INDONESIAN HEALTH ISSUE

E-ISSN: 2828-2809

TAK-003 Dengue Vaccine Efficacy and Safety: A Systematic Literature Review Using PRISMA

Galih Muchlis Hermawan[1*], Syuharul Qomar[2], Iga Putri Imansari[3]

[1,2] PKU Muhammadiyah Delanggu General Hospital, Indonesia

[3] RSGM Soelastri, Indonesia

Email korespondensi: galihmh777@gmail.com

ARTICLE INFO

Article History:

Received:
19 Januari 2026
Accepted:
3 Februari 2026
Published:
3 Februari 2026

Kata Kunci:
TAK-003;
Dengue Vaccine;
Efektivitas;
Keamanan;
PRISMA

Keywords:
TAK-003;
Dengue Vaccine;
Efficacy;
Safety;
PRISMA

ABSTRAK

Latar Belakang: *Dengue* merupakan masalah kesehatan masyarakat global dengan beban penyakit yang tinggi di wilayah endemis dan non-endemis. Meskipun vaksin dengue telah dikembangkan, bukti mengenai efektivitas dan keamanan vaksin TAK-003 dilaporkan secara terfragmentasi dengan variasi hasil berdasarkan serotipe, usia, status serologis awal, serta desain studi. **Tujuan:** Penelitian ini bertujuan untuk menganalisis dan mensintesis bukti ilmiah terkait efektivitas dan keamanan vaksin dengue tetravalen TAK-003 berdasarkan studi uji klinis dan data dunia nyata. **Metode:** *Systematic Literature Review* dilakukan pada Januari 2025 dengan mengikuti pedoman PRISMA. Pencarian literatur dilakukan pada basis data ScienceDirect, PubMed, ProQuest, dan ClinicalKey dengan total 1.011 skrining awal. Setelah proses penghapusan duplikasi, penyaringan judul dan abstrak, dan evaluasi kelayakan full-text, artikel disertakan apabila memenuhi kriteria inklusi: (1) secara eksplisit meneliti TAK-003, (2) melaporkan luaran efektivitas, imunogenisitas, dan/atau keamanan, (3) menggunakan desain uji klinis, observasional, atau surveilans pasca peredaran, dan (4) tersedia dalam full-text berbahasa Inggris. Artikel non-empiris, studi hewan, komentar, dan ulasan naratif dikecualikan. **Hasil:** Sebanyak lima artikel berkualitas tinggi dari jurnal Scopus Q1 memenuhi kriteria inklusi. Analisis tematik mengidentifikasi lima tema utama, yaitu keamanan dan imunogenisitas TAK-003 saat dikoadministrasikan dengan vaksin lain, konsistensi manufaktur dengan respons imun yang stabil, efektivitas jangka panjang dalam mencegah infeksi dengue dan rawat inap hingga 4,5 tahun, perlindungan tetravalen terhadap keempat serotipe dengue, dan profil keamanan yang baik berdasarkan data pasca peredaran dengan mayoritas kejadian ikutan bersifat ringan. **Kesimpulan:** Vaksin TAK-003 menunjukkan efektivitas dan keamanan yang menguntungkan baik dalam uji klinis maupun di dunia nyata. Walaupun variasi efektivitas antar serotipe dan kelompok usia masih ditemukan, bukti yang tersedia mendukung peran TAK-003 sebagai strategi pencegahan dengue yang menjanjikan.

ABSTRACT

Background: *Dengue is a global public health problem with a high disease burden in both endemic and non-endemic regions. Although dengue vaccines have been developed, evidence regarding the efficacy and safety of the TAK-003 vaccine remains fragmented, with variations across serotypes, age groups, baseline serostatus, and study designs.*

Objective: *This study aims to analyze and synthesize scientific evidence on the efficacy and safety of the tetravalent dengue vaccine TAK-003 based on clinical trial data and real-world evidence.* ***Methods:*** *A Systematic Literature Review was conducted in January 2025 in accordance with PRISMA guidelines. Literature searches were performed in the ScienceDirect, PubMed, ProQuest, and ClinicalKey databases, yielding a total of 1,011 initial records. After duplicate removal, title and abstract screening, and full-text eligibility assessment, studies were included if they: (1) explicitly investigated TAK-003, (2) reported outcomes related to efficacy, immunogenicity, and/or safety, (3) employed clinical trial, observational, or post-marketing surveillance designs, and (4) were available as full-text articles in English. Non-empirical studies, animal studies, commentaries, and narrative reviews were excluded.* ***Results:*** *Five high-quality articles from Scopus Q1 journals met the inclusion criteria. The thematic analysis identified five main themes: the safety and immunogenicity of TAK-003 when co-administered with other vaccines, manufacturing consistency with stable immune responses, long-term effectiveness in preventing dengue infection and hospitalization for up to 4.5 years, tetravalent protection against all four dengue serotypes, and a favorable safety profile based on post-marketing data, with most adverse events being mild.* ***Conclusion:*** *The TAK-003 vaccine demonstrates favorable efficacy and safety profiles in both clinical trials and real-world settings. Although variability in effectiveness across serotypes and age groups persists, the available evidence supports TAK-003 as a promising strategy for dengue prevention.*

