VACCINE DELIVERY RESEARCH DIGEST

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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{Abstract & START Commentary} {Full Article}

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{Abstract & START Commentary} {Full Article}

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{Abstract & START Commentary} {Full Article}

- The contextual factors influencing vaccine deliver and uptake during the initial introduction of RTS,S/AS01 malaria vaccine in western Kenya were evaluated.

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{Abstract & START Commentary} {Full Article}

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{Abstract & START Commentary} {Full Article}

- Contextual factors and strategies associated with Rwanda's implementation of rotavirus vaccines and a program to prevent mother-to-child transmission of HIV were identified using a mixed methods study approach.

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{Abstract & START Commentary} {Full Article}

- The prevalence of zero-dose children aged 12-35 months among underserved populations of Ethiopia was estimated.

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{Abstract & START Commentary} {Full Article}

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13 Effective interventions for improving routine childhood immunisation in low and middle-income countries: a systematic review of systematic reviews.

{Abstract & START Commentary} {Full Article}

- Systematic reviews of any intervention on routine childhood immunization outcomes in low- and middle-income countries were identified, and effectiveness of interventions was assessed.

14 What would have happened anyway? Population data source considerations when estimating background incident rates of adverse events following immunisation to inform vaccine safety. {Abstract & START Commentary} {Full Article}

- A retrospective cohort analysis of hospital admissions, emergency department visits, and general practice consultations were identified and compared to estimate background incident rates for conditions considered as potential adverse events following immunization.

Appendix

Details of Articles

1. Last-mile delivery increases vaccine uptake in Sierra Leone.

Meriggi N, Voors M, Levine M, Ramakrishna V, Kangbai D, Rozelle M, et al.
Nature. 2024 Mar 22;627(8004):612-619.
PubMed ID: 38480877

ABSTRACT

Less than 30% of people in Africa received a dose of the COVID-19 vaccine even 18 months after vaccine development. Here, motivated by the observation that residents of remote, rural areas of Sierra Leone faced severe access difficulties, we conducted an intervention with last-mile delivery of doses and health professionals to the most inaccessible areas, along with community mobilization. A cluster randomized controlled trial in 150 communities showed that this intervention with mobile vaccination teams increased the immunization rate by about 26 percentage points within 48-72 h. Moreover, auxiliary populations visited our community vaccination points, which more than doubled the number of inoculations administered. The additional people vaccinated per intervention site translated to an implementation cost of US $33 per person vaccinated. Transportation to reach remote villages accounted for a large share of total intervention costs. Therefore, bundling multiple maternal and child health interventions in the same visit would further reduce costs per person treated. Current research on vaccine delivery maintains a large focus on individual behavioural issues such as hesitancy. Our study demonstrates that prioritizing mobile services to overcome access difficulties faced by remote populations in developing countries can generate increased returns in terms of uptake of health services.

WEB: 10.1038/s41586-024-07158-w
IMPACT FACTOR: 64.8
CITED HALF-LIFE: 10.1

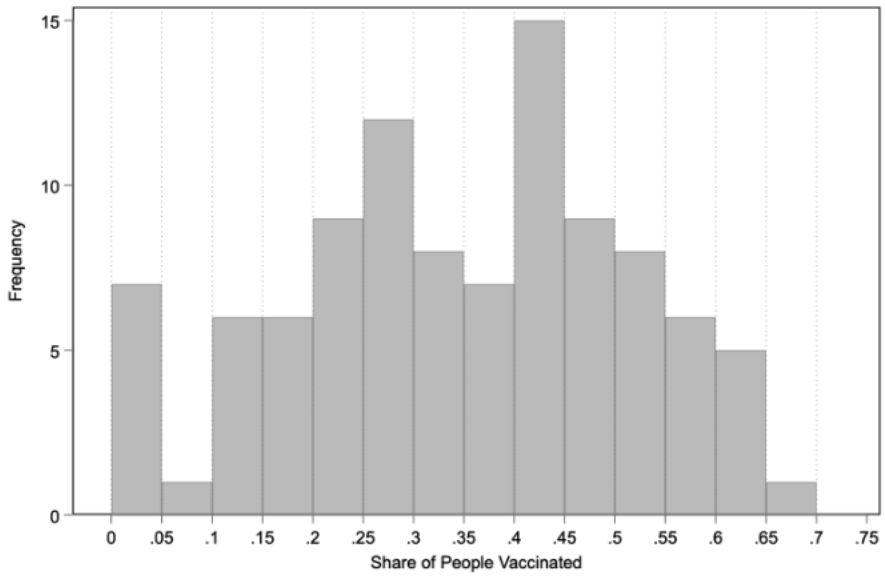
START COMMENTARY

Meriggi et al. conducted this trial in conjunction with the Sierra Leone Ministry of Health and Sanitation (MoHS) after data from Sierra Leone indicated that an individual in Sierra Leone would need to travel an average 3 ½ hours of each way to reach a vaccination center where they could receive a COVID-19 vaccine with the cost of the journey exceeding a week of wages. Researchers identified communities located more than 5 miles from the nearest peripheral health unit catchment and randomized them to intervention or control. In the intervention communities, a social mobilization team met with community leaders to engender support for the vaccine clinic, then asked

them to convene a community meeting where the social mobilization team spoke directly to village residents about vaccine benefits, addressed concerns, and provided details about the location and timing of the vaccination clinic. MoHS staff then set up a 48–72-hour mobile vaccine clinic at a central community location. The vaccination rate, based on village residents who received the vaccine, was an underestimate of the number of vaccines administered as individuals from neighboring villages other non-residents received the vaccine. There was wide variation in vaccination rates among intervention villages, with some villages having no increase after village authorities refused to allow or discouraged participation, highlighting the importance of community engagement in vaccine programs (Figure 1.2).

1.2 Variation in Endline Vaccination Rate

Figure A2: Variation in Endline Vaccination Rate



Notes: This figure provides a histogram of the vaccination rate (i.e share of adults that took the vaccine at the end of the study from those enumerated during the census) in the 100 treatment villages.

