VACCINE DELIVERY RESEARCH DIGEST

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1. Determinants of Malaria Vaccine Acceptance: A Systematic Review and Meta-Analysis of Awareness, Acceptance, Hesitancy, and Willingness to Pay.

Bushi G, Khatib M, S R, Kaur I, Sharma A, Iqbal S, et al.

Immun Inflamm Dis. 2025 May 14;13(5):e70205.

PubMed ID: 40365988

ABSTRACT

BACKGROUND: Malaria is a life-threatening disease caused by Plasmodium parasites, transmitted through the bites of infected female Anopheles mosquitoes. It remains a major global health issue, with 263 million cases and 597,000 deaths in 2023, primarily affecting young children and pregnant women. This review evaluates awareness, acceptance, hesitancy, and willingness to pay (WTP) for the RTS,S/AS01 malaria vaccine, along with the key factors influencing these outcomes.

METHODS: A comprehensive literature search was conducted in Web of Science, PubMed, and Embase, covering publications up to 18 June 2024. Observational studies assessing awareness, acceptance, hesitancy, and WTP for the malaria vaccine in endemic regions were included. Two independent reviewers screened the studies. Data extraction was performed using Nested Knowledge software and analyzed with R v.4.4. Pooled prevalences were estimated using random-effects models, and heterogeneity was assessed with the I^2 statistic.

RESULTS: Eighteen studies with 21,975 participants provided insights into malaria vaccine dynamics: 32% awareness (95% CI, 18%-50%), 83% acceptance (95% CI, 75%-89%), 14% hesitancy (95% CI, 7%-26%), and 58% WTP (95% CI, 34%-79%). Key determinants of acceptance included age, where younger adults (18-24 years) showed lower acceptance (OR = 0.64, 95% CI, 0.35-0.93). Employment, particularly farmers, had higher acceptance rates (OR = 3.20, 95% CI, 1.00-7.40). Lower socioeconomic status and larger family sizes were associated with decreased acceptance (OR = 0.18, 95% CI, 0.02-0.38).

CONCLUSION: This review revealed an 83% acceptance rate for the malaria vaccine, with variability in awareness (32%), hesitancy (14%), and willingness to pay (58%). Age, employment, and socioeconomic status were significant determinants of acceptance. However, due to potential publication bias and high heterogeneity, these findings should be cautiously interpreted. The results highlight the necessity for targeted interventions to enhance vaccine acceptance. Further research is required to elucidate factors that influence vaccine acceptance.

WEB: 10.1002/iid3.70205
IMPACT FACTOR: 3.1
CITED HALF-LIFE: 2.7

START COMMENTARY

Studies that reported malaria vaccine acceptance (89%), awareness (78%), hesitancy (56%), willingness to pay (50%), and factors associated with acceptance (50%) were included, and participants were categorized as caregivers or children <5 years old or self-respondents. The pooled prevalence of willingness to pay (WTP) for malaria vaccine was higher among caregivers of children <5 years than among self-respondents (78% and 47%, respectively). Caregivers who had recently had malaria or whose child had recently had malaria were more likely to indicate vaccine acceptance, and higher perceived susceptibility to malaria was associated with higher vaccine acceptance. Low prevalence of vaccine awareness among both categories of participants highlights the need for targeted education interventions.

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2. Real-world effectiveness of RSVpreF vaccination during pregnancy against RSV-associated lower respiratory tract disease leading to hospitalisation in infants during the 2024 RSV season in Argentina (BERNI study): a multicentre, retrospective, test-negative, case-control study.

Pérez Marc G, Vizzotti C, Fell D, Di Nunzio L, Olszevicki S, Mankiewicz S, et al.

Lancet Infect Dis. 2025 May 08.

PubMed ID: 40339585

ABSTRACT

BACKGROUND: In March, 2024, Argentina became the first country to implement a national maternal immunisation programme with bivalent respiratory syncytial virus (RSV) prefusion F vaccine (RSVpreF) as the primary strategy to prevent RSV disease among infants. We aimed to evaluate vaccine effectiveness against RSV-associated lower respiratory tract disease (LRTD) and severe LRTD leading to hospitalisation among infants during the first season after implementation.

METHODS: A multicentre, retrospective, test-negative, case-control study was done during the 2024 RSV season in 12 hospitals across Argentina (BERNI study). We included infants aged 6 months or younger who were hospitalised with LRTD between April 1 and Sept 30, 2024, and tested for RSV using PCR or indirect immunofluorescence; cases were infants with any positive RSV test and controls were PCR-confirmed negative for RSV. Infants were considered born to an RSVpreF-vaccinated pregnant woman if RSVpreF was received between 32+0/7 weeks and 36+6/7 weeks of gestation and 14 days or more before delivery. We estimated vaccine effectiveness against RSV-associated LRTD requiring hospitalisation (primary outcome) and RSV-associated severe LRTD requiring hospitalisation (key secondary outcome) by comparing the odds of RSVpreF vaccination during pregnancy among infant cases versus controls using multilevel logistic regression adjusted for potential confounders.

FINDINGS: Of 633 infants hospitalised for LRTD between April 1 and Sept 30, 2024, 505 (286 cases and 219 controls) met full eligibility criteria for inclusion in the primary vaccine effectiveness analysis; 51 (18%) cases and 109 (50%) controls were born to individuals who received RSVpreF during pregnancy. Vaccine effectiveness against RSV-associated LRTD leading to infant hospitalisation was 78·6% (95% CI 62·1-87·9) from birth to age 3 months and 71·3% (53·3-82·3) from birth to age 6 months. Effectiveness against RSV-associated severe LRTD leading to hospitalisation was 76·9% (45·0-90·3) from birth to age 6 months. Three RSV-associated in-hospital deaths occurred, all among infants whose mothers did not receive RSVpreF during pregnancy.