INTRODUCTION

Vaccination has long been recognized as one of the most effective public health interventions, significantly reducing morbidity and mortality from infectious diseases worldwide (Alanazi *et al*., 2024). Through systematic immunization programs, many previously devastating diseases have been brought under control or nearly eliminated (Lindstrand *et al*., 2021). Despite these achievements, vector-borne viral diseases continue to pose major challenges to global health systems. Dengue fever, in particular, remains a persistent and expanding threat due to rapid urbanization, climate change, and increased global mobility (Abbasi, 2025; Nakhaie, 2026). The disease places a substantial burden on healthcare systems, especially in low and middle-income countries located in tropical and subtropical regions. Consequently, the development of safe and effective dengue vaccines has become a critical priority in global disease prevention strategies (Shafie *et al*., 2024).

Dengue is caused by infection with the dengue virus, which consists of four antigenically distinct serotypes that circulate simultaneously in many endemic regions (Roy & Bhattacharjee, 2021). Infection with one serotype provides long-term immunity only to that specific serotype, while subsequent infection with a different serotype may increase the risk of severe disease. This complex immunological interaction has made dengue vaccine development particularly challenging compared to other viral diseases. Unlike many vaccine-preventable infections, there is no clearly defined immune correlate of protection for dengue. Evaluating vaccine efficacy requires large-scale clinical trials with long follow-up periods to assess both

protection and potential safety risks (Salmon *et al*., 2021).

The first licensed dengue vaccine represented a significant milestone but also revealed critical limitations in dengue vaccine development (Idris, 2021). Safety concerns emerged when increased risks of severe dengue were observed in individuals without prior dengue exposure who received the vaccine. This finding necessitated strict pre-vaccination screening and restricted use only to seropositive individuals, limiting its public health applicability. The requirement for laboratory confirmation before vaccination reduced feasibility in many endemic regions with limited diagnostic capacity. Consequently, a substantial unmet need remains for a dengue vaccine that can be safely administered regardless of prior infection status (Sharp, 2022).

TAK-003 is a live-attenuated tetravalent dengue vaccine developed to overcome many of the limitations observed in earlier vaccine candidates (Hou *et al*., 2022). It is based on a dengue virus serotype 2 backbone engineered to induce immune responses against all four serotypes. The vaccine has been evaluated extensively in clinical development programs involving diverse populations and age groups. Its two-dose schedule offers a practical advantage for immunization programs compared to more complex regimens. Importantly, TAK-003 was designed to provide protection irrespective of baseline serostatus, which could enable wider and more equitable vaccine deployment (Wilder-Smith *et al*., 2025).

Clinical trials have showed that TAK-003 provides substantial protection against virologically confirmed dengue and dengue-related hospitalization. Evidence suggests that the vaccine confers durable protection over multiple years, although efficacy may vary across age groups and viral serotypes (López-Medina *et al*., 2022). Protection against severe disease and hospitalization has been consistently reported as one of its strongest benefits. However, some variability in efficacy against specific serotypes and in younger children has been observed, as the need for continued monitoring.

Although numerous clinical trials and observational studies have evaluated the efficacy and safety of the TAK-003 dengue vaccine, findings across studies remain heterogeneous and difficult to interpret when examined individually (Tricou *et al*., 2024). Variations are evident in reported vaccine performance across different dengue serotypes, age groups, baseline serostatus, and follow-up periods. Some studies emphasize strong protection against hospitalization and severe disease, while others highlight reduced or variable efficacy in specific populations or serotypes. In addition, evidence from clinical trials and post-marketing surveillance is often reported separately, limiting a comprehensive of the holistic benefit-risk profile of TAK-003. To date, while previous meta-analyses, such as Flacco *et al.* (2024), have quantitatively summarized aspects of TAK-003 efficacy, no systematic literature review has integratively synthesized both clinical trial and real-world post-marketing evidence (Flacco *et al*., 2024). Therefore, a Systematic Literature Review (SLR) is warranted to systematically identify, synthesize, and structurally analyze the available evidence on the efficacy and safety of the TAK-003 dengue vaccine. This SLR contributes uniquely by:

1) Integrating fragmented evidence from both clinical trials and post-marketing surveillance studies to provide a comprehensive overview of TAK-003 efficacy and safety;
2) Identifying consistent patterns and sources of variability across dengue serotypes, age groups, and baseline serostatus;

3) Providing evidence-based insights to inform immunization policies, programmatic decisions, and future dengue vaccine research.