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2. Immunogenicity of RV1 and RV5 vaccines administered in standard and interchangeable mixed schedules: a randomized, double-blind, non-inferiority clinical trial in Mexican infants.

Macías-Parra M, Vidal-Vázquez P, Reyna-Figueroa J, Rodríguez-Weber M, Moreno-Macías H, Hernández-Benavides I, et al.

Front Public Health. 2024 Mar 12;12:1356932.

PubMed ID: 38463163

ABSTRACT

INTRODUCTION: Rotavirus-associated diarrheal diseases significantly burden healthcare systems, particularly affecting infants under five years. Both Rotarix™ (RV1) and RotaTeq™ (RV5) vaccines have been effective but have distinct application schedules and limited interchangeability data. This study aims to provide evidence on the immunogenicity, reactogenicity, and safety of mixed RV1-RV5 schedules compared to their standard counterparts.

METHODS: This randomized, double-blind study evaluated the non-inferiority in terms of immunogenicity of mixed rotavirus vaccine schedules compared to standard RV1 and RV5 schedules in a cohort of 1,498 healthy infants aged 6 to 10 weeks. Participants were randomly assigned to one of seven groups receiving various combinations of RV1, and RV5. Standard RV1 and RV5 schedules served as controls of immunogenicity, reactogenicity, and safety analysis. IgA antibody levels were measured from blood samples collected before the first dose and one month after the third dose. Non-inferiority was concluded if the reduction in seroresponse rate in the mixed schemes, compared to the standard highest responding scheme, did not exceed the non-inferiority margin of -0.10. Reactogenicity traits and adverse events were monitored for 30 days after each vaccination and analyzed on the entire cohort.

RESULTS: Out of the initial cohort, 1,365 infants completed the study. Immunogenicity analysis included 1,014 infants, considering IgA antibody titers ≥20 U/mL as seropositive. Mixed vaccine schedules demonstrated non-inferiority to standard schedules, with no significant differences in immunogenic response. Safety profiles were comparable across all groups, with no increased incidence of serious adverse events or intussusception.

CONCLUSION: The study confirms that mixed rotavirus vaccine schedules are non-inferior to standard RV1 and RV5 regimens in terms of immunogenicity and safety. This finding supports the flexibility of rotavirus vaccination strategies, particularly in contexts of vaccine shortage or logistic constraints. These results contribute to the global effort to optimize rotavirus vaccination programs

for broader and more effective pediatric coverage.Clinical trial registration: ClinicalTrials.gov, NCT02193061.

WEB: 10.3389/fpubh.2024.1356932
IMPACT FACTOR: 5.2
CITED HALF-LIFE: 2.3

START COMMENTARY

This study by Macias-Parra et al. adds to evidence from a 2017 study in the United States that found mixed vaccine schedules were non-inferior to standard rotavirus vaccine (RV1 and RV5) schedules. The seven vaccine schedules tested were: Group 1: RV1 + RV1 + placebo; Group 2: RV5 + RV5 + RV5; Group 3: RV1 + RV5 + RV5; Group 4: RV5 + RV1 + RV1; Group 5: RV5 + RV5 + RV1; Group 6: RV5 + RV1 + RV5; and Group 7: RV1 + RV5 + RV1. Immunogenicity responses can be found in Figure 2. Since infants in low- and middle income countries have lower seroconversion rates after receiving the standard rotavirus schedules compared to those in high income countries, this study provides context-specific information about the immunogenicity of mixed RV1 and RV5 vaccine schedules among Mexican infants.

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3. Systematic review of social determinants of childhood immunisation in low- and middle-income countries and equity impact analysis of childhood vaccination coverage in Nigeria.

Williams S, Akande T, Abbas K.

PLoS One. 2024 Mar 08;19(3):e0297326.

PubMed ID: 38446836

ABSTRACT

BACKGROUND: Nigeria has a high proportion of the world's underimmunised children. We estimated the inequities in childhood immunisation coverage associated with socioeconomic, geographic, maternal, child, and healthcare characteristics among children aged 12-23 months in Nigeria using a social determinants of health perspective.

METHODS: We conducted a systematic review to identify the social determinants of childhood immunisation associated with inequities in vaccination coverage among low- and middle-income countries. Using the 2018 Nigeria Demographic and Health Survey (DHS), we conducted multiple logistic regression to estimate the association between basic childhood vaccination coverage (1-dose BCG, 3-dose DTP-HepB-Hib (diphtheria, tetanus, pertussis, hepatitis B and Haemophilus influenzae type B), 3-dose polio, and 1-dose measles) and socioeconomic, geographic, maternal, child, and healthcare characteristics in Nigeria.

RESULTS: From the systematic review, we identified the key determinants of immunisation to be household wealth, religion, and ethnicity for socioeconomic characteristics; region and place of residence for geographic characteristics; maternal age at birth, maternal education, and household head status for maternal characteristics; sex of child and birth order for child characteristics; and antenatal care and birth setting for healthcare characteristics. Based of the 2018 Nigeria DHS analysis of 6,059 children aged 12-23 months, we estimated that basic vaccination coverage was 31% (95% CI: 29-33) among children aged 12-23 months, whilst 19% (95% CI:18-21) of them were zero-dose children who had received none of the basic vaccines. After controlling for background characteristics, there was a significant increase in the odds of basic vaccination by household wealth (AOR: 3.21 (2.06, 5.00), $p < 0.001$) for the wealthiest quintile compared to the poorest quintile, antenatal care of four or more antenatal care visits compared to no antenatal care (AOR: 2.87 (2.21, 3.72), $p < 0.001$), delivery in a health facility compared to home births (AOR 1.32 (1.08, 1.61), $p = 0.006$), relatively older maternal age of 35-49 years compared to 15-19 years (AOR: 2.25 (1.46, 3.49), $p < 0.001$), and maternal education of secondary or higher education compared to no formal education (AOR: 1.79 (1.39, 2.31), $p < 0.001$). Children of Fulani ethnicity in comparison to children of Igbo ethnicity had lower odds of receiving basic vaccinations (AOR: 0.51 (0.26, 0.97), $p = 0.039$).