INTERPRETATION: These real-world estimates for the 2024 RSV season in Argentina show high RSVpreF effectiveness against RSV-associated LRTD and severe LRTD leading to hospitalisation from birth to age 3 months and sustained to age 6 months.

FUNDING: Pfizer.

WEB: 10.1016/S1473-3099(25)00156-2
IMPACT FACTOR: 36.4
CITED HALF-LIFE: 4.4

START COMMENTARY

Respiratory syncytial virus (RSV) vaccine coverage among pregnant individuals in Argentina reached 60% by August 2024 after a national RSV maternal immunization program was instituted in March 2024 in Argentina. When compared with those who did not receive the RSV vaccine, those who were vaccinated for RSV during pregnancy were more likely to have received another recommended vaccine during pregnancy (96% vs 77%). Among infants hospitalized with RSV, 33% of those whose mother received the RSV vaccine and 75% of those whose mother did not progressed to severe lower respiratory tract disease (LRTD), with 22% and 14%, respectively, requiring ICU care for more than 4 hours. Infants born to those who received an RSV vaccine during pregnancy generally had less severe illness across all measures (Table 4).

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3. Using an analogue-digital hybrid clinical data management platform during a two-dose preventive Ebola virus vaccine trial in Goma, the Democratic Republic of the Congo.

Brindle H, Tetsa-Tata D, Edwards T, Choi E, Kasonia K, Aboubacar S, et al.

PLOS Glob Public Health. 2025 May 04;5(5):e0004487.

PubMed ID: 40315243

ABSTRACT

Clinical trials in settings with intermittent or non-existent internet and power connectivity, for example during humanitarian emergencies, present challenges in the synchronisation of data across different sites, in addition to accessing a centralised database in real-time. To overcome these, we designed a novel hybrid analogue/digital data management system which was deployed during the rapid implementation of a Phase III evaluation of a two-dose preventative vaccine for Ebola virus disease in Goma, Democratic Republic of the Congo, from 2019 to 2022. We provided study participants with an Enhanced Participant Record Card (EPRC) that served as eligibility for, and confirmation of, vaccination and was used in combination with Open Data Kit (ODK) electronic case report forms to create an off-grid study participant management system. To understand the utility of the EPRC, we analysed data from 15,327 study participants who received both vaccines and various types of prompts or reminders to return for dose 2, including home visits, telephone calls, or short messaging service (SMS). A total of 53% participants referred to the date on the EPRC as a prompt to return for dose 2 and 36.1% mentioned this as the only prompt. A multivariable generalised linear mixed-effects model showed that those who were not working, those aged 45-64 years or who had a chronic medical condition identified prior to receiving dose 2 were more likely to use the date on the EPRC as a prompt. Our findings demonstrate the utility of this system in the facilitation of decentralised data collection in off-grid locations that may be useful for future trials in complex humanitarian settings. Clinical Trials Registration Number: ClinicalTrials.gov NCT01128790.

WEB: 10.1371/journal.pgph.0004487

IMPACT FACTOR: 2.3

CITED HALF-LIFE: 4.4

START COMMENTARY

The Enhanced Participant Reference Card (EPRC) was designed to meet study requirements for a tool that could be used across multiple study sites in areas where access to internet was not always possible. These requirements included: 1) assigning unique study identification numbers to participants, 2) providing a way to accurately link the unique ID on all case reporting forms across multiple visits over time, 3) ensuring that the individual was the same person seen at previous visits, 4) assisting in managing the vaccination clinic flow, 5) tracking vaccine eligibility and exclusions, 6)

reminding patients of timing of future visits, 7) providing information about how to contact the study team in case of adverse events, 8) providing documentation of study participation to healthcare providers outside of the vaccine clinic, 9) and complying with data protection protocols. Constraints included working without a reliable internet connection, consistent power supply, or real-time data synchronization between local devices or a central database, and identifying when participants attended different study sites or clinics. The EPRC was given to participants during study registration, and had a photograph, vaccination card information, and a sticker with a unique study ID (Figure 2). Study staff used a ticket punching tool to punch boxes printed on the sticker as the participant completed study steps. Participants would provide the card at each visit so the study team at any site would have the information needed to meet their needs.

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4. Effect of the 13-valent pneumococcal conjugate vaccine on pneumococcal carriage in rural Gambia 10 years after its introduction: A population-based cross-sectional study.

Osei I, Mendy E, van Zandvoort K, Sarwar G, Nuredin I, Bruce J, et al.

Vaccine. 2025 May 18;56:127181.
PubMed ID: 40300436

ABSTRACT

BACKGROUND: Sub-Saharan Africa has a high burden of pneumococcal diseases. Pneumococcal carriage precedes invasive disease and transmission. The introduction of pneumococcal conjugate vaccines (PCVs) has significantly reduced global vaccine-type (VT) pneumococcal disease, but data on PCVs' long-term impact on VT serotypes in Africa are limited. We aimed to evaluate PCV13's long-term effect on pneumococcal carriage in rural Gambia.

METHODS: From January to November 2022, we conducted a population-based, cross-sectional pneumococcal carriage survey in Central and Upper River Regions of The Gambia. We collected data on demographic characteristics, clinical history, risk factors, and PCV status. Nasopharyngeal swabs were taken from randomly selected household members of all ages. Streptococcus pneumoniae was isolated and serotyped using standard methods. We measured the prevalence of pneumococcal carriage by specific age groups, PCV13 vaccination status, and the proportions of different pneumococcal outcomes among carriers. We performed multivariable logistic regression to examine factors associated with VT carriage.

