lower rates in rural areas with limited healthcare access, a trend similarly observed in Nigeria (Adedokun et al., 2017), Bangladesh (Amin et al., 2022), and Naha et al. (2025). In Indonesia, TT vaccination is initiated at the first antenatal visit, with two doses given at least four weeks apart for previously unvaccinated mothers and a single booster for those with prior immunization (Dalle et al., 2021). The resulting maternal antibodies are transferred trans placentally, providing effective neonatal protection against tetanus.

In resource-limited settings, cost-effectiveness analyses (CEAs) from Ethiopia and South Asia (Memirie et al., 2019; Rogers et al., 2022) show that maternal TT/Td vaccination is highly cost-effective, with costs below USD 100–300 per DALY averted. However, outcomes are influenced by uncertainties such as vaccine price, cold chain capacity, maternal uptake, and data accuracy. Local vaccine production further enhances cost-efficiency, with manufacturing costs ranging from USD 0.98 to 4.85 per dose (Munira et al., 2019). Despite existing applications of sensitivity and cost-utility analyses for other maternal vaccines (e.g., pertussis and influenza) (Botwright et al., 2023), few studies compare TT/Td cost-effectiveness by dosage adherence. Moreover, limited primary data on distribution costs only USD 0.55–0.64 per dose in Indonesia and Malawi (Procter et al., 2020) highlight the need for contextual economic evaluations. Therefore, a systematic review is warranted to assess the cost-effectiveness of maternal TT/Td immunization considering parameter uncertainty and local health system variations, providing an evidence base for sustainable policy decisions.

OBJECTIVE

The aim of this systematic review is to evaluate the cost-effectiveness of maternal tetanus toxoid (TT) and tetanus-diphtheria (Td) vaccination in developing countries.

METHODS

This systematic review assesses the cost-effectiveness of maternal Tetanus Toxoid (TT) and Tetanus-Diphtheria (Td) vaccination by examining economic outcomes and contextual variations to support evidence-based policymaking in developing countries. The review follows the PICOS framework (Population, Intervention, Comparison, Outcomes, Study design) and uses secondary data sourced from PubMed, ScienceDirect, Crossref, Scopus, and

ISSN: 2614-3488 (print); 2614-3496 (online) Vol.9 No.2. January 2026. Page.446-458

Wiley. Article searches employed Mesh-adjusted keywords and Boolean operators (AND, OR, AND NOT) to refine results. The mean keywords included: pregnant women*, antenatal care*, tetanus toxoid*, Tetanus-Diphtheria Vaccine*, immunization program*, Partial-dose, Developing Countries, Cost-Benefit Analysis*, and Cost-Effectiveness Analysis*.

Tabel 1. *PICOS Framework*

Population	Intervention	Comparation	Outcome	Study Design
Pregnant Women in Developing Countries	Tetanus Toxoid or Tetanus-Diphtheria Immunization	Without Immunization/ Incomplete Dose/ Alternative Immunization Strategy (Routine Vs Campaign)	1. Cost-effectiveness 2. Cost-utility 3. Economic evaluation 4. Health outcomes in developing countries 5. DALY averted ICER (incremental cost-effectiveness ratio)	Economic evaluation studies (cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis)

The article selection process for this systematic review was carried out in two stages: title and abstract screening, followed by full-text screening. Both stages were conducted independently by two reviewers (AC and NS), with disagreements resolved through discussion with a third reviewer (AZ or TR) to reach consensus. Inclusion criteria consisted of studies conducting cost-effectiveness or cost-utility analyses (CEA/CUA) of Tetanus Toxoid (TT) or Tetanus-Diphtheria (Td) vaccination in developing countries, based on World Bank or UN classifications, and published in English. Non-empirical works such as editorials, commentaries, or letters were excluded.