CONCLUSIONS: Basic vaccination coverage is below target levels for all groups. Children from the poorest households, of Fulani ethnicity, who were born in home settings, and with young mothers with no formal education nor antenatal care, were associated with lower odds of basic vaccination in Nigeria. We recommend a proportionate universalism approach for addressing the immunisation barriers in the National Programme on Immunization of Nigeria.

WEB: 10.1371/journal.pone.0297326
IMPACT FACTOR: 3.7
CITED HALF-LIFE: 7.3

START COMMENTARY

Vaccination coverage among children 12-23 months in Nigeria was significantly lower among those living in rural compared to urban areas for all included vaccines (Figure 2). Children in the richest quintile living in rural areas had lower odds of having received basic vaccines than children in the poorest quintile living in urban areas. Authors posit that proximity to healthcare facilities in urban settings make it more likely that mothers in urban areas access preventive healthcare services, including immunization services.

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4. Maternal GBS vaccination for preventing group B streptococcus disease in newborns: A mini review of current evidence.

Kokori E, Olatunji G, Komolafe R, Ogieuhi I, Oyebiyi B, Ajayi I, et al.

Int J Gynaecol Obstet. 2024 Mar 06.

PubMed ID: 38445529

ABSTRACT

Group B streptococcus (GBS) poses a significant threat to neonates, leading to morbidity and mortality. Intrapartum antibiotics, although effective, have limitations, prompting the exploration of maternal vaccination. This study reviews the current evidence for maternal GBS vaccination in the prevention of early-onset GBS disease in newborns. A search on Google Scholar, PubMed, and Scopus identified studies assessing the impact of maternal GBS vaccination on early-onset GBS disease. Inclusion criteria comprised English-language clinical trials or observational studies. Data extraction included study details, immunogenicity profiles, effectiveness, safety outcomes, and relevant findings. Qualitative synthesis was employed for data analysis. Five studies meeting the inclusion criteria were reviewed. Maternal GBS vaccines demonstrated efficacy with sustained immunogenicity. Adverse events, although documented, were predominantly non-severe. Variability in immune responses and maternal-to-infant antibody ratios show the need for tailored vaccination approaches. Long-term follow up and surveillance are essential to assess persistence and identify unintended effects. Positive outcomes in vaccine efficacy support GBS vaccination integration into maternal health programs. Implementation challenges in diverse healthcare infrastructures require tailored approaches, especially in resource-limited settings. Overcoming cultural barriers and ensuring healthcare provider awareness are crucial for successful vaccination.

WEB: 10.1002/ijgo.15465

IMPACT FACTOR: 3.8

CITED HALF-LIFE: 7.0

START COMMENTARY

While use of antibiotics during labor and delivery has led to a decrease in early onset group B streptococcus disease in the United States, GBS still accounts for a substantial portion of worldwide preterm births. Kokori et al. argue that maternal vaccination could provide broader sustained protection for both the mother and neonate. While the authors state that occurrence of non-severe adverse events are a concern, they do not include information regarding type and frequency of adverse events in the five included studies.

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5. Enhanced cholera surveillance to improve vaccination campaign efficiency.

Xu H, Zou K, Dent J, Wiens K, Malembaka E, Bwire G, et al.

Nat Med. 2024 Mar 05.

PubMed ID: 38443690

ABSTRACT

Systematic testing for Vibrio cholerae O1 is rare, which means that the world's limited supply of oral cholera vaccines (OCVs) may not be delivered to areas with the highest true cholera burden. Here we used a phenomenological model with subnational geographic targeting and fine-scale vaccine effects to model how expanding V. cholerae testing affected impact and cost-effectiveness for preventive vaccination campaigns across different bacteriological confirmation and vaccine targeting assumptions in 35 African countries. Systematic testing followed by OCV targeting based on confirmed cholera yielded higher efficiency and cost-effectiveness and slightly fewer averted cases than status quo scenarios targeting suspected cholera. Targeting vaccine to populations with an annual incidence rate greater than 10 per 10,000, the testing scenario averted 10.8 (95% prediction interval (PI) 9.4-12.6) cases per 1,000 fully vaccinated persons while the status quo scenario averted 6.9 (95% PI 6.0-7.8) cases per 1,000 fully vaccinated persons. In the testing scenario, testing costs increased by US$31 (95% PI 25-39) while vaccination costs reduced by US$248 (95% PI 176-326) per averted case compared to the status quo. Introduction of systematic testing into cholera surveillance could improve efficiency and reach of global OCV supply for preventive vaccination.

WEB: 10.1038/s41591-024-02852-8

IMPACT FACTOR: 82.9

CITED HALF-LIFE: 5.7

START COMMENTARY

Modeled scenarios evaluated the impact and cost-effectiveness of preventive vaccination campaigns in areas with a confirmed cholera outbreak based on either clinical definition of cholera with no confirmatory lab testing or two testing strategies: 1) a centralized testing scenario defined as systematic testing with culture in a single reference laboratory, and 2) a decentralized testing scenario using a combination of rapid detection tests and culture. Table 2 shows projected cholera cases averted, oral cholera vaccine campaign efficiency and percent of cases averted across targeting thresholds of 1, 2, and 10 cases per 10,000 people by model scenario. The model projected that systematic decentralized testing could reduce the combined cost of testing and vaccine campaigns across all target thresholds compared to the clinical definition scenario.

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6. Malaria vaccine efficacy, safety, and community perception in Africa: a scoping review of recent empirical studies.

Chutiyami M, Saravanakumar P, Bello U, Salihu D, Adeleye K, Kolo M, et al.

Infection. 2024 Mar 05.

PubMed ID: 38441731

ABSTRACT

AIM: The review summarizes the recent empirical evidence on the efficacy, safety, and community perception of malaria vaccines in Africa.

METHODS: Academic Search Complete, African Journals Online, CINAHL, Medline, PsychInfo, and two gray literature sources were searched in January 2023, and updated in June 2023. Relevant studies published from 2012 were included. Studies were screened, appraised, and synthesized in line with the review aim. Statistical results are presented as 95% Confidence Intervals and proportions/percentages.