RESEARCH METHOD

This study employed a Systematic Literature Review (SLR) approach in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Agrawal, 2024). The review was conducted in January 2025 to comprehensively synthesize available scientific evidence on the efficacy and safety of the dengue vaccine candidate TAK-003. The literature search was conducted using four major and credible scientific databases: ScienceDirect, PubMed, ProQuest, and ClinicalKey. These databases were selected to ensure comprehensive coverage of peer-reviewed biomedical and clinical research related to dengue vaccination and TAK-003. The search strategy applied combinations of keywords, including “TAK-003,” “dengue vaccine,” “efficacy,” and “safety.” Search query variations were adjusted to the specific syntax of each database to ensure search accuracy and replicability. The publication period was restricted to articles published between 2020 and January 2026, including early online publications available ahead of print, to ensure chronological consistency with the review period.

The initial search yielded a total of 1,011 articles, consisting of 133 articles from ScienceDirect, 28 from PubMed, 842 from ProQuest, and 8 from ClinicalKey. All retrieved records underwent both automatic and manual deduplication to remove duplicate publications. Following deduplication, the study selection process was conducted in multiple stages in accordance with the PRISMA framework. The first-stage screening involved reviewing article titles and abstracts to assess their relevance to the objectives of this systematic review. After this initial screening, 285 articles remained for further evaluation, comprising 27 articles from ScienceDirect, 10 from PubMed, 240 from ProQuest, and 8 from ClinicalKey.

The second-stage screening consisted of full-text assessment to identify studies that were directly aligned with the purpose of this review. Articles were included if they met the following criteria:

1. Explicitly examined TAK-003,
2. Reported outcomes related to vaccine efficacy, immunogenicity, and/or safety,
3. Employed clinical trial, observational, or post-marketing surveillance study designs, and
4. Were published in peer-reviewed journals and available in full-text English.

Studies were excluded if they did not specifically assess TAK-003, did not report efficacy or safety outcomes, were review articles without original empirical data, conference abstracts, editorials, commentaries, or animal and in vitro studies. After applying these criteria, 61 articles remained, consisting of 12 articles from ScienceDirect, 10 from PubMed, 33 from ProQuest, and 6 from ClinicalKey.

A subsequent final-stage selection was conducted to minimize the risk of bias and enhance the internal validity of the review. At this stage, articles were excluded if they demonstrated high risk of bias, incomplete or inconsistently reported outcome data, insufficient methodological transparency, or outcomes that were not directly comparable across studies.This additional filtering step resulted in the exclusion of 56 articles, leaving 5 studies for qualitative synthesis.

To address methodological rigor, a formal quality assessment was performed for all studies that passed the full-text screening stage. Randomized controlled trials were assessed using the Cochrane Risk of Bias 2 (RoB 2) tool, while non-

randomized studies were evaluated using the ROBINS-I tool. Each study was independently assessed across relevant domains, including selection bias, performance bias, detection bias, attrition bias, and reporting bias. Studies categorized as having a high overall risk of bias were excluded from the final synthesis. Only studies demonstrating low to moderate risk of bias and high relevance to the review objectives were retained.

Although journal quartile ranking (Scopus Q1) was not used as a primary inclusion criterion, all five included studies were published in Scopus Quartile 1 journals, as strong peer-review standards and reporting quality. This characteristic was considered a supporting indicator of publication quality rather than a methodological selection criterion. Data extraction and evaluation were conducted independently by the research team using Microsoft Word (Schmidt *et al*., 2021). The final qualitative synthesis prioritized studies with robust methodological design, transparent reporting, low risk of bias, and clinically relevant efficacy and safety outcomes, thereby reducing the potential for selection bias and enhancing the credibility of the review findings.