RESULTS: Overall, 4087 participants were enrolled; the prevalence of pneumococcal carriage was 32.1% (95% CI: 29.34% - 35.03%). The estimated prevalence of PCV13 VT carriage was 6.4% (95% CI: 5.48% - 7.47%). Children aged 5-9 years had the highest VT carriage prevalence at 13.6% (95% CI: 10.34% - 17.56%). Among fully PCV-vaccinated children under 10, the odds of VT carriage in 5-9-year-olds were 1.60 times higher than in infants aged 0-11 months [AOR = 1.60, 95% CI:1.06-2.41]. The prevalence of VT carriage was similar among fully PCV-vaccinated and unvaccinated children under 10 years of age. Serotypes 19F, 3 and 6A were the most abundant VTs; 19F and 3 were the most prevalent among <5 and 5-14-year-old children, respectively.

CONCLUSIONS: Ten years after the introduction of PCV13 in the Gambia, residual VT carriage persists, particularly in age groups in whom direct protection from immunization in infancy has waned. A booster dose or catch-up vaccinations could aid control of VT circulation.

WEB: 10.1016/j.vaccine.2025.127181
IMPACT FACTOR: 4.5
CITED HALF-LIFE: 7.9

START COMMENTARY

Overall pneumococcal carriage was highest among the youngest age groups and decreased with age, with prevalence among those <5 years, 5-14 years, and ≥15 years of 64%, 35%, and 14%, respectively (Table 1). Authors report that the prevalence of vaccine type (VT) carriage among children <5 years old decreased by 32% between 2009 and 2022, with decreases of 6%, 5%, and 2% in those aged 5-14, 15-44, and ≥45 years, respectively. These changes provide evidence of the indirect effect of pneumococcal conjugate vaccine (PCV) in children on older age groups. Serotypes 19F, 3, and 6A accounted for >60% of all PCV13 VT carriage. The prevalence of pneumococcal carriage with any serotype was lower among those who had received at least 2 doses of PCV13 compared to those who had received less than 2 doses (52% and 73%, respectively) in children under 10 years. The estimated prevalence of non-vaccine type (NVT) pneumococcal carriage in the entire population was 24.1%, and prevalence decreased with age.

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5. Incidence rates of malaria, meningitis, and mortality in children younger than 5 years: a prospective cohort study in Ghana and Kenya before the roll-out of the RTS,S/AS01E malaria vaccine from 2016 to 2022.

Asante K, Bozonnat M, Savic M, Owusu-Agyei S, Kaali S, Otieno W, et al.

Lancet Glob Health. 2025 Apr 28;13(5):e859-e869.
PubMed ID: 40288396

ABSTRACT

BACKGROUND: The RTS,S/AS01E malaria vaccine was introduced in selected communities of Ghana, Kenya, and Malawi in 2019 under a WHO-coordinated pilot programme. The scarcity of background disease incidence rates might hamper the assessment of vaccine safety and effectiveness. We aimed to determine the incidence rates of malaria, meningitis, and death, and health outcomes leading to hospital admission in children younger than 5 years enrolled before RTS,S/AS01E implementation. Interim results from EPI-MAL-002 up to Oct 5, 2018, were reported previously. Here, we report results from the final analysis of the pre-vaccine introduction study.

METHODS: This disease surveillance study combined two approaches: (1) prospective cohort event monitoring (home visits scheduled to mimic a future four-dose RTS,S/AS01E vaccination schedule [ie, a simulated vaccination schedule], with additional visits after the simulated schedule and continuous disease monitoring of outpatient visits and hospital admission) in children enrolled in two age groups (6-12 weeks [6-12W] and 5-17 months [5-17M]), and (2) hospital-based disease surveillance for children not enrolled in the prospective cohort, in three sites in Ghana and Kenya. Key outcomes were rates of meningitis, malaria, adverse events of special interest, other adverse events leading to hospital admission, all-cause mortality, and malaria-attributable mortality.

FINDINGS: The final analysis included 23 427 children: 9032 in the 6-12W age group, 9694 in the 5-17M age group, and 4701 in hospital-based disease surveillance. In the 5-17M age group (corresponding to the WHO-recommended age for RTS,S/AS01E vaccination), the incidence rates of meningitis and cerebral malaria within an at-risk period of 1 year after the simulated vaccination schedule were both equal to 28 (95% CI 9-65) per 100 000 person-years. There were 11 (0·1%) children with an adverse event of special interest during hospital admission. In the 5-17M age group, the all-cause mortality rate was 643 (95% CI 531-771) per 100 000 person-years.

INTERPRETATION: Observed incidence of meningitis and cerebral malaria were in the previously published range, whereas childhood mortality was lower, suggesting that the recent efforts to reduce mortality in children younger than 5 years have been impactful. Data from this study have public health use and will form the baseline evidence for ongoing evaluation of the benefit-risk of RTS,S/AS01E.

FUNDING: GSK and PATH.

WEB: 10.1016/S2214-109X(25)00022-1
IMPACT FACTOR: 20.0
CITED HALF-LIFE: 4.3

START COMMENTARY

In the active surveillance cohort of children 5-17 months of age, nearly 60% of children were diagnosed with malaria during the study period. Of these, <2% were severe malaria cases and <0.1% had cerebral malaria (Table 1). Approximately 20% of children in the active surveillance cohort were admitted to the hospital at some point during the study, and the most common reasons for hospitalization were anemia (1.5%), gastrointestinal disorders/infection (1.1%), and lower respiratory infection (0.8%) (Table 3). The study investigated baseline incidence of 15 adverse events of special interest (AESIs) chosen in collaboration with pediatricians working in sub-Saharan Africa based on AESIs observed with other vaccines or hypothetical association with the RTS, S/AS01E vaccine. These include acute disseminated encephalomyelitis, encephalitis, Guillain Barre syndrome, generalized convulsive seizure, juvenile arthritis, and Kawasaki disease (Supplementary appendix 1). 12 AESIs were reported in the 5-17 month age group in the active surveillance cohort, with 5 generalized convulsive seizure events, 3 anaphylaxis events, 2 episodes of acute disseminated encephalomyelitis, and one each of intussusception and type 1 diabetes.