RESULTS: Sixty-six (N = 66) studies met the inclusion criteria. Of the vaccines identified, overall efficacy at 12 months was highest for the R21 vaccine (N = 3) at 77.0%, compared to the RTS,S vaccine (N = 15) at 55%. The efficacy of other vaccines was BK-SE36 (11.0-50.0%, N = 1), ChAd63/MVA ME-TRAP (- 4.7-19.4%, N = 2), FMP2.1/AS02A (7.6-9.9%, N = 1), GMZ2 (0.6-60.0%, N = 5), PfPZ (20.0-100.0%, N = 5), and PfSPZ-CVac (24.8-33.6%, N = 1). Injection site pain and fever were the most common adverse events (N = 26), while febrile convulsion (N = 8) was the most reported, vaccine-related Serious Adverse Event. Mixed perceptions of malaria vaccines were found in African communities (N = 17); awareness was generally low, ranging from 11% in Tanzania to 60% in Nigeria (N = 9), compared to willingness to accept the vaccines, which varied from 32.3% in Ethiopia to 96% in Sierra Leone (N = 15). Other issues include availability, logistics, and misconceptions.

CONCLUSION: Malaria vaccines protect against malaria infection in varying degrees, with severe side effects rarely occurring. Further research is required to improve vaccine efficacy and community involvement is needed to ensure successful widespread use in African communities.

WEB: 10.1007/s15010-024-02196-y

IMPACT FACTOR: 7.5

CITED HALF-LIFE: 4.5

START COMMENTARY

Of 66 included studies, 47 were randomized controlled trials or clinical trials, 17 were surveys, one was a case-control study, and one was a mixed methods study. Study populations included individuals from 16 countries in Africa: Tanzania, Kenya, The Gambia, Burkina Faso, Gabon, Ghana, Ethiopia, Mozambique, Mali, Nigeria, Uganda, Malawi, Togo, Sierra Leone, Senegal, and Equatorial Guinea. Half of included studies (n=33) reported on vaccine efficacy of the various malaria vaccines (Table 1) and 36 studies reported information about vaccine safety (Table 2). Vaccine acceptance was generally high but varied across studies (Table 3).

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7. Could less be more? Accounting for fractional-dose regimens and different number of vaccine doses when measuring the impact of the RTS, S/AS01E malaria vaccine.

Westercamp N, Osei-Tutu L, Schuerman L, Kariuki S, Bollaerts A, Lee C, et al.

J Infect Dis. 2024 Mar 04.

PubMed ID: 38438123

ABSTRACT

BACKGROUND: The RTS, S/AS01E malaria vaccine (RTS, S) is recommended for children in moderate-to-high Plasmodium falciparum malaria transmission areas. This phase 2b trial (NCT03276962) evaluates RTS, S fractional- and full-dose regimens in Ghana and Kenya.

METHODS: 1500 children aged 5-17 months were randomised (1:1:1:1:1) to receive RTS, S or rabies control vaccine. RTS, S groups received two full RTS, S doses at month (M)0/M1 followed by either full (groups R012-20, R012-14-26) or fractional (1/5) doses (groups Fx012-14-26, Fx017-20-32).

RESULTS: At M32 post-first dose, vaccine efficacy (VE) against clinical malaria (all episodes) ranged from 38% (R012-20; 95%CI: 24-49) to 53% (R012-14-26; 95%CI: 42-62). Vaccine impact estimates (cumulative number of malaria cases averted/1000 children vaccinated) were 1344 (R012-20), 2450 (R012-14-26), 2273 (Fx012-14-26), 2112 (Fx017-20-32). To account for differences in vaccine volume (fractional- versus full-dose), in a post-hoc analysis, we also estimated cases averted/1000 RTS, S full-dose equivalents: 336 (R012-20), 490 (R012-14-26), 874 (Fx012-14-26), 880 (Fx017-20-32).

CONCLUSIONS: VE against clinical malaria was similar in all RTS, S groups. Vaccine impact accounting for full-dose equivalence suggests that using fractional-dose regimens could be a viable dose-sparing strategy. If borne out through trial end (M50), these observations underscore the means to reduce cost per regimen with a goal of maximising impact and optimising supply.

WEB: 10.1093/infdis/jiae075

IMPACT FACTOR: 6.4

CITED HALF-LIFE: 9.5

START COMMENTARY

Study results do not demonstrate improved efficacy of fractional regimens compared to full-dose regimens. However, there were no statistically significant differences in vaccine efficacy between

full-dose and fractional regimens through 32 months of follow-up. Authors calculated malaria cases averted per 1000 full vaccine doses (by volume) administered, with each fractional dose counting as 0.2 of a full dose and found that the impact of fractional dose regimens was more substantial compared to full dose regimens when volume of vaccine administered was considered.

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8. Integration of the RTS,S/AS01 malaria vaccine into the Essential Programme on Immunisation in western Kenya: a qualitative longitudinal study from the health system perspective.

Hill J, Bange T, Hoyt J, Kariuki S, Jalloh M, Webster J, et al.

Lancet Glob Health. 2024 Mar 18;12(4):e672-e684.

PubMed ID: 38430916

ABSTRACT

BACKGROUND: Malaria accounts for over half a million child deaths annually. WHO recommends RTS,S/AS01 to prevent malaria in children living in moderate-to-high malaria transmission regions. We conducted a qualitative longitudinal study to investigate the contextual and dynamic factors shaping vaccine delivery and uptake during a pilot introduction in western Kenya.

METHODS: The study was conducted between Oct 3, 2019, and Mar 24, 2022. We conducted participant and non-participant observations and in-depth interviews with health-care providers, health managers, and national policymakers at three timepoints using an iterative approach and observations of practices and processes of malaria vaccine delivery. Transcripts were coded by content analysis using the consolidated framework for implementation research, to which emerging themes were added deductively and categorised into challenges and opportunities.