RESULTS

The systematic literature review was conducted following PRISMA guidelines through identification, screening, eligibility, and inclusion is presented in Figure 1

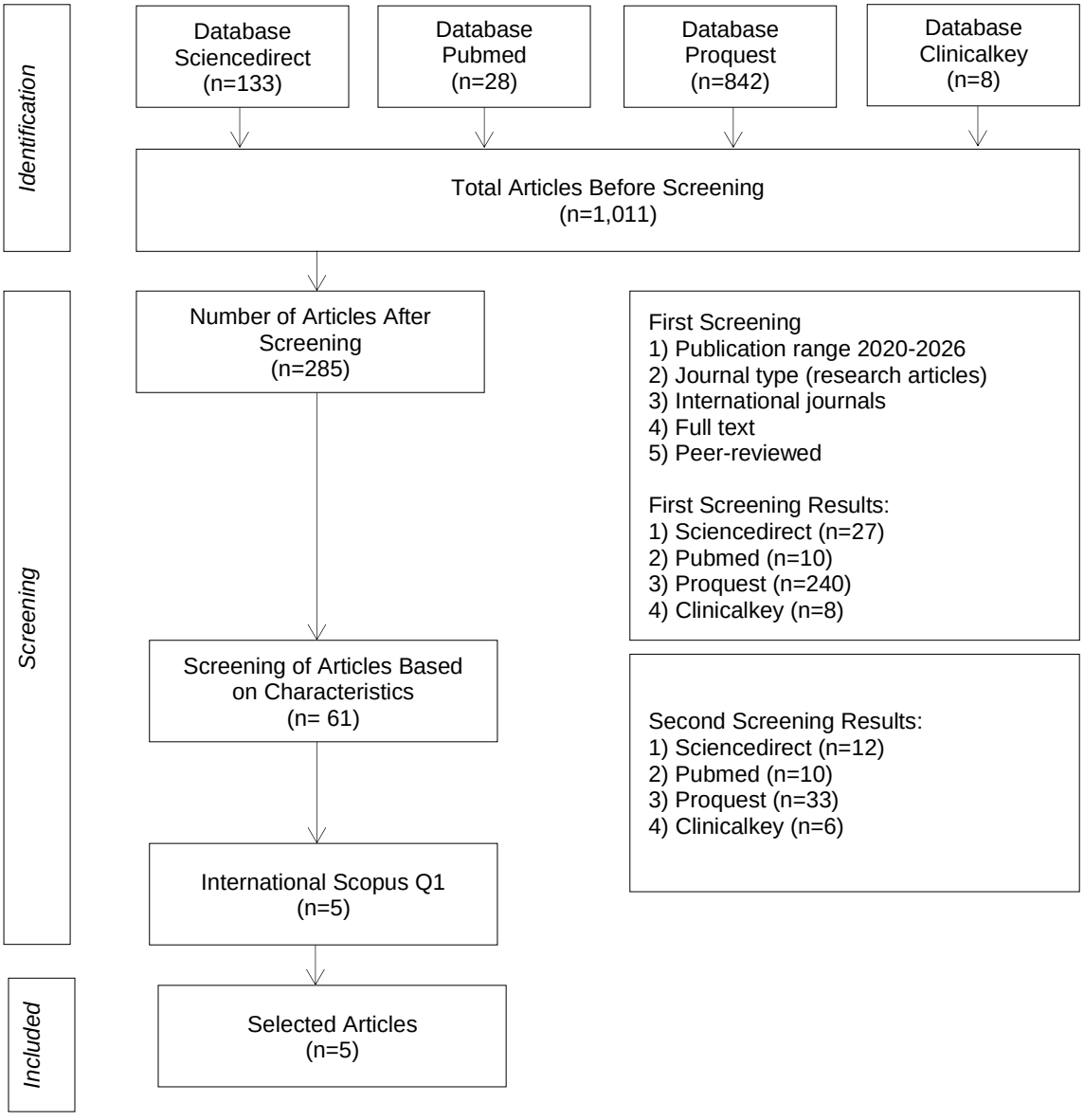

Figure 1. PRISMA Diagram

From the literature search process, five articles were identified that met the predefined inclusion criteria and were aligned with the objectives of this study, namely to evaluate the efficacy and safety profile of the tetravalent dengue vaccine TAK-003. All selected articles were subsequently categorized into key thematic areas to facilitate systematic synthesis and interpretation, as presented in Table 1, and 2.