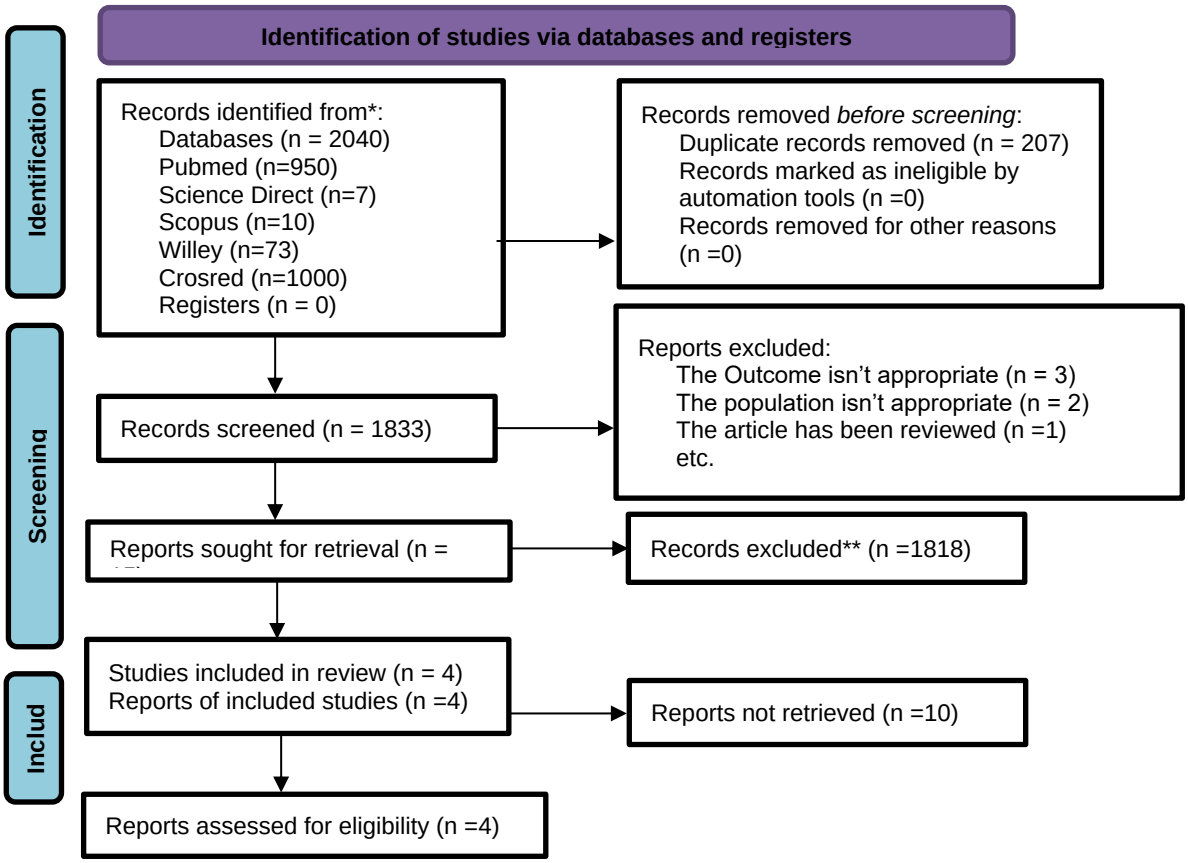
Articles that met these criteria underwent data extraction following the PRISMA 2020 framework. The reporting quality of included studies was then evaluated using the CHEERS 2022 checklist, which consists of 28 items assessing methodological and reporting rigor in health economic evaluations. This approach ensured that only studies meeting high-quality standards were included for further analysis.

RESULTS

A total of 2,040 articles were identified from five databases PubMed, ScienceDirect, Scopus, Wiley, and Crossref using a MeSH-adjusted keywords. After removing 207 duplicates via Rayyan, 1,833 records remained for title and abstract screening. Of these, 1,818 were excluded as irrelevant, leaving 15 articles for full-text review. Following assessment based on inclusion and exclusion criteria, four studies met all requirements and were included in the final narrative synthesis of this systematic review.

Journal Of Nursing Practice
https://thejnp.org/
ISSN: 2614-3488 (print); 2614-3496 (online) Vol.9 No.2. January 2026. Page.446-458

Figure 1. *Systematic Review and Meta-analysis Flowchart diagram*



Tabel 2. Summary of Results of the Economic Evaluation Study of Maternal Immunization Tetanus Toxoid (TT) / Tetanus-Diphtheria (Td)

No.	Author (Year)	Country	Target Population	Intervention	Comparation	Outcome	Economic Evaluation	Uncertainty factor	Model & Perspective	Conclusion
1	*Peter Berman (1991)*	Indonesia	Pregnant women in Aceh	Routine EPI immunization	Mass campaigns	Routine immunization is more cost-efficient	Economic evaluation of the CEA (Cost-Effectiveness Analysis)	Estimates of the effectiveness, costs, and coverage of immunization programs and their impact on neonatal mortality	Cost-effectiveness and cost-benefit analysis & Economic and public health perspectives	*Cost-effective*
2	*Sartori et al. (2016)*	Brasil	Pregnant women in the 3rd trimester	Tdap vaccine 1 dose	Without the Tdap vaccine	USD 15,600 per life-year saved – rated very cost-effective	Cost-Effectiveness Analysis (CEA)	The main uncertain factors are vaccine effectiveness, cost, and disease incidence, which influence the results of the cost-effectiveness analysis.	*Decision tree, Social & Health*	*Very cost-effective*
3	*Griffiths et al. (2004)*	Pakistan	Women of reproductive age	SIAs (additional TT)	Routine immunizations	USD 2.43–6.39 per DALY averted is highly cost-effective	Cost-Effectiveness Analysis (CEA).	Neonatal tetanus incidence rate, Case fatality rate (CFR), TT vaccine efficacy, Duration of immunity per TT dose, Actual vaccination coverage in the field	*State-transition*, Health	*Cost-effective*
4	*Laing et al. (2020)*	13 countries	Women of reproductive age	TTCV campaign & additional interventions	*Status quo*	*USD 2,900 per death averted, USD 45 per life year gained is very cost-effective*	Cost-Effectiveness Analysis (CEA)	Among the uncertainties involved in this study are limited data on maternal mortality, estimates of neonatal mortality rates, and limited cost estimates.	*Hybrid model, Global Health*	*Very cost-effective*