FINDINGS: We conducted 112 in-depth interviews with 60 participants (25 health-care providers, 27 managers, and eight policy makers). Health-care providers highlighted limitations in RTS,S/AS01 integration into routine immunisation services due to the concurrent pilot evaluation and temporary adaptations for health reporting. Initial challenges related to the complexity of the four-dose schedule (up to 24-months); however, self-efficacy increased over time as the health-care providers gained experience in vaccine delivery. Low uptake of the fourth dose remained a challenge. Health managers cited insufficient trained immunisation staff and inadequate funding for supervision. Confidence in the vaccine increased among all participant groups owing to reductions in malaria frequency and severity.

INTERPRETATION: Integration of RTS,S/AS01 into immunisation services in western Kenya presented substantial operational challenges most of which were overcome in the first 2 years, providing important lessons for other countries. Programme expansion is feasible with intensive staff training and retention, enhanced supervision, and defaulter-tracing to ensure uptake of all doses.

FUNDING: PATH via World Health Organization; Gavi, the Vaccine Alliance; The Global Fund; and Unitaid.

WEB: 10.1016/S2214-109X(24)00013-5
IMPACT FACTOR: 34.3
CITED HALF-LIFE: 3.6

START COMMENTARY

Study locations were purposively selected to represent variations in malaria prevalence, and sublocations were chosen based on measles vaccination coverage as a proxy indicator for health system capacity and access to immunization services. The Consolidated Framework for Implementation Research was used to assess challenges and opportunities for malaria vaccine integration into the Essential Programme on Immunisation (EPI) in Kenya (Table 2). Hill et al. found that challenges changed over time and strong leadership at the national and local levels was key to program success.

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9. Perspectives on development and advancement of new tuberculosis vaccines.

da Costa C, Benn C, Nyirenda T, Mpabalwani E, Grewal H, Ahmed R, et al.

Int J Infect Dis. 2024 Mar 10:106987.

PubMed ID: 38417616

ABSTRACT

Tuberculosis (TB) remains a leading cause of death worldwide and is estimated to have caused 1.3 million deaths worldwide in 2022. Approximately one quarter of the world's population are infected with Mycobacterium tuberculosis, of whom up to 10% will progress to developing active TB disease. Achieving the World Health Organization End TB Strategy targets of a 95% reduction in TB mortality and a 90% reduction in TB incidence worldwide by 2035 remains a daunting task. The continuing spread of multidrug-resistant TB adds another obstacle to achieving global TB control. Larger funding pledges coupled with technological advances have recently enabled the enhancement of TB vaccine development efforts. These are yielding a pipeline of over 17 products currently in different stages of clinical trials. Emerging promising phase I and II trial results and advancement to phase III trials have necessitated "vaccine preparedness" in parallel so that a smooth transition from any positive clinical trial result to phase IV evaluation and implementation into policy and practice can follow. Promotion of a human rights-based approach, which recognizes and upholds the fundamental rights of all affected by the disease, is essential to ensure universal access to quality TB vaccines, regardless of their background or personal circumstances.

WEB: 10.1016/j.ijid.2024.106987

IMPACT FACTOR: 8.4

CITED HALF-LIFE: 2.6

START COMMENTARY

In this brief report, da Costa et al. describe current vaccine research for tuberculosis. Tables 1-4 provide an overview of vaccines in trial and their mechanisms of action. Authors emphasize the importance of vaccine preparedness, advocating for establishing the groundwork for regulatory approval, manufacturer capacity building, and distribution planning for optimal rollout of a future vaccine once trials are complete.

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10. Understanding rapid implementation from discovery to scale: Rwanda's implementation of rotavirus vaccines and PMTCT in the quest to reduce under-5 mortality.

Sayinzoga F, Hirschhorn L, Ntawukuriryayo J, Beyer C, Donahoe K, Binagwaho A.

BMC Pediatr. 2024 Feb 29;23(Suppl 1):649.

PubMed ID: 38413897

ABSTRACT

BACKGROUND: Over the last eight decades, many evidence-based interventions (EBIs) have been developed to reduce amenable under-5 mortality (U5M). Implementation research can help reduce the lag between discovery and delivery, including as new EBIs emerge, or as existing ones are adapted based on new research. Rwanda was the first low-income African country to implement the rotavirus vaccine (RTV) and also adopted Option B+ for effective prevention of mother-to-child transmission (PMTCT) before the World Health Organization's (WHO) recommendation. We use implementation research to identify contextual factors and strategies associated with Rwanda's rapid uptake of these two EBIs developed or adapted during the study period.

METHODS: We conducted a mixed methods case study informed by a hybrid implementation research framework to understand how Rwanda outperformed regional and economic peers in reducing U5M, focusing on the implementation of health system-delivered EBIs. The research included review of existing literature and data, and key informant interviews to identify implementation strategies and contextual factors that influenced implementation outcomes. We extracted relevant results from the broader case study and used convergent methods to understand successes and challenges of implementation of RTV, a newly introduced EBI, and PMTCT, an adapted EBI reflecting new research.

RESULTS: We found several cross-cutting strategies that supported the rapid uptake and implementation of PMTCT, RTV, and leveraging facilitating contextual factors and identifying and addressing challenging ones. Key implementation strategies included community and stakeholder involvement and education, leveraging of in-country research capacity to drive adoption and adaptation, coordination of donors and implementing partners, data audit and feedback of coverage, a focus on equity, and integration into pre-existing systems, including community health workers and primary care. The availability of donor funding, culture of evidence-based decision-making, preexisting accountability systems, and rapid adoption of innovation were facilitating contextual factors.

CONCLUSION: Implementation strategies which are generalizable to other settings were key to success in rapidly achieving high acceptability and coverage of both a new and an evolving EBI.

Choosing strategies which leverage their facilitating factors and address barriers are important for other countries working to accelerate uptake of new EBIs and implement needed adaptations based on emerging evidence.

