VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE GATES FOUNDATION

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DECEMBER 2024

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{Abstract & START Commentary} {Full Article}

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- Challenges facing health sector planning and budgeting in Kenya and how they affect immunisation service delivery at the county level were examined.

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11 An evaluation of the surveillance system for monitoring and reporting adverse events following immunization in Kebbi State, Northern Nigeria: a mixed method approach.

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13 A prospective, multicenter study of hepatitis B birth-dose vaccine with or without hepatitis B immunoglobulin in preventing mother-to-child transmission of hepatitis B virus in Ethiopia.
{Abstract & START Commentary} {Full Article}

- Birth-dose hepatitis B vaccine with or without hepatitis B immunoglobulin was found to significantly reduced the risk of mother to child transmission of hepatitis B in this study.

14 Safety of hepatitis E vaccine in pregnancy: an emulated target trial following a mass reactive vaccination campaign in Bentiu internally displaced persons camp, South Sudan.
{Abstract & START Commentary} {Full Article}

- The association between vaccination against hepatitis E in pregnancy and fetal loss was assessed in a cohort of vaccinated and unvaccinated pregnant people.

15 Update on Vaccine-Derived Poliovirus Outbreaks - Worldwide, January 2023-June 2024.
{Abstract & START Commentary} {Full Article}

- An update on circulating vaccine-derived poliovirus type 1 (cVDPV1) and type 2 (cVDPV2) outbreaks was provided.

Appendix

Details of Articles

1. Private sector engagement for immunisation programmes: a pragmatic scoping review of 25 years of evidence on good practice in low-income and middle-income countries.

Sharma G, Morgan C, Wanyoike S, Kenyon S, Sheel M, Jain M, et al.

BMJ Glob Health. 2024 Nov 15;8(Suppl 5).

PubMed ID: 39542515

ABSTRACT

INTRODUCTION: Many National Immunisation Programmes attempt to leverage the private sector ; however, there is limited consolidated and synthesised documentation on good practices, gaps and lessons learnt. A 2017 WHO guidance document recommended best practices for private sector engagement (PSE) in immunisation. We conducted a pragmatic scoping review to identify gaps, update and consolidate evidence on promising practices in PSE for vaccination.

METHODS: Building on two previous reviews published in 2011 and 2017, we conducted a pragmatic scoping review of peer-reviewed publications from low-income and middle-income countries since September 2016 in PubMed that pertained to PSE and immunisation service delivery. We extracted and analysed findings using a new analytical framework covering motivations, enablers and barriers, risks and challenges, and engagement mechanisms.

RESULTS: We collated over 80 well-documented analyses of PSE for vaccination, derived from 54 peer-reviewed publications from 1998 to 2016 included in prior reviews, 21 new publications from 24 countries published since 2016 and 1 new systematic review. The level of PSE was mixed, ranging from 3%-4% to >60% of all childhood vaccinations. Promising practices for PSE included using governance and policy to leverage private providers' motivations and including them in programme efforts. Planning and monitoring efforts were effective when linked with regulatory requirements based on national standards for services, reporting and performance monitoring. Information systems were effective when they included private sector services in vaccine monitoring and surveillance. Challenges identified included ensuring compliance with national schedules and standards and minimising financial exclusion. Few studies documented successful public-private partnership models or other innovative financing models.

CONCLUSION: The published evidence captures numerous strategies to facilitate stronger immunisation programme engagement with the private sector. Stronger PSE can potentially reach zero-dose and underimmunised populations in low-resource settings and build resilient systems. Untapped opportunities exist for more structured testing of approaches to inform global guidance.

WEB: 10.1136/bmjgh-2023-014728

IMPACT FACTOR: 7.1

CITED HALF-LIFE: 3.2

START COMMENTARY

Authors extracted information about underlying motivations of private providers to engage in immunization services. Profit opportunities and the desire to offer essential services to local communities were important to many private providers. In Bangladesh, providers reported profits made from service fees as a key motivator for participation while also reporting that providing essential services improved the reputation of the facility and increased their social standing in the community. In Afghanistan and Sudan, involvement in vaccine provisions linked facilities to opportunities for government support for training, facility renovations, equipment and supplies, and quality improvement opportunities. Efforts to expand the private sector's role in immunization services can build on these findings.