Table 3. Data Charting

Article Identity	Author/Title	Vaccination Strategy	Case/Death Prevented	Cost-Effectiveness (ICER/QALY/ or LYS)	Conclusion
A1	(Peter Berman, 1991) Maternal Tetanus Immunization in Aceh Province, Sumatra: The Cost-Effectiveness of Alternative Strategies Indonesia	EPI Routines and TT Mass Campaigns	40.6 Deaths Prevented in Aceh	US$ 27–125 per death prevented	Cost-effective
A2	(Sartori et al., 2016) Cost-effectiveness analysis of universal maternal immunization with tetanus-diphtheria-acellular pertussis (Tdap) vaccine in Brazil	1 Dose of Tdap During Third Trimester of Pregnancy	661 cases and 24 deaths prevented in one year	US$ 15.600 per life year saved (LYS)	Very cost-effective
A3	(Griffiths et al., 2004) Incremental cost-effectiveness of supplementary immunization activities to prevent neonatal tetanus in Pakistan	Additional TT SIAs for women of reproductive age	224 neonatal deaths prevented (2001–2034)	US$ 3.61 per DALY averted (95% CI: 2.43–6.39)	Cost-effective
A4	(Laing et al., 2020) An investment case for maternal and neonatal tetanus elimination	TTCV Vaccine Campaign (TT/Td) with Intervention	70,000 neonatal deaths averted 4.4 million LYS (Life Year Saved)	US$ 2,900 per death averted, US$ 45 per LYS	Very Cost-effective

Tabel 4. Critical Appraisal CHEERS 2022

No	CHEERS Statement Item	Peter Berman (1991)	Sartori et al. (2016)	Griffiths et al. (2004)	Laing et al. (2020)
1	Title	1	1	1	1
2	Abstract	1	1	1	1
3	Background and objectives	1	1	1	1
4	Health economic analysis plan	0	1	1	1
5	Study population	1	1	1	1
6	Setting and location	1	1	1	1
7	Comparators	1	1	1	1
8	Perspective	0	1	1	0
9	Time horizon	1	1	1	1
10	Discount rate	0	1	1	1
11	Selection of outcomes	1	1	1	1
12	Measurement of outcomes	1	1	1	1
13	Valuation of outcomes	1	1	1	1
14	Measurement and valuation of resources and costs	1	1	1	1
15	Currency, price date, and conversion	1	1	1	1
16	Rationale and description of model	0	1	1	1
17	Analytics and assumptions	1	1	1	1
18	Characterizing heterogeneity	1	0	0	0
19	Characterizing	0	0	0	1

	distributional effects				
20	Characterizing uncertainty	1	1	1	1
21	Approach to engagement with patients and others affected by the study	1	0	0	0
22	Study parameters	1	1	1	1
23	Summary of main results	1	1	1	1
24	Effect of uncertainty	1	1	1	1
25	Effect of engagement with patients and others affected by the study	1	0	0	0
26	Study findings, limitations, generalizability, and current knowledge	1	1	1	1
27	Source of funding	1	1	1	1
28	Conflicts of interest	0	1	1	1
	% of Yes	78,6%	85,7%	85,7%	85,7%
	Overall Quality	Good	Verry Good	Verry Good	Verry Good

Based on the results of the analysis of four articles evaluated using CHEERS guidelines, maternal immunization TT/Td has excellent quality articles there are three with grade A (85.7%) and articles with good quality there is one article with grade B (78.6%). The results of the included articles were concluded that TT/Td maternal immunization is a highly economically viable intervention, both at national and global levels. The interventions undertaken also support more responsive, efficient, and inclusive health systems, especially in developing countries with limited health resources and infrastructure.