Table 1. Thematic Analysis (n=5)

Theme	Article Number
Co-administration of TAK-003 with other vaccines maintains immunogenicity and safety	1, 4
Manufacturing consistency ensures stable immunogenicity and acceptable safety of TAK-003	2
Long-term efficacy of TAK-003 in preventing dengue infection and hospitalization in endemic settings	3
TAK-003 provides sustained protection across multiple dengue serotypes	1, 2, 3, 4
Real-world post-marketing surveillance confirms favorable safety profile of TAK-003	5

Table 2. Data Extraction (n=5)

No	Title, Authors, Year	Sample, Instruments, and Research Design	Results
1	A randomized phase 3 trial of the immunogenicity and safety of coadministration of a live-attenuated tetravalent dengue vaccine (TAK-003) and an inactivated hepatitis a (HAV) virus vaccine in a dengue non-endemic country. (Tricou, Eyre, *et al*., 2023)	Sample: 900 healthy adults (18-60 years) in the UK. Instruments: Randomized, observer-blind phase 3 trial; measurement of anti-HAV sero protection and neutralizing antibody titers. Design: Three-group comparison (HAV+Placebo, TAK-003+Placebo, or TAK-003+HAV) to test non-inferiority.	Results showed that HAV seroprotection rates were non-inferior when co-administered with TAK-003 (98.7%) compared to HAV alone (97.1%). By Day 120, 90.9-96.8% of TAK-003 recipients were seropositive for all four dengue serotypes. Co-administration was well-tolerated with no significant safety risks.
2	Consistency of immunogenicity in three consecutive lots of a	Sample: 923 healthy US adults.	Eight of 12 equivalence comparisons were met; failures in others were attributed to loss

	tetravalent dengue vaccine candidate (TAK-003): A randomized placebo-controlled trial in US adults. (Tricou, Winkle, *et al*., 2023)	Instruments: Randomized, placebo-controlled trial evaluating three different manufacturing lots of TAK-003. Design: Participants received two doses (Day 0 and 90) to evaluate lot-to-lot equivalence and safety.	of statistical power rather than vaccine issues. All lots elicited high tetravalent seropositivity (up to 97.5% at Day 120). The data supports the consistency of the manufacturing process and acceptable safety.
3	Long-term efficacy and safety of a tetravalent dengue vaccine (TAK-003): 4.5-year results from a phase 3, randomised, double-blind, placebo-controlled trial. (Tricou *et al*., 2024)	Sample: 20,099 healthy participants (4-16 years) across eight dengue-endemic countries. Instruments: RT-PCR testing for febrile illnesses and active surveillance over 4.5 years. Design: Double-blind, randomized (2:1 TAK-003 to placebo) phase 3 trial.	Cumulative vaccine efficacy (VE) was 61.2% against virologically confirmed dengue and 84.1% against hospitalization. TAK-003 showed long-term protection against all four serotypes in seropositive individuals, and against DENV-1 and DENV-2 in dengue-naive individuals.
4	Immunogenicity and safety of the live-attenuated tetravalent dengue vaccine (TAK-003) co-administered with recombinant 9-valent human papillomavirus vaccine. (El Hindi *et al*., 2025)	Sample: 614 healthy participants (9 to <15 years) in Thailand. Instruments: Phase 3, open-label, randomized trial measuring HPV IgG levels and dengue seropositivity. Design: Comparison between co-administration (TAK-003 + 9vHPV) and 9vHPV alone.	Non-inferiority (NI) was demonstrated for all HPV types when co-administered. Dengue seropositivity rates were ≥ 99.6% for all serotypes. The study supports integrating TAK-003 into existing immunization programs alongside HPV vaccines.
5	Retrospective analysis of one year of passive safety surveillance data following implementation of the dengue vaccine, Qdenga®	Sample: 156,676 doses administered to 112,345 individuals (ages 4-102) in	AEFI incidence rate was low (1.9/1000). Most events were non-serious (95.1%), such as rash, myalgia, and headache, and were more common after

	(TAK-003) at private vaccination centers, in Buenos Aires, Argentina. (Castellano *et al*., 2025)	Argentina. Instruments: Retrospective, observational, multicenter study using passive surveillance of AEFI. Design: Analysis of reported adverse events per 1000 doses, stratified by age and severity.	the first dose. Very few serious events were reported, confirming a favorable safety profile in a real-world setting.

DISCUSSION

Based on the results of the systematic literature review, five major analytical themes describe the efficacy and safety profile of the tetravalent dengue vaccine TAK-003 across clinical trial and real-world settings. Unlike a purely descriptive synthesis, this discussion critically compares inter-study findings, population subgroups, and clinical outcomes, situating the observed variability in vaccine performance within its broader clinical and policy.

First, co-administration of TAK-003 with other vaccines consistently maintains immunogenicity and safety across different age groups and vaccine platforms. Tricou, Eyre *et al*. (2023) demonstrated that co-administration of TAK-003 with the inactivated hepatitis A (HAV) vaccine in healthy adults did not compromise immune responses to either vaccine, with non-inferior HAV seroprotection and high dengue seropositivity across all four serotype (Tricou, Eyre, *et al*., 2023). Similar findings were reported by 19 El Hindi *et al*. (2025), who observed dengue seropositivity rates ≥99.6% for all serotypes following co-administration with the 9-valent human papillomavirus (9vHPV) vaccine in adolescents (El Hindi *et al*., 2025). Comparatively, these studies indicate that TAK-003 exhibits immunological compatibility across distinct vaccine platforms (inactivated vs recombinant), showing that immune interference is unlikely to be a limiting factor in integrated immunization programs. These findings align with broader vaccine co-administration evidence reported by 21 Mondelli (2023) and reinforce the feasibility of incorporating TAK-003 into existing national immunization schedules without additional safety concerns (Mondelli, 2023; Patel *et al*., 2023).