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2. Progress Toward Measles Elimination - Worldwide, 2000-2023.

Minta A, Ferrari M, Antoni S, Lambert B, Sayi T, Hsu C, et al.

MMWR Morb Mortal Wkly Rep. 2024 Nov 14;73(45):1036-1042.

PubMed ID: 39541251

ABSTRACT

Measles vaccination effectively prevents measles, a highly contagious disease that can cause severe complications and death and requires high population immunity to interrupt transmission. This report describes measles elimination progress during 2000-2023. During 2000-2023, an estimated 60.3 million measles deaths were averted by vaccination. However, despite commitment from all six World Health Organization regions to eliminate measles, no region has successfully achieved and maintained measles elimination as of the end of 2023. During the COVID-19 pandemic, estimated global coverage with the first dose of measles-containing vaccine (MCV1) declined to 81%, the lowest level since 2008. MCV1 coverage improved to 83% in 2022 but was unchanged in 2023. From 2022 to 2023, estimated measles cases increased 20% worldwide, from 8,645,000 to 10,341,000; the number of countries experiencing large or disruptive outbreaks increased from 36 to 57. Estimated measles deaths decreased 8%, from 116,800 in 2022 to 107,500 in 2023, primarily because an increased number of cases occurred in countries with lower risk for death. The stagnation in MCV1 coverage means millions of children remain unprotected, leading to increases in cases and outbreaks. Coverage with measles-containing vaccine (MCV) is lower, and measles incidence is higher, in low-income countries and countries experiencing fragile, conflict-affected, and vulnerable settings, which exacerbate inequities. Urgent and targeted efforts are needed to ensure that all children receive 2 MCV doses and that surveillance is strengthened to hasten progress toward measles elimination.

WEB: 10.15585/mmwr.mm7345a4

IMPACT FACTOR: 21.0

CITED HALF-LIFE: 3.6

START COMMENTARY

First dose measles-containing vaccine (MCV1) coverage was 64%, 86%, and 94% in low-, middle- , and high-income countries, respectively, and was 67% in countries containing fragile, conflict-affected, and vulnerable settings (FCV). No region regained 2019 MCV1 coverage levels by the end of 2023. Only two measles genotypes were identified among a total of 3,373 sequenced samples from 74 countries in 2023 (74% and 26% genotypes D8 and B3, respectively).

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3. Population-level health impact of hypothetical waning 1-dose human papillomavirus vaccination and 2-dose mitigation strategies in a high cervical cancer burden setting.

Burger E, Laprise J, Portnoy A, Spencer J, Sy S, Regan M, et al.

J Natl Cancer Inst Monogr. 2024 Nov 12;2024(67):379-386.
PubMed ID: 39529530

ABSTRACT

BACKGROUND: We simulated the impact of hypothetical waning scenarios of a 1-dose human papillomavirus (HPV) vaccination paired with switching to 2-dose mitigation strategies guided by empirical vaccine trial reporting timelines.

METHODS: Using 2 independent mathematical models fitted to a high-burden setting, we projected the cumulative cervical cancer cases averted over 85 years for alternative HPV vaccination scenarios under 2 program adoption timelines: 1) de novo introduction of a 1-dose HPV vaccination and 2) a switch from an existing 2-dose HPV vaccination program to a 1-dose vaccination. We assumed 80% vaccination coverage with the bivalent vaccine and an average duration of a 1-dose HPV vaccine protection of either 30 or 25 years with 100% efficacy. We varied the eligible age group(s) at program introduction and the 2-dose mitigation (single-age cohort or multi-age cohort). If needed for mitigation, reintroduction of 2-dose vaccination was assumed to occur in 2036 (ie, 30 years after initiation of the Costa Rica Vaccine Trial).

RESULTS: Under both vaccine adoption timelines, the models projected that countries could achieve the same level of health benefits by switching to 2 doses in 2036 using a multi-age cohort approach as with initiating a 2-dose or 1-dose vaccination program with no waning. With only a single-age cohort 2-dose mitigation approach, 98%-99% of cases would be prevented compared with the health benefits of 2 doses or a noninferior, durable 1 dose.

CONCLUSIONS: Countries hesitant to adopt a 1-dose HPV vaccination program may have opportunities to leverage the benefits and efficiency of a 1-dose schedule while awaiting longer-term reporting from 1-dose durability studies, including Costa Rica Vaccine Trial.