DISCUSSION

Article Characteristics

From a total of 2,040 articles found through scientific database searches, four articles ultimately met the inclusion criteria and were included in the narrative analysis. The articles cover studies in various developing countries such as Indonesia, Pakistan, Brazil, as well as several countries in the African region. These four studies presented the results of economic evaluations against TT/Td maternal immunization strategies with different approaches, including descriptive models, decision trees, state-transition models, and hybrid models.

The main findings suggest that TT/Td vaccine administration, both through routine immunization programs and campaigns, is generally highly cost-effective, with estimated costs per death averted ranging from USD 27 to USD 2,900 and costs per life-year saved (LYS) ranging from USD 45 to USD 15,600. In addition, two studies reported cost-effectiveness based on disability-adjusted life years (DALY) indicators, with results that also showed high efficiency (e.g., USD 3.61 per DALY averted in Pakistan).

Cost-Effectiveness of Full-Dose TT/Td Vaccine

The reviewed studies consistently confirm that administering the full-dose TT/Td vaccine to pregnant women is a highly cost-effective intervention across diverse economic settings. For instance, Griffiths et al. (2004) in Pakistan reported that supplementary immunization activities achieved a cost of only USD 3.61 per DALY averted, demonstrating remarkable efficiency. Similarly, Laing et al. (2020) estimated a cost of USD 2,900 per death averted and USD 45 per life-year saved (LYS), placing the intervention well within the WHO's highly cost-effective threshold (<1× GDP per capita). Even in high-income contexts, such as Brazil, a single dose of Tdap administered during the third trimester yielded favourable cost-

effectiveness results, with an estimated cost of USD 15,600 per LYS (Sartori et al., 2016), confirming the global applicability of this maternal immunization strategy.

The strong economic justification for TT/Td immunization is further reinforced by Procter et al. (2020), who demonstrated through a systematic review that the non-vaccine delivery cost in low-income countries ranges between USD 0.55 and USD 0.64 per dose. These figures, encompassing expenses for logistics, health worker training, cold chain maintenance, and public awareness activities, indicate that maternal vaccination is not only clinically effective but also financially sustainable. When integrated into existing primary healthcare services, such interventions reduce operational redundancy and enhance program efficiency, making them particularly suitable for resource-limited settings where maximizing health outcomes per unit cost is essential.

Cross country evidence further supports these findings. In Ethiopia, expanding maternal immunization coverage by 20% resulted in an ICER of approximately USD 168 per DALY averted far below the WHO cost-effectiveness benchmark of 0.4× GDP per capita indicating substantial economic efficiency (Media et al., 2019). Similarly, Mai et al. (2022) in Vietnam found that the cost per TT/Td dose ranged from USD 1.49 for school-based programs to USD 3.86 for outreach services, identifying school-based delivery as the most cost-effective approach. In Indonesia, Berman (1991) reported that routine immunization under the Expanded Program on Immunization (EPI) framework achieved lower costs (USD 27–125 per death averted) compared to mass campaigns, underscoring the advantage of leveraging existing healthcare systems. Collectively, these studies demonstrate that full-dose TT/Td vaccination is a highly cost-effective and impactful intervention for reducing maternal and neonatal mortality. Nonetheless, persistent gaps in vaccination coverage and inadequate data recording systems in many low- and middle-income countries, as noted by Johns et al. (2024), highlight the need for improved documentation and data quality to support stronger, evidence-based maternal immunization policies.

Influence of Parameter Uncertainty

The results of the economic evaluation studies (Articles A1, A2, A3, and A4) indicate that parameter uncertainty plays a critical role in influencing the interpretation and reliability of cost-effectiveness analyses. Such uncertainty reflects the inherent complexity of real-world health interventions, where outcomes depend on variations in model assumptions, input data quality, and field implementation dynamics. One of the main sources of uncertainty lies in the estimation of vaccine effectiveness. Sartori et al. (2016) noted that the protective effect of the Tdap vaccine against tetanus and pertussis in neonates is highly dependent on the timing of administration and the maternal immune response, both of which can vary considerably. Similarly, Laing et al. (2020) acknowledged that their model considered only the direct impact of TTCV vaccination, excluding the potential contribution of complementary interventions such as clean delivery practices. Moreover, the study emphasized that innovations like TT-Uniject™ are not yet widely implemented, creating additional uncertainty in projecting program outcomes.