Second, manufacturing consistency emerges as a critical determinant of reliable immunogenicity outcomes. The randomized, placebo-controlled trial by Tricou, Winkle, *et al*. (2023) assessed immunogenic equivalence across three consecutive manufacturing lots and reported consistently high tetravalent seropositivity rates, reaching up to 97.5% at Day 120 (Tricou, Winkle, *et al*., 2023). Although not all predefined equivalence margins were met, comparative analysis suggests that these deviations were statistically driven rather than clinically meaningful, as no systematic reduction in serotype-specific immune responses was observed. This conclusion is supported by Jackson *et al*. (2018), who similarly reported robust and comparable immune responses across multiple vaccine lots (Jackson *et al*., 2018). From a regulatory and supply-chain perspective, this consistency is particularly important for

large-scale deployment in endemic regions, where batch-to-batch variability could undermine public confidence and program effectiveness.

Third, TAK-003 demonstrates sustained long-term efficacy, although with notable variation across clinical endpoints and population subgroups. Tricou *et al*. (2024) reported a cumulative vaccine efficacy of 61.2% against virologically confirmed dengue and a substantially higher efficacy of 84.1% against dengue-related hospitalization over a 4.5-year follow-up period (Tricou *et al*., 2024). This divergence highlights an important clinical distinction: while TAK-003 provides moderate protection against overall dengue infection, it offers stronger protection against severe disease outcomes. Such findings suggest that the public health value of TAK-003 lies primarily in reducing disease severity and healthcare burden rather than achieving complete infection prevention. This differential efficacy has direct implications for policy-makers, as vaccines with higher effectiveness against hospitalization may still be highly cost-effective in endemic settings with limited healthcare capacity.

Fourth, comparative analysis across studies reveals heterogeneity in vaccine performance by dengue serotype and baseline serostatus. Long-term protection against all four serotypes was consistently observed among baseline seropositive individuals, whereas protection in seronegative participants was predominantly sustained for DENV-1 and DENV-2 13 (Tricou *et al*., 2024). This pattern suggests that pre-existing immunity enhances the breadth of vaccine-induced protection, a finding that aligns with immunological priming theories and contrasts with earlier concerns surrounding dengue vaccines in seronegative populations. Evidence from (Tricou, Eyre, *et al*., 2023; Tricou, Winkle, *et al*., 2023) and (El Hindi *et al*., 2025) further supports this observation, as high seropositivity rates were more uniform in populations with prior dengue exposure. These differences show the need for specific vaccination strategies, particularly in regions with heterogeneous dengue transmission intensity.

Fifth, real-world post-marketing surveillance provides critical external validation of clinical trial findings. 20, Castellano *et al*. (2025) analyzed more than 156,000 administered doses of Qdenga® (TAK-003) in Argentina and reported a low incidence of adverse events following immunization (1.9 per 1,000 doses), with most events being mild and self-limiting (Castellano *et al*., 2025). When compared with safety profiles reported in controlled clinical trials, these findings show no signal of increased risk in routine programmatic use. The concordance between real-world and trial-based safety data strengthens confidence in the overall benefit-risk profile of TAK-003 and supports its broader implementation in national dengue control programs (Flacco *et al*., 2024).

Meta-analysis was not conducted in this review due to substantial heterogeneity across the included studies. Differences in study design (randomized trials vs observational surveillance), outcome definitions (virologically confirmed dengue vs hospitalization), follow-up duration, population age structure, baseline serostatus, and serotype-specific reporting precluded meaningful statistical pooling of effect estimates. Conducting a meta-analysis under such conditions could have produced misleading summary estimates and reduced the interpretability of the findings. Therefore, a structured qualitative synthesis was deemed the most appropriate analytical approach to preserve clinical.