WEB: 10.1186/s12887-023-03888-4
IMPACT FACTOR: 2.4
CITED HALF-LIFE: 5.0

START COMMENTARY

Sayinzoga et al. used an explanatory mixed methods approach that included key informant interviews, a literature search on reduction of under 5 mortality in Rwanda focused on uptake and implementation of evidence-based interventions, and utilization of quantitative data from Demographic and Health Surveys (DHS). Table 2 highlights strategies used to achieve acceptability, feasibility, fidelity, effectiveness and coverage, and equity outcomes for rotavirus vaccine implementation. These include community education and engagement to increase acceptability, identifying and preemptively addressing gaps in cold chain management to address feasibility issues, and planning for delivery of vaccines to children in remote areas to ensure equitable distribution of vaccines. Table 3 highlights strategies implemented for preventing mother-to-child HIV transmission, including providing clear guidelines and establishing monitoring programs to track loss-to-follow-up.

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11. High prevalence of zero-dose children in underserved and special setting populations in Ethiopia using a generalize estimating equation and concentration index analysis.

Biks G, Shiferie F, Tsegaye D, Asefa W, Alemayehu L, Wondie T, et al.

BMC Public Health. 2024 Feb 26;24(1):592.

PubMed ID: 38395877

ABSTRACT

BACKGROUND: Globally, according to the World Health Organization (WHO) 2023 report, more than 14.3 million children in low- and middle-income countries, primarily in Africa and South-East Asia, are not receiving any vaccinations. Ethiopia is one of the top ten countries contributing to the global number of zero-dose children.

OBJECTIVE: To estimate the prevalence of zero-dose children and associated factors in underserved populations of Ethiopia.

METHODS: A cross-sectional vaccine coverage survey was conducted in June 2022. The study participants were mothers of children aged 12-35 months. Data were collected using the CommCare application system and later analysed using Stata version 17. Vaccination coverage was estimated using a weighted analysis approach. A generalized estimating equation model was fitted to determine the predictors of zero-dose children. An adjusted odds ratio (AOR) with 95% confidence interval (CI) and a p-value of 0.05 or less was considered statistically significant.

RESULTS: The overall prevalence of zero-dose children in the study settings was 33.7% (95% CI: 34.9%, 75.7%). Developing and pastoralist regions, internally displaced peoples, newly formed regions, and conflict-affected areas had the highest prevalence of zero-dose children. Wealth index (poorest [AOR = 2.78; 95% CI: 1.70, 4.53], poorer [AOR = 1.96; 95% CI: 1.02, 3.77]), single marital status [AOR = 2.4; 95% CI: 1.7, 3.3], and maternal age (15-24 years) [AOR = 1.2; 95% CI: 1.1, 1.3] were identified as key determinant factors of zero-dose children in the study settings. Additional factors included fewer than four Antenatal care visits (ANC) [AOR = 1.3; 95% CI: 1.2, 1.4], not receiving Postnatal Care (PNC) services [AOR = 2.1; 95% CI: 1.5, 3.0], unavailability of health facilities within the village [AOR = 3.7; 95% CI: 2.6, 5.4], women-headed household [AOR = 1.3; 95% CI:1.02, 1.7], low gender empowerment [AOR = 1.6; 95% CI: 1.3, 2.1], and medium gender empowerment [AOR = 1.7; 95% CI: 1.2, 2.5].

CONCLUSION: In the study settings, the prevalence of zero-dose children is very high. Poor economic status, disempowerment of women, being unmarried, young maternal age, and underutilizing antenatal or post-natal services are the important predictors. Therefore, it is recommended to target tailored integrated and context-specific service delivery approach. Moreover,

extend immunization sessions opening hours during the evening/weekend in the city administrations to meet parents' needs.

WEB: 10.1186/s12889-024-18077-w
IMPACT FACTOR: 4.5
CITED HALF-LIFE: 5.5

START COMMENTARY

The vaccine coverage survey was administered to caregivers of children less than 5 years residing in underserved settings in Ethiopia, including pastoral regions, developing regions, newly established regions, hard-to-reach areas in agrarian regions, conflict-affected areas, urban slums, and refugees/internally displaced peoples. The survey was administered in five local languages by researchers with intensive training on the sampling approach and interviewing techniques. Over 3,600 caregivers were included across the targeted regions, and the prevalence of zero-dose and under-immunized children by setting can be found in Figure 1. Geographic variations were noted among population domains, with penta-1 coverage of more than 90% among those living in urban areas, which authors attributed to greater access to immunization services. Authors conclude that variability in uptake demonstrate the need for regional and context-specific vaccination strategies.
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12. The role of global health partnerships in vaccine equity: A scoping review.

Nunes C, McKee M, Howard N.

PLOS Glob Public Health. 2024 Feb 24;4(2):e0002834.
PubMed ID: 38386621

ABSTRACT

The emergence of global health partnerships (GHPs) towards the end of the twentieth century reflected concerns about slow progress in access to essential medicines, including vaccines. These partnerships bring together governments, private philanthropic foundations, NGOs, and international agencies. Those in the vaccine field seek to incentivise the development and manufacture of new vaccines, raise funds to pay for them and develop and support systems to deliver them to those in need. These activities became more critical during the COVID-19 pandemic, with the COVAX Facility Initiative promoting global vaccine equity. This review identifies lessons from previous experiences with GHPs. Findings contribute to understanding the emergence of GHPs, the mechanisms they leverage to support global access to vaccines, and the inherent challenges associated with their implementation. Using Arksey and O'Malley's method, we conducted a scoping review to identify and synthesise relevant articles. We analysed data thematically to identify barriers and opportunities for success. We included 68 eligible articles of 3,215 screened. Most (65 [95%]) were discussion or review articles describing partnerships or programmes they supported, and three (5%) were commentaries. Emerging themes included policy responses (e.g., immunisation mandates), different forms of partnerships arising in vaccine innovation (e.g., product development partnerships, public-private partnerships for access), and influence on global governance decision-making processes (e.g., the rising influence of foundations, diminishing authority of WHO, lack of accountability and transparency, creation of disease silos). If global health partnerships are to maximise their contributions, they should: (1) increase transparency, especially regarding their impacts; (2) address the need for health systems strengthening; and (3) address disincentives for cooperative vaccine research and development partnerships and encourage expansion of manufacturing capacity in low and middle-income countries.