Uncertainties also arise from vaccine logistics and distribution cost estimations, as highlighted by Berman (1991) and Laing et al. (2020). Variations in transportation costs, cold chain efficiency, and health worker training expenses can significantly affect total program costs, especially when local primary data are unavailable. Such inaccuracies can distort Incremental Cost-Effectiveness Ratio (ICER) calculations and lead to misinterpretations of intervention efficiency. Similarly, Griffiths et al. (2004) identified that assumptions about local epidemiological parameters such as case fatality rates, vaccine efficacy, and immunization coverage substantially influence cost-effectiveness outcomes. Even small changes in these assumptions can produce large variations in results, emphasizing the need for robust sensitivity

analyses. Deterministic and probabilistic approaches are therefore essential to capture the range of possible outcomes and assess the stability of conclusions under different scenarios.

In resource-limited settings, simulation-based modeling remains a practical tool for addressing data gaps, but its credibility depends on transparency in assumptions and comprehensive sensitivity testing. To strengthen the robustness of economic evaluations, clear communication of methodological choices and underlying uncertainties is essential for guiding responsible policy formulation. Complementary evidence from Vietnam further demonstrates that the school-based vaccination strategy offers the lowest delivery cost at USD 1.49 per dose, compared to USD 1.76 for facility-based and USD 3.86 for outreach services (Mai et al., 2022). Supporting this, a systematic review reported that TT/Td vaccine delivery costs in low-income countries range from USD 0.55 to USD 0.64 per dose including logistics, training, and cold chain maintenance indicating that integrating maternal immunization into existing primary health services is both feasible and economically sustainable without imposing excessive financial burdens on healthcare systems.

Contextual Variation Between Countries

The cost-effectiveness evaluation of TT/Td maternal immunization showed the existence of significant variation between countries, confirming the importance of a local context-based approach in program planning and implementation. Factors such as health infrastructure, access to antenatal services, government policies, to geographical conditions play a major role in determining the reach and efficiency of immunization programmes. The studies of Tilahun et al., 2025, through a multilevel analysis in six developing countries, found that the determinants of maternal vaccination coverage differed meaningfully between regions, depending on the socio-economic characteristics and health system structure in each country.

Studies in low- and middle-income countries exhibit diverse distribution strategies with varying degrees of efficiency. (Yaya et al., 2020) in Sierra Leone showed that TT vaccination coverage is strongly influenced by access to ANC services, education level, and geographical location. In Indonesia, (Peter Berman, 1991) found that routine immunization integrated into ANC services is more cost-effective than mass campaigns, as it can leverage existing infrastructure and reduce additional logistical costs. Similar was found in Vietnam in the study (Mai et al., 2022), which showed that the distribution strategy through health facilities (US$1.76 per dose) or schools (US$1.49 per dose) was more efficient than the outreach approach (US$3.86), especially in mountainous areas requiring higher logistical incentives. In contrast, in countries with more established health systems, the efficiency of vaccination programs is achieved through the integration of record-keeping systems and strong primary service outreach.

In Brazil, (Sartori et al., 2016) reported that administration of a single dose of Tdap in the third trimester of pregnancy resulted in an ICER value of US$15,600 per life-year saved (LYS). Although relatively high, this intervention was nevertheless considered highly cost-effective in the local context, as the support of medical record keeping and primary services allowed for efficient and targeted implementation. Meanwhile, in Pakistan, intensive strategies such as Supplementary Immunization Activities (SIAs) are actually more economically rational. (Griffiths et al., 2004), showed that SIAs for women of reproductive age only cost US$3.61 per DALY averted, as it is able to reach populations that are not yet integrated into the formal health system. (Laing et al., 2020), through a study in 13 countries, showed that large-scale TT/Td vaccination programs have high impact potential preventing about 70,000 deaths and generating 4.4 million LYS. However, these approaches rely on epidemiological assumptions and global parameters that do not always correspond to local realities. For example, some assumptions do not consider clean delivery practices or variation in neonatal mortality rates between countries. Therefore, the TT/Td vaccination strategy cannot be

universally generalized. The success and efficiency of the program is strongly influenced by the geographical, social, economic conditions, and the structure of the healthcare system in each country. Maternal immunization policies need to be contextually designed to be not only clinically effective, but also efficient and sustainable in their implementation.

Impact of Full Dose Non-compliance

The evaluation of TT/Td maternal immunization cost-effectiveness across countries demonstrates considerable variation, underscoring the critical role of local context in shaping program efficiency. Factors such as healthcare infrastructure, access to antenatal services, community engagement, and policy support significantly influence immunization outcomes. Tilahun et al. (2025) showed that determinants of vaccination coverage vary across developing regions, reflecting differences in socioeconomic and health system characteristics. Similarly, Yaya et al. (2020) in Sierra Leone highlighted that coverage among pregnant women is influenced by contextual elements including education level, access to antenatal care (ANC), and geographic location. These findings emphasize the necessity of adopting context-sensitive strategies in designing and implementing maternal immunization programs.