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6. Safety of RTS,S/AS01E malaria vaccine up to 1 year after the third dose in Ghana, Kenya, and Malawi (EPI-MAL-003): a phase 4 cohort event monitoring study.

Haine V, Oneko M, Debois M, Ndeketa L, Agyapong P, Boahen O, et al.

Lancet Glob Health. 2025 May 24;13(6):e995-e1005.
PubMed ID: 40288377

ABSTRACT

BACKGROUND: RTS,S/AS01E has been successfully administered to over two million children since 2019 through the Malaria Vaccine Implementation Programme (MVIP). In this Article, we report the safety results of a study evaluating RTS,S/AS01E safety and effectiveness in real-world settings.

METHODS: EPI-MAL-003 is an ongoing phase 4 disease surveillance study with prospective cohort event monitoring and hospital-based surveillance, done in the setting of routine health-care practice in Ghana, Kenya, and Malawi and fully embedded in the MVIP. The study design was dependent on the cluster-randomised vaccine implementation. In active surveillance, we enrolled children younger than 18 months from exposed (where RTS,S/AS01E was offered) and unexposed clusters. The coprimary endpoints were the occurrence of predefined adverse events of special interest and aetiology-confirmed meningitis. We report primary and secondary safety results up to 1 year after the primary vaccine schedule (three doses). The study is registered with ClinicalTrials.gov, NCT03855995.

FINDINGS: The first participant was enrolled on March 21, 2019. The cutoff date for the current analysis was 1 year after the third RTS,S/AS01E dose for each participant. In total, 44 912 children (19 993 in Ghana, 11 990 in Kenya, and 12 929 in Malawi) were included in the analysis set for the cluster-randomised comparison: 22 508 from exposed clusters and 22 404 from unexposed clusters. Incidence rates (expressed per 100 000 person-years) for generalised convulsive seizures and intussusception were similar between vaccinated and unvaccinated children. Aetiology-confirmed meningitis was reported in two children: one case of bacterial meningitis due to Streptococcus pneumoniae in an RTS,S/AS01E-vaccinated child in the exposed clusters, and one case of viral meningitis due to human herpesvirus 6 in an unvaccinated child in the unexposed clusters. Both cases occurred within 12 months after vaccination in children in the cluster-design analysis set, leading to incidence rates of 4·1 (95% CI 0·1-23·0) per 100 000 person-years in RTS,S/AS01E-vaccinated children and 4·0 (0·1-22·6) per 100 000 person-years in unvaccinated children, and a country-adjusted incidence rate ratio (IRR) of 0·96 (95% CI 0·06-15·34; p=0·98). Cerebral malaria cases were reported for four (<0·1%) of 20 639 RTS,S/AS01E-vaccinated children in the exposed clusters and two (<0·1%) of 22 137 unvaccinated children in the unexposed clusters. These included three and two cases occurring within 12 months after the primary vaccination, in RTS,S/AS01E-

vaccinated children and unvaccinated children, respectively (IRR 1·43, 95% CI 0·24-8·58, p=0·70). Incidence rates for all-cause mortality were 659·7 (95% CI 561·5-770·3) in vaccinated children versus 724·5 (622·3-838·8) in unvaccinated children, with similar incidence rates for boys and girls.

INTERPRETATION: We found no evidence of vaccination being associated with an increased risk of meningitis, cerebral malaria, or mortality among vaccinated children, and no new safety risks were identified.

FUNDING: GSK.

WEB: 10.1016/S2214-109X(25)00096-8
IMPACT FACTOR: 20.0
CITED HALF-LIFE: 4.3

START COMMENTARY

This phase 4 study was conducted to evaluate safety of the RTS, S/AS01E malaria vaccine after findings in a phase 3 trial in seven sub-Saharan African countries that approximately 25% of children had at least one serious adverse event, with 0.3% thought to be attributable to the vaccine. Increased risk for febrile seizures, all-cause mortality among girls, meningitis, and cerebral malaria were noted in the earlier trial, and, while these were considered most likely to be chance findings, the Strategic Advisory Group of Experts on Immunization and the World Health Organization's Malaria Policy Advisory Group recommended further safety testing in real-world settings before wide-spread vaccine use. This study of safety was nested within a phase 4 disease surveillance study among children enrolled in active surveillance, which included home visits, and continuous monitoring of outpatient visits and hospitalizations. Only 0.1% in both the vaccinated and unvaccinated group had ≥ 1adverse event of special interest. Incidence of AESIs were not significantly different between the vaccinated and unvaccinated groups over one year of follow-up (Table 3), providing evidence that the RTS, S/AS01E is safe for use in young children.

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7. Effectiveness of a single-dose mass dengue vaccination in Cebu, Philippines: Final results of a 5-year case-control study.

Agrupis K, Crisostomo M, Daag J, Sarol J, Lopez M, Florendo K, et al.

Vaccine. 2025 May 18;56:127142.
PubMed ID: 40279922

ABSTRACT

BACKGROUND: In mid-2017, the Philippine Department of Health launched a vaccination program of nine- to fourteen-year-old children using CYD-TDV (Dengvaxia, Sanofi) in Cebu province. The vaccination program was discontinued after only one dose was given. Until 2020, the interim vaccine effectiveness against hospitalized virologically confirmed dengue (VCD) and dengue with warning signs was 26 % and 51 %, respectively. In this report, we assess vaccine protection through February 2023.

METHODS: From 15 February 2018 to 28 February 2023, we conducted a case-control study in Cebu province. Children residing in Cebu who were eligible to participate in the dengue mass vaccination in mid-2017 and subsequently admitted to any of four participating public hospitals with suspected dengue were enrolled. A blood sample was collected for dengue RT-PCR and clinical and socio-demographic information were obtained. Children hospitalized with VCD were followed until discharge and their illness classified according to WHO 2009 criteria as dengue, dengue with warning signs and severe dengue. To estimate the level of vaccine protection, vaccination status was compared between VCD cases and neighborhood controls of the same sex and age-group.