WEB: 10.1371/journal.pgph.0002834
IMPACT FACTOR: N/A
CITED HALF-LIFE: N/A

START COMMENTARY

Authors describe the lack of empiric studies examining the roles of global health partnerships (GHPs) in improving access to medications and pandemic preparedness/pandemic response.

Authors note that evidence suggests that project development partnerships and GHPs provide opportunities to close equity gaps through leveraging skills and experiences of each partner. To ensure GHPs can be evaluated, authors advocate for transparency regarding decision-making processes, with data made publicly available regarding funding arrangements, geographical scope, research and development spending, and profit margins. They also argue for the inclusion of equity goals to address issues with technology transfer and manufacturing conditions in low- and middle-income countries (LMICs).

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13. Effective interventions for improving routine childhood immunisation in low and middle-income countries: a systematic review of systematic reviews.

Jain M, Duvendack M, Shisler S, Parsekar S, Leon M.

BMJ Open. 2024 Feb 19;14(2):e074370.

PubMed ID: 38365291

ABSTRACT

OBJECTIVE: An umbrella review providing a comprehensive synthesis of the interventions that are effective in providing routine immunisation outcomes for children in low and middle-income countries (L&MICs).

DESIGN: A systematic review of systematic reviews, or an umbrella review.

DATA SOURCES: We comprehensively searched 11 academic databases and 23 grey literature sources. The search was adopted from an evidence gap map on routine child immunisation sector in L&MICs, which was done on 5 May 2020. We updated the search in October 2021.

ELIGIBILITY CRITERIA: We included systematic reviews assessing the effectiveness of any intervention on routine childhood immunisation outcomes in L&MICs.

DATA EXTRACTION AND SYNTHESIS: Search results were screened by two reviewers independently applying predefined inclusion and exclusion criteria. Data were extracted by two researchers independently. The Specialist Unit for Review Evidence checklist was used to assess review quality. A mixed-methods synthesis was employed focusing on meta-analytical and narrative elements to accommodate both the quantitative and qualitative information available from the included reviews.

RESULTS: 62 systematic reviews are included in this umbrella review. We find caregiver-oriented interventions have large positive and statistically significant effects, especially those focusing on short-term sensitisation and education campaigns as well as written messages to caregivers. For health system-oriented interventions the evidence base is thin and derived from narrative synthesis suggesting positive effects for home visits, mixed effects for pay-for-performance schemes and inconclusive effects for contracting out services to non-governmental providers. For all other interventions under this category, the evidence is either limited or not available. For community-oriented interventions, a recent high-quality mixed-methods review suggests positive but small effects. Overall, the evidence base is highly heterogenous in terms of scope, intervention types and outcomes.

CONCLUSION: Interventions oriented towards caregivers and communities are effective in improving routine child immunisation outcomes. The evidence base on health system-oriented interventions is scant not allowing us to reach firm conclusions, except for home visits. Large evidence gaps exist and need to be addressed. For example, more high-quality evidence is needed for specific caregiver-oriented interventions (eg, monetary incentives) as well as health system-oriented (eg, health workers and data systems) and community-oriented interventions. We also need to better understand complementarity of different intervention types.

WEB: 10.1136/bmjopen-2023-074370
IMPACT FACTOR: 2.9
CITED HALF-LIFE: 4.0

START COMMENTARY

Inclusion criteria for this review were broad, with studies examining a wide range of vaccine-related outcomes, including: the impact of interventions on coverage rates or timeliness of vaccinations; third dose of DPT, pentavalent or measles vaccine; other immunizations coverage outcomes; and intermediate outcomes such as attitudes about vaccination and access to immunizations. Studies that focused solely on high income countries were excluded. Table 2 provides a summary of findings across the 62 included systematic reviews.

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14. What would have happened anyway? Population data source considerations when estimating background incident rates of adverse events following immunisation to inform vaccine safety.

Clothier H, Shetty A, Mesfin Y, Mackie M, Pearce C, Buttery J.

Vaccine. 2024 Feb 26;42(5):1108-1115.

PubMed ID: 38262811

ABSTRACT

INTRODUCTION: Understanding background incident rates of adverse events following immunisation (AEFI) is essential to rapidly detect, evaluate, respond to, and communicate about vaccine safety concerns, especially for new vaccines. Creating estimates based on geographic specific population level data is increasingly important, as new AEFI presentations will be subject to the same local influences of population demography, exposures, health system variations and level of health care sought.

METHODS: We conducted a retrospective cohort analysis of hospital admissions, emergency department presentations and general practice consultations from 2015 to 2019-before introduction of COVID-19, Mpox or Shingrix vaccination-to estimate background incident rates for 37 conditions considered potential AEFI of special interest (AESI). Background incident rates per 100,000 population were calculated and presented as cases expected to occur coincidentally 1 day, 1 week and 6 weeks post-vaccination, by life-stage age-groups and presenting healthcare setting. We then assessed the proportional contribution of each data source to inform each AESI background rate estimate.

RESULTS: 16,437,156 episodes of the 37 AESI were identified. Hospital admissions predominantly informed 19 (51%) of AESI, including exclusively ADEM and CVST; 8 AESI (22%) by primary care, and 10 (27%) a mix. Four AESI (allergic urticaria, Bell's palsy, erythema multiform and sudden death) were better informed by emergency presentations than admissions, but conversely 11 AESI (30%) were not captured in ICD-10 coded emergency presentations at all.

CONCLUSIONS: Emergent safety concerns are inevitable in population-wide implementation of new vaccines, therefore understanding local background rates aids both safety signal detection as well as maintaining public confidence in vaccination. Hospital and primary care data sources can be interrogated to inform expected background incident rates of adverse events that may occur following vaccination. However, it is necessary to understand which data-source provides best intelligence according to nature of condition and presenting healthcare setting.