Evidence from several countries further supports the importance of integrating immunization into existing healthcare systems to enhance cost effectiveness. In Indonesia, Berman (1991) found that routine immunization embedded within ANC services was more cost-effective than mass campaigns, as it leveraged existing infrastructure and reduced logistical overheads. A study by Mai et al. (2022) in Vietnam similarly revealed substantial cost variation based on delivery methods ranging from USD 1.49 for school-based programs to USD 3.86 for outreach reflecting geographic and infrastructural influences. Conversely, Griffiths et al. (2004) demonstrated that in Pakistan, where routine coverage remains low and neonatal tetanus risk high, Supplementary Immunization Activities (SIAs) were more economically viable (USD 3.61 per DALY averted). Meanwhile, Sartori et al. (2016) in Brazil found that administering one Tdap dose during the third trimester was highly efficient due to strong primary healthcare systems and integrated medical records, despite higher ICER values (USD 15,600 per LYS).

Comprehensive analyses, such as Laing et al. (2020) involving 13 countries, further highlight that large-scale vaccination programs can have a major global impact preventing an estimated 70,000 deaths and generating 4.4 million life years saved yet relly on generalized assumptions that may not reflect local realities. Accordingly, the decisions regarding TT/Td vaccination strategies should not be universally applied but rather tailored to each country's geographical, economic, and health system contexts. Context-based policy evaluation ensures that maternal immunization programs are not only clinically effective but also operationally feasible and economically efficient within local settings.

Limitations and Policy Implications

Although the findings from Articles A1, A2, A3, and A4 consistently demonstrate that full-dose TT/Td maternal vaccination is a highly cost-effective intervention, several methodological and implementation limitations must be acknowledged when translating these results into public policy. A major methodological gap lies in the limited use of primary data, particularly concerning vaccine logistics and distribution costs. For instance, Laing et al. (2020) and Mai et al. (2022) included only incremental costs in their analyses, omitting essential operational expenditures such as health worker training, cold chain maintenance, transportation to remote areas, and new delivery technologies like TT-Uniject™. This exclusion risks underestimating total program costs and distorting the true cost-effectiveness ratio. Moreover, studies such as those by Sartori et al. (2016) and Griffiths et al. (2004) did not perform probabilistic sensitivity analyses, which are crucial for assessing uncertainty in parameters like

vaccine efficacy, coverage rates, and unit costs potentially leading to overly deterministic conclusions that do not fully represent real-world conditions.

Beyond methodological issues, challenges related to demand generation and community participation significantly affect program effectiveness. Nguyen et al. (2022) found that limited awareness and low willingness to pay among women of reproductive age in Vietnam hindered coverage expansion, especially outside routine healthcare facilities. Similarly, Yusuf et al. (2022) and Ropero Alvarez et al. (2021) identified systemic barriers, including weak inter-agency coordination, inadequate monitoring, and insufficient public communication, all of which contribute to persistently low full-dose coverage in several regions. These findings underline the need for stronger community engagement and targeted risk communication strategies to complement systemic interventions and improve immunization uptake among vulnerable populations.

Variations in outcome measures such as deaths prevented, life-years saved (LYS), or DALYs complicate comparisons and meta-analysis, highlighting the need for standardized evaluation metrics (Vaccines, MDPI, 2023; Johns et al., 2024). Nonetheless, evidence confirms that TT/Td maternal immunization is highly cost-effective and significantly reduces neonatal tetanus mortality. Policies in developing countries should prioritize routine antenatal vaccination, integrate programs into primary healthcare, adapt outreach strategies to local contexts, and implement robust digital monitoring systems to ensure effective, sustainable, and accountable program delivery.

CONCLUSION

This systematic review concludes that full dose maternal Tetanus Toxoid (TT) and Tetanus-Diphtheria (Td) immunization is a highly cost-effective intervention for reducing neonatal mortality in developing countries. Both routine and campaign-based strategies demonstrate strong economic efficiency, though program outcomes depend on local health infrastructure and antenatal care coverage. However, limited primary data and inconsistent indicators hinder comprehensive evaluation. Thus, maternal immunization policies should be data-driven and adapted to local health system contexts to ensure effectiveness and sustainability.

ACKNOWLEDGMENT

We extend our sincere gratitude to our supervisors, colleagues, and the Faculty of Health Sciences, Universitas ‘Aisyiyah Yogyakarta, for their academic and logistical support. This study received no external funding.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest; all research activities and findings were conducted independently without external influence.

REFERENCES

Adedokun, S. T., Uthman, O. A., Adekanmbi, V. T., & Wiysonge, C. S. (2017). Incomplete childhood immunization in Nigeria: A multilevel analysis of individual and contextual factors. *BMC Public Health*, *17*(1), 1–10. https://doi.org/10.1186/s12889-017-4137-7.