FINDINGS: We included 584 VCD cases and 1168 controls in the analysis. Of the 584 cases, 397 (67·8 %) presented as dengue with warning sign (DWS), 8 (1·4 %) had severe dengue, and 1 (0·2 %) died. All four dengue virus serotypes were detected, but serotype 3 was the most common (287/584 or 49·1 %). Receipt of one dose of CYD-TDV was associated with 21 % (95 % CI, -7 to 41 %; p = 0·1129) overall protection against hospitalized VCD and 31 % (95 % CI, 6 to 49 %; p < 0·0001) protection against more severe presentations of dengue (dengue with warning signs and severe dengue).

CONCLUSION: A single dose of CYD-TDV conferred extended protection against more severe presentations of dengue. The study is limited by an absence of baseline dengue serostatus of the participants prior to vaccination but a large majority in this this cohort were likely dengue seropositive.

WEB: 10.1016/j.vaccine.2025.127142
IMPACT FACTOR: 4.5
CITED HALF-LIFE: 7.9

START COMMENTARY

Presumptive signs and symptoms of dengue that were assessed among vaccinated and unvaccinated individuals hospitalized with virologically confirmed dengue (VCD) were nausea or vomiting, rash, headache, retroorbital pain, myalgia, anorexia, arthralgia, malaise, watery stools, and flushed skin; warning signs were abdominal pain, persistent vomiting, lethargy, restlessness, bleeding, and enlarged liver. Those who had received the dengue vaccine were less likely to experience any of the presumptive symptoms or warning signs of dengue except persistent vomiting (Table 2). A significantly higher proportion of those who were not vaccinated had dengue with warning signs when compared to those who were vaccinated (70% vs 58%). Authors note that an interim analysis indicated 51% effectiveness of one dose and suggest that the current estimate of 31% indicates waning immunity.

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8. Systematic review and meta-analysis of interventions to increase the uptake of vaccines recommended during pregnancy.

Regan A, Uwimana H, Rowe S, Olsanska E, Agnew B, Castillo E, et al.

NPJ Vaccines. 2025 Apr 22;10(1):76.

PubMed ID: 40253502

ABSTRACT

Although immunization during pregnancy can protect mothers and their infants from vaccine-preventable morbidity and mortality, vaccination rates are often poor. We systematically reviewed the literature from inception to July 4, 2023, for randomized and non-randomized quasi-experimental studies estimating the effects of interventions to increase vaccination during pregnancy. Of 9331 studies screened, 36 met inclusion criteria, including 18 demand-side interventions, 11 supply-side interventions, and seven multi-level (demand and supply-side) interventions. Demand-side interventions commonly addressed patient education, showing modest improvement (pooled RR 1.18; 95% CI: 1.04, 1.33; I2 = 63.1%, low certainty). Supply-side interventions commonly implemented Assessment-Feedback-Incentive-eXchange interventions with little improvement (pooled RR 1.13; 95% CI: 0.96, 1.33; I2 = 94.0%, low certainty). Multi-level interventions were modestly effective in increasing vaccination (pooled RR 1.62; 95% CI: 1.09, 2.42; I2 = 97%, very low certainty). Interventions identified in the literature mostly resulted in low to moderate increases in vaccination with likely high heterogeneity and low to very low certainty in the findings.

WEB: 10.1038/s41541-025-01120-1

IMPACT FACTOR: 7.0

CITED HALF-LIFE: 2.7

START COMMENTARY

Patient-level (demand-side) interventions evaluated were clinic-based patient education (n=9), reminders (n=3), cash incentives (n=2), persuasive messaging with patient education (n=2), and patient-held immunization records (n=1). Overall results and results by intervention type can be found in Figure 2. All but 2 studies on patient education interventions and all studies on persuasive messaging and education were conducted in the USA while all studies on conditional cash transfer and patient-held medical record were conducted in low- and middle-income countries, so careful consideration should be given to context when interpreting results.

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9. Incorporating vaccines into vaccination schedules around the world: A scoping review.

de Melo Araújo A, Oliveira T, Souza J, da Fonseca Victer T, Rangel P, Duarte C, et al.
Vaccine. 2025 May 12;54:127132.
PubMed ID: 40250066

ABSTRACT

INTRODUCTION: Over the past 50 years, immunization initiatives and programs promoted by member countries of the World Health Organization have prevented approximately 154 million deaths, 146 million of which would have occurred among children under 5 years of age. The development of vaccines and implementing global immunization strategies against vaccine-preventable diseases have been instrumental in enhancing global health security.

OBJECTIVE: To analyze the process of integrating new vaccines into vaccination schedules worldwide.

METHODOLOGY: This study is a scoping review, conducted in accordance with the 2024 Joanna Briggs Institute Manual for Evidence Synthesis and reported following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses - Extension for Scoping Reviews RESULTS: The search strategy yielded 2432 citations, with 688 removed due to duplication. Consequently, 1744 titles and abstracts were assessed, resulting in 75 studies being included in the review. The majority of these studies found that the assessment process for incorporating new vaccines primarily aims at reducing costs and/or promoting collective and individual social and economic benefits, with most focusing on the vaccination schedule for children up to 12 years of age. To evaluate the social and economic aspects, the predominant strategies were cost-effectiveness and cost-benefit analyses of new vaccine incorporation. The most frequently employed tools included the incremental cost-effectiveness ratio, years of life lost adjusted for disability, years of life adjusted for quality, and the Markov model.

FINAL CONSIDERATIONS: The process of vaccine incorporation has been shown to extend beyond immediate health impacts, encompassing social improvements and cost optimization capable of producing long-term effects.