WEB: 10.1093/jncimonographs/lgae039
IMPACT FACTOR: 10.0
CITED HALF-LIFE: 12.1

START COMMENTARY

Figures 2 and 3 shows cumulative cervical cancer cases averted by 2068, 2088, and 2108 for mitigation strategies among countries introducing an HPV vaccination program for the first time in

2024 (de novo) and countries switching from a 2-dose HPV vaccination schedule to a 1-dose vaccination schedule in 2024 (switcher). HPV vaccination coverage of 40% vs base case (80%) prevented ~40% fewer cases across all modeled scenarios while increasing coverage to 90% prevented an additional 6% of cases. In low coverage areas, a multi-age cohort mitigation approach had a higher proportion of cases averted when compared with a single-age cohort mitigation approach (Table 1).

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4. Evaluating potential program cost savings with a single-dose HPV vaccination schedule: a modeling study.

Slavkovsky R, Mvundura M, Debellut F, Naddumba T.

J Natl Cancer Inst Monogr. 2024 Nov 12;2024(67):371-378.
PubMed ID: 39529523

ABSTRACT

BACKGROUND: There is limited evidence on the magnitude of the potential program cost savings associated with the World Health Organization-endorsed single-dose schedule for the human papillomavirus (HPV) vaccine. The objective of this analysis was to model the delivery and vaccine procurement cost implications of the new schedule.

METHODS: The analysis leveraged primary data during a study evaluating the HPV vaccine delivery costs and operational context in 5 countries (Ethiopia, Guyana, Rwanda, Sri Lanka, and Uganda) implementing a two-dose schedule. To estimate the cost for the single-dose schedule, we adjusted the two-dose schedule cost estimates to account for differences in the frequency of activities, whether activities differed by HPV vaccine dose or session, and differences in relative quantity or storage volume of HPV vaccines delivered. We estimated the cost per dose and cost per adolescent receiving the full (single-dose or two-dose) vaccination schedule in 2019 US dollars from a health system perspective.

RESULTS: Modeled results found that cost per dose would increase under a single-dose schedule, whereas cost per adolescent receiving the full schedule would decrease. The financial cost for vaccine procurement and delivery per adolescent receiving the full schedule ranged from $9.64 (Sri Lanka) to $23.43 (Guyana) under a two-dose schedule and decreased to $4.84 and $12.34, respectively, under a single-dose schedule, reflecting savings up to 50%. For economic costs, the range for a single-dose schedule was $7.86 (Rwanda) to $28.53 (Guyana).

CONCLUSION: A single-dose HPV vaccination schedule could provide cost savings to immunization programs and enhance program affordability and sustainability.

WEB: 10.1093/jncimonographs/lgae037
IMPACT FACTOR: 10.0
CITED HALF-LIFE: 12.1

START COMMENTARY

Costs associated with program planning, social mobilization, training, vaccine distribution and storage, and service delivery were included in the analysis. Combined vaccine delivery and

procurement costs per adolescent vaccinated decreased by at least 40% in all five countries when moving from a 2-dose schedule to a single-dose schedule. Delivery and procurement costs per adolescent to deliver the full HPV vaccination schedule under a two-dose and single-dose schedule for each of the five countries are shown in Figure 1.

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5. Community-based participatory research (CBPR) approaches in vaccination promotion: a scoping review.

Zhang Y, Xie Y, Yang L, Cheung K, Zhang Q, Li Y, et al.

Int J Equity Health. 2024 Nov 06;23(1):227.

PubMed ID: 39501299

ABSTRACT

BACKGROUND: Community-based participatory research (CBPR) is a collaborative research approach that engages academic researchers and community stakeholders as equal partners in all research steps to address community concerns and achieve health equity. The CBPR approach has been widely used in vaccination promotion programmes. However, the elements and steps of CBPR-based programmes varied among studies. The purpose of this scoping review was to synthesize the elements and steps, and establish an implementation framework to guide the utilisation of CBPR approaches in vaccination promotion.