WEB: 10.1016/j.vaccine.2024.01.025
IMPACT FACTOR: 5.5
CITED HALF-LIFE: 7.2

START COMMENTARY

This study investigated data from emergency room visits, hospital discharge reports, and primary care visits in Melbourne, Australia, to assess which source provided the best estimates of potential incident adverse events following immunization (AEFI). They found that rates differed for each setting due to the way data was recorded, and the best source of data differed depending on the AEFI of concern. They stressed the importance of understanding the health system structure and rules for how data are recorded to better understand which rate should be used as the background rate of an event for the purposes of assessing AEFI. Tables 2, 3, and 4 show the expected rate of hospital admissions, expected rate of emergency room visits, and expected rate of primary care visits per 100,000 persons vaccinated by risk-window period and age category, respectively.

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Additional Articles of Interest

1 Rethinking immunization programs through the life course approach. {Full Article}
2 A paired measles-rubella catch-up campaign in Sichuan China to stop an outbreak and strengthen local immunization programs. {Full Article}
3 Parents' perspectives on dental team as advisors to promote HPV vaccination among Spanish adolescents. {Full Article}
4 Community engagement in vaccination promotion: A systematic review and meta-analysis. {Full Article}
5 Impact of a research-action on vaccination indicators in the state of Minas Gerais, Brazil. {Full Article}
6 Prevalence of errors causing events allegedly attributable to vaccination/immunization: systematic review and meta-analysis. {Full Article}
7 Strategies to increase the coverage of influenza and pneumonia vaccination in older adults: a systematic review and network meta-analysis. {Full Article}
8 Rates and determinants of Rotavirus vaccine uptake among children in Italy: a cross-sectional study within the 2022 OBVIOUS* project. {Full Article}
9 Migration and infant immunization timeliness in New Zealand: Evidence from the Growing Up in New Zealand study. {Full Article}
10 Prevalence of Human Papillomavirus (HPV) and HPV Type Distribution in Penile Samples in Young Men in Denmark: Results 10 Years After Implementation of a Girls-Only HPV Vaccination Program. {Full Article}
11 Effectiveness of educational interventions for healthcare workers on vaccination dialogue with older adults: a systematic review. {Full Article}
12 Exploring the processes and mechanisms by which nonprofit organizations orchestrate global innovation networks: A case study of the COVAX program. {Full Article}
13 Using freeze-preventive cold boxes in rural Nepal: A study of equipment performance, acceptability, system fit, and cost. {Full Article}
14 Systems vaccinology studies - achievements and future potential. {Full Article}
15 Population-based cross-sectional study of factors influencing full vaccination status of children aged 12- 23 months in a rural district of the Upper East Region, Ghana. {Full Article}
16 Pneumococcal vaccine uptake among high-risk adults and children in Italy: results from the OBVIOUS project survey. {Full Article}
17 Immunization coverage and its associated factors among children aged 12-23 months in Ethiopia: An umbrella review of systematic review and meta-analysis studies. {Full Article}

18 Landscaping analysis of immunization progress and program structures in selected middle income Southeast Asian countries. {Full Article}
19 Leaky bodies, vaccination and three layers of memory: bio-immune, social-collective and lived experience. {Full Article}
20 Establishing priorities to strengthen National Immunization Technical Advisory Groups in Latin America and the Caribbean. {Full Article}
21 Health system barriers to the first dose of measles immunization in Ethiopia: a qualitative study. {Full Article}
22 Promoting informed decision making about maternal pertussis vaccination: the systematic development of an online tailored decision aid and a centering-based group antenatal care intervention. {Full Article}
23 Co-administration of the adjuvanted recombinant zoster vaccine with other adult vaccines: An overview. {Full Article}
24 Retrospective cohort study exploring the impact of universal Tuberculosis (TB) vaccination cessation on the epidemiology of paediatric TB in Ireland, 2011-2021. {Full Article}
25 The immune status of migrant populations in Europe and implications for vaccine-preventable disease control: a systematic review and meta-analysis. {Full Article}
26 Geospatial and multilevel clustering of zero-dose children in Kikwit, Democratic Republic of the Congo in 2022. {Full Article}
27 BCG vaccination and multiple sclerosis risk: A Norwegian cohort study. {Full Article}
28 Reducing the equity gap in under-5 mortality through an innovative community health program in Ethiopia: an implementation research study. {Full Article}
29 Novel therapeutic approaches for the management of hepatitis infections. {Full Article}
30 Tuberculosis vaccine developments and efficient delivery systems: A comprehensive appraisal. {Full Article}
31 Strategies for Improving Vaccine Communication and Uptake. {Full Article}
32 Can side effect expectations be assessed implicitly? A comparison of explicit and implicit expectations of vaccination side effects. {Full Article}
33 A Practical Guide to Full Value of Vaccine Assessments. {Full Article}
34 Complex interplay of science reasoning and vaccine hesitancy among parents in Shanghai, China. {Full Article}
35 From Qualitative Research to Quantitative Preference Elicitation: An Example in Invasive Meningococcal Disease. {Full Article}
36 Progress Toward Measles Elimination - World Health Organization Eastern Mediterranean Region, 2019-2022. {Full Article}
37 Prediction of effectiveness of universal rotavirus vaccination in Southwestern Vietnam based on a dynamic mathematical model. {Full Article}

38 2022 Polio outbreak, Rockland County, NY: Cost evaluation of strategies to prevent future outbreaks of vaccine-preventable diseases. {Full Article}

39 Trend of measles-rubella vaccination coverage and impact on measles epidemiology in the Savannah Region, Ghana; 2018-2022: A secondary data analysis. {Full Article}

Appendix

The literature search for the April 2024 Vaccine Delivery Research Digest was conducted on March 17, 2024. We searched English language articles indexed by the US National Library of Medicine and published between February 15, 2024 and March 14, 2024. The search resulted in 455 items.

SEARCH TERMS

(((((vaccine[tiab] OR vaccines[tiab] OR vaccination[tiab] OR immunization[tiab] OR immunisation[tiab] OR vaccine[mesh] OR immunization[mesh]) 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[LA]) (“2024/15/02”[PDAT] : “2024/14/03”[PDAT]))