WEB: 10.1016/j.vaccine.2025.127132
IMPACT FACTOR: 4.5
CITED HALF-LIFE: 7.9

START COMMENTARY

Integration of the HPV vaccine into vaccination schedules was the subject of 20% of included studies (n=15), with rotavirus and pneumococcal vaccine representing 17% each (n=13). The main objectives, strategies, and supports used in decision-making were evaluated using qualitative data analysis methods and are presented as a conceptual map in Figure 2. The impact of vaccine-preventable diseases on the health system and the investment required to procure vaccines were the most frequently cited economic considerations. The importance of incorporating expert voices and reviewing scientific evidence were noted in 25% of studies. Studies about the incorporation of the COVID-19 vaccine into vaccine schedules were excluded because the emergence of the pandemic is not typical of circumstances under which vaccines are incorporated into the routine schedule.

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10. A roadmap of priority evidence gaps for the co-implementation of malaria vaccines and perennial malaria chemoprevention.

Grant J.

Malar J. 2025 Apr 18;24(1):126.
PubMed ID: 40247263

ABSTRACT

Progress in malaria control will rely on deployment and effective targeting of combinations of interventions, including malaria vaccines and perennial malaria chemoprevention (PMC). Several countries with PMC programmes have introduced malaria vaccination into their essential programmes on immunizations, but empirical evidence on the impact of combining these two interventions and how best to co-implement them are lacking. At the American Society of Tropical Medicine and Hygiene 2023 annual meeting, a stakeholder meeting was convened to identify key policy, operational and research gaps for co-implementation of malaria vaccines and PMC. Participants from 11 endemic countries, including representatives from national malaria and immunization programmes, the World Health Organization, researchers, implementing organizations and funders attended. Identified evidence gaps were prioritized to select urgent issues to inform co-implementation. The output of these activities is a strategic roadmap of priority malaria vaccine and PMC co-implementation evidence gaps, and solutions to address them. The roadmap was presented to stakeholders for feedback at the 2024 Multilateral Initiative on Malaria meeting and revised accordingly. The roadmap outlines four key areas of work to address urgent evidence gaps for co-implementation: (1) support to the global and national policy process, (2) implementation support and research, (3) clinical studies, and (4) modelling. Together, these areas will provide practical guidance on the co-implementation of the interventions, and robust evidence to inform decision-making on how best to design, optimize and scale-up co-implementation in different contexts, including if and in what contexts the co-implementation is cost-effective, and the optimal schedule for co-implementation. This will work towards supporting the policy process on co-implementation of malaria vaccines and PMC, and achieving the most impactful use of available resources for the prevention of malaria in children.

WEB: 10.1186/s12936-025-05347-0
IMPACT FACTOR: 2.4
CITED HALF-LIFE: 7.1

START COMMENTARY

Modelling studies suggest that combining malaria vaccination with perennial malaria chemoprevention (PMC) will provide better protection against malaria than either intervention

individually (Figure 2), but there is uncertainty about how to co-implement the intervention in resource-limited settings to optimize impact. The roadmap of priority evidence gaps for the co-implementation of malaria vaccines and perennial malaria chemoprevention outlines methods, outputs, and outcomes to support the cost-effective scale-up of these interventions (Figure 3). Input from those with practical experiences implementing malaria vaccine and PMC, results from observational studies in real-world settings, and results from clinical studies that assess safety and optimal timing of interventions are highlighted as keys to successful outcomes.

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11. Global, regional, and national trends of measles burden and its vaccination coverage among children under 5 years old: An updated systematic analysis from the Global Burden of Disease Study 2021.

Chen W, Du M, Deng J, Liu M, Liu J.

Int J Infect Dis. 2025 May 16;156:107908.
PubMed ID: 40246060

ABSTRACT

OBJECTIVES: This study examines trends in measles burden and measles-containing vaccine (MCV) coverage among children under 5 years old, with a focus on the impact of the COVID-19 pandemic.

METHODS: We analyzed measles incidence, mortality, and disability-adjusted life years (DALYs) in children under 5 years old using Global Burden of Disease 2021 data and MCV coverage in 204 countries from the Global Health Data Exchange. Trends from 1990 to 2021 were assessed through estimated annual percentage change (EAPC) at global, regional, and national levels.

RESULTS: In 2021, measles caused 4.1 million cases, 48.1 thousand deaths, and 4.2 million DALYs among children under 5 years old globally. From 1990 to 2021, incidence, mortality, and DALYs declined by over 90%, but low socio-demographic index regions continued to bear the highest burden. During the COVID-19 pandemic (2019-2021), the global measles burden declined overall, but mortality (EAPC = 155.55, 95% confidence interval [CI]: 53.89-324.38) and DALY rates (EAPC = 146.94, 95% CI: 46.25-316.94) in East Asia increased. The pandemic also disrupted vaccination, with MCV1 coverage declining (EAPC = -2.08, 95% CI: -3.30 to -0.85), reversing previous trends in 68 countries (33.33%) for MCV1 and 50 countries (24.51%) for MCV2.

CONCLUSION: Global measles incidence has declined over the past 30 years, but regional disparities persist. The COVID-19 pandemic disrupted vaccination efforts, raising the risk of outbreaks among children. Enhanced efforts are critical to achieving measles elimination.

WEB: 10.1016/j.ijid.2025.107908
IMPACT FACTOR: 4.8
CITED HALF-LIFE: 3.4

START COMMENTARY

During the COVID-19 pandemic (2019-2021), measles burden in children under 5 years declined, global incidence decreased by 37% and mortality and DALYs each decreased by 21% between 2019 and 2021. However, 10 countries experienced an increase in measles incidence and DALYs,

and 11 had increased mortality rates (Figures 1 and 2). When compared to pre-pandemic coverage, measles vaccine coverage for dose 1 and dose 2 was lower in 75 and 68 countries, respectively in 2021. Authors suggest that the declining measles burden at the same time as measles vaccine coverage was decreasing was likely due to the effect of COVID-19 prevention measures such as masking and social distancing on measles spread. This explanation is supported by the increase in global measles cases in 2023 after COVID-19 prevention measures were lifted.