CONCLUSION AND RECOMMENDATION

Based on the findings of this systematic literature review, TAK-003 shows a robust and favorable efficacy-safety profile across clinical trial and real-world. Evidence consistently shows that TAK-003 can be co-administered with other vaccines without compromising immunogenicity or safety, exhibits stable manufacturing consistency with high tetravalent seropositivity, provides sustained long-term protection against dengue infection and hospitalization particularly in endemic settings and induces broad immune responses across all four dengue serotypes. Furthermore, post-marketing surveillance data confirm a low incidence of mostly non-serious adverse events, reinforcing its acceptable safety profile in routine use. Collectively, these findings support the inclusion of TAK-003 in national and regional dengue immunization programs, including integration with existing vaccination schedules. Future research is recommended to continue long-term effectiveness monitoring, assess performance in diverse epidemiological settings, and evaluate real-world impact on dengue transmission and healthcare burden to optimize vaccination strategies and policy decision-making.

REFERENCES

Abbasi, E. (2025). The impact of climate change on travel-related vector-borne diseases: A case study on dengue virus transmission. *Travel Medicine and Infectious Disease*, *65*(March), 102841. https://doi.org/10.1016/j.tmaid.2025.102841

Agrawal. (2024). Analysis and recommendation system-based on PRISMA checklist to write systematic review. *Assessing Writing*, *61*, 100866.

Alanazi, F. T. H., Alharbi, B. N., Aljuaid, T. H., Alammar, F. A., Almarzouq, Y. F., Albalawi, I., Almutairi, M. N., Alshaghroud, S. M., Alhaosawi, M. E., Albalawi, M. A. S., & Alorf, A. A. (2024). The impact of vaccinations on disease prevention: A comprehensive analysis of their role in enhancing global public health and reducing morbidity and mortality rates. *International Journal of Health Sciences*, *8*(S1), 1885–1907. https://doi.org/10.53730/ijhs.v8ns1.15436

Castellano, V. E., Diana Menéndez, S., Ochoa, J., Burgos, F., Fernadez, F., Gigliotti, R., Díaz, M., & Bonvehí, P. (2025). Retrospective analysis of one year of passive safety surveillance data following implementation of the dengue vaccine, Qdenga® (TAK-003) at private vaccination centers, in Buenos Aires, Argentina. *Vaccine: X*, *27*(November). https://doi.org/10.1016/j.jvacx.2025.100749

El Hindi, T., Anugulruengkitt, S., Lapphra, K., Limkittikul, K., Tangsathapornpong, A., Galindo-Tsoukas, C., Hellwig, M., Roubinis, N., Schuring, R., Biswal, S., & Folschweiller, N. (2025). Immunogenicity and safety of the live-attenuated tetravalent dengue vaccine (TAK-003) co-administered with recombinant 9-valent human papillomavirus vaccine. *Vaccine*, *62*(March), 127558. https://doi.org/10.1016/j.vaccine.2025.127558

Flacco, M. E., Bianconi, A., Cioni, G., Fiore, M., Calò, G. L., Imperiali, G., Orazi, V., Tiseo, M., Troia, A., Rosso, A., & Manzoli, L. (2024). Immunogenicity, Safety and Efficacy of the Dengue Vaccine TAK-003: A Meta-Analysis. *Vaccines*, *12*(7), 1–13. https://doi.org/10.3390/vaccines12070770

Hou, J., Ye, W., & Chen, J. (2022). Current Development and Challenges of Tetravalent Live-Attenuated Dengue Vaccines. *Frontiers in Immunology*, *13*(February), 1–13. https://doi.org/10.3389/fimmu.2022.840104

Idris. (2021). An update on dengue vaccine development, challenges, and future perspectives. *Expert Opinion on Drug Discovery*, *16*(1), 47–58.

Jackson, L. A., Rupp, R., Papadimitriou, A., Wallace, D., Raanan, M., & Moss, K. J. (2018). A phase 1 study of safety and immunogenicity following intradermal administration of a tetravalent dengue vaccine candidate. *Vaccine*, *36*(27), 3976–3983. https://doi.org/10.1016/j.vaccine.2018.05.028

Lindstrand, A., Cherian, T., Chang-Blanc, D., Feikin, D., & O'brien, K. L. (2021). The World of Immunization: Achievements, Challenges, and Strategic Vision for the Next Decade. *Journal of Infectious Diseases*, *224*(Suppl 4), S452–S467. https://doi.org/10.1093/infdis/jiab284

López-Medina, E., Biswal, S., Saez-Llorens, X., Borja-Tabora, C., Bravo, L., Sirivichayakul, C., Vargas, L. M., Alera, M. T., Velásquez, H., Reynales, H., Rivera, L., Watanaveeradej, V., Rodriguez-Arenales, E. J., Yu, D., Espinoza, F., Dietze, R., Fernando, L. K., Wickramasinghe, P., Duarte Moreira, E., … Borkowski, A. (2022). Efficacy of a Dengue Vaccine Candidate (TAK-003) in Healthy Children and Adolescents 2 Years after Vaccination. *Journal of Infectious Diseases*, *225*(9), 1521–1532. https://doi.org/10.1093/infdis/jiaa761

Mondelli, M. U. (2023). Does co-administration of vaccines interfere with immune responses? The jury is still out. *Clinical Microbiology and Infection*, *29*(12), 1482–1484. https://doi.org/10.1016/j.cmi.2023.09.022

Nakhaie. (2026). Dengue Fever: Viral, Environmental, and Human Factors Driving Expansion and Pandemic Risk. *Reviews in Medical Virology*, *36*(1), 70088.