Amin, M. B., Roy, N., Meem, A. E., Hossain, E., & Aktarujjaman, M. (2022). Trends and determinants of taking tetanus toxoid vaccine among women during last pregnancy in Bangladesh: Country representative survey from 2006 to 2019. *PLoS ONE*, *17*(10 October). https://doi.org/10.1371/journal.pone.0276417.

Botwright, S., Win, E. M., Kapol, N., Benjawan, S., & Teerawattananon, Y. (2023). Cost-Utility Analysis of Universal Maternal Pertussis Immunisation in Thailand: A Comparison of Two Model Structures. *PharmacoEconomics*, *41*(1), 77–91. https://doi.org/10.1007/s40273-022-01207-w.

Dalle, A., Jaya, H. N., & Yakub, A. S. (2021). Pemberian Imunisasi Tetanus Toxoid (Tt) Pada Ibu Hamil Dan Wanita Usia Subur (Wus). Jadwal Tabel Imunisasi TT, 13. Diakses dari: https://e-modul.poltekkes-mks.ac.id/file/modul/perawat-mks/imunisasi-tetanus.pdf.

Griffiths, U. K., Wolfson, L. J., Quddus, A., Younus, M., & Hafiz, R. A. (2004). Incremental cost-effectiveness of supplementary immunization activities to prevent neonatal tetanus in Pakistan. Incremental Cost-Effectiveness of Supplementary Immunization Activities to Prevent Neonatal Tetanus in Pakistan, 82(9), 643–651. https://doi.org/DOI:10.1590/S0042-96862004000900005.

Johns, N. E., Blumenberg, C., Kirkby, K., Allorant, A., Costa, F. D. S., Danovaro-Holliday, M. C., Lyons, C., Yusuf, N., Barros, A. J. D., & Hosseinpoor, A. R. (2024). Comparison of Wealth-Related Inequality in Tetanus Vaccination Coverage before and during Pregnancy: A Cross-Sectional Analysis of 72 Low- and Middle-Income Countries. *Vaccines*, *12*(4). https://doi.org/10.3390/vaccines12040431.

Johns, N. E., Cata-Preta, B. O., Kirkby, K., Arroyave, L., Bergen, N., Danovaro-Holliday, M. C., Santos, T. M., Yusuf, N., Barros, A. J. D., & Hosseinpoor, A. R. (2023). Inequalities in Immunization against Maternal and Neonatal Tetanus: A Cross-Sectional Analysis of Protection at Birth Coverage Using Household Health Survey Data from 76 Countries. *Vaccines*, *11*(4). https://doi.org/10.3390/vaccines11040752.

Jones, C. E., Yusuf, N., Ahmed, B., Kassogue, M., Wasley, A., & Kanu, F. A. (2024). Progress Toward Achieving and Sustaining Maternal and Neonatal Tetanus Elimination — Worldwide, 2000–2022. *MMWR. Morbidity and Mortality Weekly Report*, *73*(28), 614–621. https://doi.org/10.15585/mmwr.mm7328a1.

Laing, S. K., Griffiths, U., Raza, A. A., Zulu, F., Yakubu, A., Bessias, S., & Ozawa, S. (2020). An investment case for maternal and neonatal tetanus elimination. *Vaccine*, *38*(9), 2241–2249. https://doi.org/10.1016/j.vaccine.2019.11.052.

Mai, V. Q., Boonstoppel, L., Vaughan, K., Schutte, C., Ozaltin, A., Hong, D. T., Khanh, N. M., Thang, H. M., Anh, T. T., & Van Minh, H. (2022). Cost of Delivering Tetanus Toxoid and Tetanus-Diphtheria Vaccination in Vietnam and the Budget Impact of Proposed Changes to the Schedule. *Global Health Science and Practice*, *10*(2), 1–13. https://doi.org/10.9745/GHSP-D-21-00482.

Memirie, S. T., Tolla, M. T., Desalegn, D., Hailemariam, M., Norheim, O. F., Verguet, S., & Johansson, K. A. (2019). A cost-effectiveness analysis of maternal and neonatal health interventions in Ethiopia. *Health Policy and Planning*, *34*(4), 289–297. https://doi.org/10.1093/heapol/czz034.

Munira, S. L., Hendriks, J. T., Atmosukarto, I. I., Friede, M. H., Carter, L. M., Butler, J. R. G., & Clements, A. C. A. (2019). A cost analysis of producing vaccines in developing countries. *Vaccine*, *37*(9), 1245–1251. https://doi.org/10.1016/j.vaccine.2018.11.050.