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12. Strengthening health security through routine vaccination policy: A comprehensive analysis of childhood vaccination laws across 194 countries.

Weets C, Wilson R, Swadley H, Katz R.

Vaccine. 2025 May 12;54:127121.
PubMed ID: 40239299

ABSTRACT

BACKGROUND: Vaccine preventable diseases (VPD) present a resurgent threat to global health security and jeopardize decades of advancements in public health and economic development. Since 1974, childhood vaccinations are estimated to have prevented 154 million deaths from VPD, yet recent declines in routine vaccination rates highlight the global population's growing vulnerability to these diseases. When paired with appropriate access to healthcare and trusted information, evidence informed enforceable policies have demonstrably improved childhood vaccination rates in countries that have recently implemented more stringent laws on routine vaccination. Here we comprehensively map and describe the current legal environment for childhood vaccination.

METHODS: We conducted a comprehensive analysis of the childhood vaccination-related policies in 194 countries. Policies were systematically identified, collated, and categorized into a publicly available tool.

RESULTS: A total of 106 countries have legally-enforceable policies requiring vaccination for at least one disease. We found that vaccines against diphtheria, measles, and tetanus were the most universally mandated, while vaccines against COVID-19 and Japanese Encephalitis were mandated by the fewest countries. In 91 countries, childhood vaccination requirements are enforced through either legal sanctions, such as monetary fines or incarceration, through exclusion from congregate settings, or through some combination of the two.

CONCLUSION: Analyses of the efficacy of childhood vaccination laws are predicated upon a comprehensive mapping of the current legal landscape related to routine immunization. Public health officials and researchers with an interest in increasing routine childhood vaccination rates in their country must know what characteristics of policy have been effective across various contexts. Our mapping of legally-enforceable childhood vaccination policies is foundational for assessing current vulnerabilities to vaccine-preventable diseases and future policy analyses.

WEB: 10.1016/j.vaccine.2025.127121
IMPACT FACTOR: 4.5
CITED HALF-LIFE: 7.9

START COMMENTARY

Overall, 12 countries require 15 or more childhood vaccinations, and 83% of those are in Central or South America. Geospatial clustering for measles, diphtheria, polio, tuberculosis, and varicella vaccine mandates can be seen in Figure 3. Measles, diphtheria, and polio requirements are evenly distributed across regions, while mandatory tuberculosis vaccination is concentrated in countries in Eastern Europe, Africa, South America, and Central America. Despite being eradicated in 1980, authors identified current laws requiring smallpox vaccination in 15 countries, and smallpox was the only required vaccine in 10 of those countries, indicating that vaccine laws are not enforced and that there is a lack of awareness about vaccine policies in these countries. 76 countries have exemptions to vaccine requirements incorporated into their legal enforcement policies, with 86% including only medical exemptions and 14% including both medical and nonmedical exemptions; exemptions likely complicate enforcement of vaccine requirements, but enforcement was not examined in this article.

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13. Vaccinology in the artificial intelligence era.

Gasperini G, Baylor N, Black S, Bloom D, Cramer J, de Lannoy G, et al.

Sci Transl Med. 2025 Apr 16;17(794):eadu3791.

PubMed ID: 40238919

ABSTRACT

Artificial intelligence (AI) has already transformed vaccine antigen design and could transform the entire vaccinology pipeline, including immune responses and emerging infectious disease prediction, manufacturing and regulatory processes, clinical trial design and implementation, and vaccine access and equity. However, realizing the promise of AI for vaccinology requires more high-quality data.

WEB: 10.1126/scitranslmed.adu3791

IMPACT FACTOR: 15.8

CITED HALF-LIFE: 6.1

START COMMENTARY

Gasperini et al. provide an overview of current and potential uses of artificial intelligence (AI) and machine learning (ML) based on a Palio 2024 scientific meeting entitled AI and Digital Transformation of Vaccinology. Table 1 describes the impact of AI use across 6 domains: antigen identification and design, immune response and infectious disease prediction, vaccine manufacturing and regulatory framework, clinical trial design, vaccine access and equity, and vaccine hesitancy. To provide insight into the use of AI to predict emerging pathogens, they described the use of EVEscape to predict SARS-CoV-2 mutations and which variants would become most prevalent.

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Additional Articles of Interest

1 Vaccination Status and Incidences of Measles, Mumps, and Rubella - Worldwide, 2014-2023. {Full Article}
2 Design, coverage and utilisation of maternity conditional cash programmes in low- and middle-income countries: a scoping review. {Full Article}
3 Country-Specific Data and Priorities for Pertussis in Latin America: Recent Findings From the Global Pertussis Initiative. {Full Article}
4 Non-specific effects of routine vaccinations on child survival between 12-59 months of age in Jigawa, Nigeria: A secondary analysis of the INSPIRING Jigawa trial. {Full Article}
5 Mathematical modeling of malaria vaccination with seasonality and immune feedback. {Full Article}
6 Protein nanocages: A new frontier in mucosal vaccine delivery and immune activation. {Full Article}
7 What vaccine inequity has taught us: a way forward through the lens of ideal and non-ideal theory. {Full Article}
8 Developing an intuitive decision support system for equitable vaccine distribution during pandemics. {Full Article}
9 Effectiveness of interventions to improve vaccine efficacy: a systematic review and meta-analysis. {Full Article}
10 Coverage and predictors of full measles-rubella immunization among children aged 24-59 months in Northern Ghana: a post measles outbreak assessment. {Full Article}
11 Global socioeconomic inequalities in vaccination coverage, supply, and confidence. {Full Article}
12 Overcoming challenges and achieving high HPV vaccination uptake in Cameroon: lessons learned from a gender-neutral and single-dose program and community engagement. {Full Article}
13 From genetic code to global health: the impact of nucleic acid vaccines on disease prevention and treatment. {Full Article}
14 Risk factors associated with zero-dose and under-immunized children, and the number of vaccination doses received by children in Ethiopia: a negative binomial regression analysis. {Full Article}
15 Chronicling the Journey of Pneumococcal Conjugate Vaccine Introduction in India. {Full Article}
16 Goals and strategies in vaccine development against tuberculosis. {Full Article}
17 Nurses' knowledge and willingness to recommend malaria vaccination to caregivers of under-5 in Nigeria: a nationwide survey. {Full Article}
18 Cost-effectiveness of a behavioral insights-informed digital campaign to increase HPV vaccination in Bangladesh. {Full Article}