Patel, S. S., Winkle, P., Faccin, A., Nordio, F., LeFevre, I., & Tsoukas, C. G. (2023). An open-label, Phase 3 trial of TAK-003, a live attenuated dengue tetravalent vaccine, in healthy US adults: immunogenicity and safety when administered during the second half of a 24-month shelf-life. *Human Vaccines and Immunotherapeutics*, *19*(2). https://doi.org/10.1080/21645515.2023.2254964

Roy, S. K., & Bhattacharjee, S. (2021). Dengue virus: Epidemiology, biology, and disease aetiology. *Canadian Journal of Microbiology*, *67*(10), 687–702. https://doi.org/10.1139/cjm-2020-0572

Salmon, D. A., Lambert, P. H., Nohynek, H. M., Gee, J., Parashar, U. D., Tate, J. E., Wilder-Smith, A., Hartigan-Go, K. Y., Smith, P. G., & Zuber, P. L. F. (2021). Novel vaccine safety issues and areas that would benefit from further research. *BMJ Global Health*, *6*, 1–11. https://doi.org/10.1136/bmjgh-2020-003814

Schmidt, L., Olorisade, B. K., McGuinness, L. A., Thomas, J., & Higgins, J. P. T. (2021). Data extraction methods for systematic review (semi)automation: A living systematic review. *F1000Research*, *10*, 401. https://doi.org/10.12688/f1000research.51117.1

Shafie, A. A., Moreira, E. D., Vidal, G., Di Pasquale, A., Green, A., Tai, R., & Yoong, J. (2024). Sustainable Dengue Prevention and Management: Integrating Dengue Vaccination Strategies with Population Perspectives. *Vaccines*, *12*(2), 1–10. https://doi.org/10.3390/vaccines12020184

Sharp. (2022). Knowledge gaps in the epidemiology of severe dengue impede vaccine evaluation. *The Lancet Infectious Diseases*, *22*(2), 42–51.

Tricou, V., Eyre, S., Ramjee, M., Collini, P., Mojares, Z., Loeliger, E., Mandaric, S., Rauscher, M., Brose, M., Lefevre, I., Folschweiller, N., & Wallace, D. (2023). A randomized phase 3 trial of the immunogenicity and safety of coadministration of a live-attenuated tetravalent dengue vaccine (TAK-003) and an inactivated hepatitis a (HAV) virus vaccine in a dengue non-endemic country. *Vaccine*, *41*(7), 1398–1407. https://doi.org/10.1016/j.vaccine.2023.01.007

Tricou, V., Winkle, P. J., Tharenos, L. M., Rauscher, M., Escudero, I., Hoffman, E., LeFevre, I., Borkowski, A., & Wallace, D. (2023). Consistency of immunogenicity

in three consecutive lots of a tetravalent dengue vaccine candidate (TAK-003): A randomized placebo-controlled trial in US adults. *Vaccine*, *41*(47), 6999–7006. https://doi.org/10.1016/j.vaccine.2023.09.049

Tricou, V., Yu, D., Reynales, H., Biswal, S., Saez-Llorens, X., Sirivichayakul, C., Lopez, P., Borja-Tabora, C., Bravo, L., Kosalaraksa, P., Vargas, L. M., Alera, M. T., Rivera, L., Watanaveeradej, V., Dietze, R., Fernando, L. K., Wickramasinghe, V. P., Moreira, E. D., Fernando, A. D., … Wallace, D. (2024). Long-term efficacy and safety of a tetravalent dengue vaccine (TAK-003): 4·5-year results from a phase 3, randomised, double-blind, placebo-controlled trial. *The Lancet Global Health*, *12*(2), e257–e270. https://doi.org/10.1016/S2214-109X(23)00522-3

Wilder-Smith, A., Cherian, T., & Hombach, J. (2025). Dengue Vaccine Development and Deployment into Routine Immunization. *Vaccines*, *13*(5), 1–12. https://doi.org/10.3390/vaccines13050483