Naha, S. K., Arpon, M. E. I., Siddique, R. T., Ripa, F. R., Hasan, M. N., & Uddin, M. J. (2025). A study of association between maternal tetanus toxoid immunization and neonatal mortality in the context of Bangladesh. *PLoS ONE*, *20*(1), 1–16. https://doi.org/10.1371/journal.pone.0316939.

Nguyen, T. H., Le, X. T. T., Nguyen, L. H., Le, H. T., Do, T. T. T., Nguyen, H. L. T., Nguyen, H. T., Latkin, C. A., Ho, C. S. H., & Ho, R. C. M. (2022). Resource mobilization for tetanus vaccination in Vietnam: Uptake, demand and willingness to pay among women

of reproductive age. *Frontiers in Public Health*, *10*. https://doi.org/10.3389/fpubh.2022.980850.

Peter Berman. (1991). Maternal Tetanus Immunization In Aceh Province, Sumatra: The Cost-E ffectiveness Of Alternative Strategies. *Strategies*, *33*(2), 185–192. https://doi.org/https://doi.org/10.1016/0277-9536(91)90179-G.

Procter, S. R., Salman, O., Pecenka, C., Gonçalves, B. P., Paul, P., Hutubessy, R., Lambach, P., Lawn, J. E., & Jit, M. (2020). A review of the costs of delivering maternal immunisation during pregnancy. *Vaccine*, *38*(40), 6199–6204. https://doi.org/10.1016/j.vaccine.2020.07.050.

Rogers, J. H., Cox, S. N., Hughes, J. P., Link, A. C., Chow, E. J., Fosse, I., Lukoff, M., Shim, M. M., Uyeki, T. M., Ogokeh, C., Jackson, M. L., Boeckh, M., Englund, J. A., Mosites, E., Rolfes, M. A., & Chu, H. Y. (2022). Trends in COVID-19 vaccination intent and factors associated with deliberation and reluctance among adult homeless shelter residents and staff, 1 November 2020 to 28 February 2021 – King County, Washington. *Vaccine*, *40*(1), 122–132. https://doi.org/10.1016/j.vaccine.2021.11.026.

Ropero Alvarez, A. M., Vilajeliu, A., Magariños, M., Jauregui, B., Guzmán, L., Whittembury, A., Cain, E., Garcia, O., Montesanos, R., & Ruiz Matus, C. (2021). Enablers and barriers of maternal and neonatal immunization programs in Latin America. *Vaccine*, *39*, B34–B43. https://doi.org/10.1016/j.vaccine.2020.07.051.

Sartori, A. M. C., de Soárez, P. C., Fernandes, E. G., Gryninger, L. C. F., Viscondi, J. Y. K., & Novaes, H. M. D. (2016). Cost-effectiveness analysis of universal maternal immunization with tetanus-diphtheria-acellular pertussis (Tdap) vaccine in Brazil. *Vaccine*, *34*(13), 1531–1539. https://doi.org/10.1016/j.vaccine.2016.02.026.

Tilahun, W. M., Geremew, H., Yohannes Abay, L., Kebie, A. B., & Simegn, M. B. (2025). Determinants of tetanus immunization among pregnant women where tetanus has not been eliminated: a multilevel analysis of 6 countries. *Frontiers in Global Women's Health*, *6*(March), 1–11. https://doi.org/10.3389/fgwh.2025.1481771.

Yaya, S., Kota, K., Buh, A., & Bishwajit, G. (2020). Prevalence and predictors of taking tetanus toxoid vaccine in pregnancy: A cross-sectional study of 8,722 women in Sierra Leone. *BMC Public Health*, *20*(1), 1–9. https://doi.org/10.1186/s12889-020-08985-y.

Yusuf, N., Steinglass, R., Gasse, F., Raza, A., Ahmed, B., Blanc, D. C., Yakubu, A., Gregory, C., & Tohme, R. A. (2022). Sustaining Maternal and Neonatal Tetanus Elimination (MNTE) in countries that have been validated for elimination – progress and challenges. *BMC Public Health*, *22*(1), 1–12. https://doi.org/10.1186/s12889-022-13110-2.

Zegeye, A. F., Tamir, T. T., Mekonen, E. G., Ali, M. S., Gonete, A. T., Techane, M. A., Wassie, M., Kassie, A. T., Ahmed, M. A., Tsega, S. S., Wassie, Y. A., Tekeba, B., & Workneh, B. S. (2024). Number of tetanus toxoid injections before birth and associated factors among pregnant women in low and middle income countries: Negative binomial poisson regression. *Human Vaccines and Immunotherapeutics*, *20*(1), 1–11. https://doi.org/10.1080/21645515.2024.2352905.