19 Dissolving microneedles in transdermal drug delivery: A critical analysis of limitations and translation challenges. {Full Article}
20 A population-level analysis of armed conflict and diphtheria at the subnational level in the WHO African Region 2017-2024. {Full Article}
21 Strategies to correct vaccine misinformation on social media for pregnant women and the impact of vaccine skepticism. {Full Article}
22 Determinants of incomplete immunization among 12-23 months old children in Ethiopia: A multilevel analysis. {Full Article}
23 BCG vaccination decline and pediatric tuberculosis rise in Brazil: spatial-temporal study. {Full Article}
24 Disease burden estimates in economic evaluation studies of respiratory syncytial virus (RSV) maternal immunization: a systematic review. {Full Article}
25 Moving beyond discovery science to a mechanistic understanding of human malaria. {Full Article}
26 Epidemiological trends of diarrheal viruses in central and western Kenya before and after Rotavirus vaccine introduction. {Full Article}
27 Vaccine-Preventable Diseases in Pediatric Age Group in India: Recent Resurgence, Implications and Solutions. {Full Article}
28 Optimising human rabies vaccine supply chains: A modelling study. {Full Article}
29 Mapping zero-dose children in Kenya - A spatial analysis and examination of the socio-demographic and media exposure determinants. {Full Article}
30 Trends and inequalities in full immunisation coverage among one-year-olds in Sierra Leone, 2008-2019. {Full Article}
31 Global Guidelines and Trends in HPV Vaccination for Cervical Cancer Prevention. {Full Article}
32 Factors associated with measles vaccine immunogenicity in children at University Teaching Hospitals, Lusaka, Zambia. {Full Article}
33 Integrating routine immunization into COVID-19 vaccination improve coverage but could create equity issues: evidence from Niger State, Nigeria. {Full Article}
34 Unveiling the complexity of vaccine hesitancy: A narrative review focusing on dengue vaccination. {Full Article}
35 Understanding caregivers' and community influencers' perspectives on the barriers to childhood immunisation in Northern Nigerian States with public-private partnerships in routine immunisation programme. {Full Article}
36 Uptake of second dose measles containing vaccine and associated factors among children aged 24-35 months in central Ethiopia: a community based cross-sectional study. {Full Article}
37 The Role of Medical Mistrust in Vaccination Decisions in Rural, Indigenous Namibian Communities. {Full Article}

38 India's universal immunization program: A review of successes, challenges, and future directions. {Full Article}

39 Geospatial analysis and scale-up modelling of the impact of mobile programming on access to essential childhood vaccinations in Yemen. {Full Article}

40 Uptake of the recently introduced vaccines among children aged 12-23 months in Ethiopia: a multilevel analysis of the 2019 Ethiopia Mini Demographic and Health Survey. {Full Article}

41 Vaccination burnout impedes the compliance with multiple-dose administration of vaccines. {Full Article}

42 Optimal control analysis for the transmission of Nipah infection with imperfect vaccination. {Full Article}

43 SEARCH Study: Text Messages and Automated Phone Reminders for HPV Vaccination in Uganda: Randomized Controlled Trial. {Full Article}

Appendix

The literature search for the June 2025 Vaccine Delivery Research Digest was conducted on May 21, 2025. We searched English language articles indexed by the US National Library of Medicine and published between April 15, 2025 and May 14, 2025. The search resulted in 417 items.

SEARCH TERMS

((((“vaccine”[tiab] OR “vaccines”[tiab] OR “vaccination”[tiab] OR “immunization”[tiab] OR “immunisation”[tiab] OR “vaccines”[MeSH Terms] OR (“vaccination”[MeSH Terms] OR “immunization”[MeSH Terms])) AND (“logistics”[tiab] OR “supply”[tiab] OR “supply chain”[tiab] OR “implementation”[tiab] OR “expenditures”[tiab] OR “financing”[tiab] OR “economics”[tiab] OR “Cost effectiveness”[tiab] OR “coverage”[tiab] OR “attitudes”[tiab] OR “belief”[tiab] OR “beliefs”[tiab] OR “refusal”[tiab] OR “Procurement”[tiab] OR “timeliness”[tiab] OR “systems”[tiab])) OR “vaccine delivery”[tiab] OR “vaccination refusal”[MeSH Terms] OR “immunization programs”[MeSH Terms] OR “zero dose”[tiab] OR “unvaccinated children”[tiab] OR “gavi”[tiab]) NOT (“in vitro”[tiab] OR “immune response”[tiab] OR “gene”[tiab] OR “chemistry”[tiab] OR “genotox*”[tiab] OR ”sequencing”[tiab] OR ”nanoparticle*”[tiab] OR “bacteriophage”[tiab] OR “exome”[tiab] OR “exogenous”[tiab] OR “electropor*“[tiab] OR”systems biology”[tiab] OR “animal model”[tiab] OR “cattle”[tiab] OR “sheep”[tiab] OR “goat”[tiab] OR “rat”[tiab] OR “pig”[tiab] OR “mice”[tiab] OR “mouse”[tiab] OR “murine”[tiab] OR “porcine”[tiab] OR “ovine”[tiab] OR “rodent”[tiab] OR “fish”[tiab])) AND “English”[Language] AND 2025/04/15:2025/05/14[Date - Publication]