METHODS: This scoping review was performed in accordance with Arksey and O'Malley's five-stage framework. A systematic search was conducted on a set of electronic databases and grey literature sources. The retrieved articles were screened according to the criteria of CBPR and vaccination promotion, and data were extracted and recorded on a calibrated and predefined form in terms of study characteristics and CBPR components. Two authors worked independently to complete literature search, study selection, and data extraction. A narrative summary was used in categorising characteristics, and the contents of the included studies were summarised through qualitative analysis.

RESULTS: A total of 8557 publications were initially screened, and 23 articles were finally included. According to the CBPR conceptual model, the elements in each CBPR component specifically for vaccination promotion included (1) the establishment of community-academic partnership (CAP)s, (2) community capacity building by partner training vaccination knowledge, research literacy, and service abilities and skills, (3) development and implementation of community-based intervention and (4) Outcome evaluation. A CAP was established between academic researchers or institutes and eight types of partners, including community service organisation-related non-government organisations (NGOs), health service institution-related NGOs, religious organisations, government agencies, educational institutions, media agencies, business agencies, and community representatives. The maintenance of CAP was achieved with four key strategies, namely, strengthening communication, forming management groups, sharing resources and information, and providing incentives. Twelve studies provided comprehensive insights into the strategies employed for intervention development, utilising either quantitative surveys, qualitative methods or a combination of both approaches. The contents of interventions included health service supports,

health education activities, social marketing campaigns, community mobilisation, interactive discussions, vaccination reminders and incentives. As for outcome evaluation, vaccination rate and the effectiveness of interventions were assessed. A considerable increase was observed in 95.7% of the included studies (22/23), and the highest increase (92.9%) was attained after the intervention. An implementation framework was generated to summarise the elements and steps of CBPR approaches for vaccination promotion.

CONCLUSIONS: This review summarised current evidence and generated an implementation framework to elucidate the elements and steps in the development and application of CBPR approaches in vaccination promotion. CBPR approaches are recommended for future vaccination promotion programmes, involving community stakeholders and research professionals, to ensure equitable access to vaccinations across diverse populations.

WEB: 10.1186/s12939-024-02278-1
IMPACT FACTOR: 4.5
CITED HALF-LIFE: 5.1

START COMMENTARY

Most included studies were conducted in the United States (n=14), which limits generalizability to low resource settings. Community partners participated in intervention delivery, intervention development, subject recruitment, and data collection in most included studies. Fewer than 22% of studies involved community partners in dissemination of findings or result interpretation. Only one study involved community partners in all six research phases. Authors suggest future studies to explore additional vaccine outcomes such as vaccine hesitancy.

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6. Routine immunization against Streptococcus pneumoniae and Haemophilus influenzae type B and antibiotic consumption in India: a dynamic modeling analysis.

Kumar C, Gleason A, Parameswaran G, Summan A, Klein E, Laxminarayan R, et al.

Lancet Reg Health Southeast Asia. 2024 Nov 05;31:100498.

PubMed ID: 39492849

ABSTRACT

BACKGROUND: Childhood vaccinations can reduce disease burden and associated antibiotic use, in turn reducing the risk of antimicrobial resistance (AMR). We retrospectively estimated the population-level reductions in antibiotic use in India following the introduction of vaccines against Streptococcus pneumoniae and Haemophilius influenzae type B in the national immunization program for children in the mid-2010s and projected future gains to 2028 if vaccination coverage were to be increased.

METHODS: Using IndiaSim, a dynamic agent-based microsimulation model (ABM) for India, we simulated the spread of Streptococcus pneumoniae and Haemophilius influenzae type B (Hib) among children to estimate reductions in antibiotic use under the scenarios of: (i) pneumococcal and Hib vaccine coverage levels equivalent to the national coverage of pentavalent diphtheria-pertussis-tetanus third dose (DPT3) compared to a baseline of no vaccination, and (ii) near-universal (90%) coverage of the vaccines compared to pre-COVID national DPT3-level coverage. Model parameters, including national DPT3 coverage rates, were based on data from the National Family Household Survey 2015-2016 and other published sources. We quantified reductions in antibiotic consumption nationally and by state and wealth quintiles.

FINDINGS: We estimate that coverage of S. pneumoniae and Hib vaccines at the same level as DPT3 in India would translate to a 61.4% [95% UI: 43.8-69.5] reduction in attributable antibiotic use compared to a baseline of zero vaccination coverage. Increases in childhood vaccination coverage between 2004 and 2016 have likely reduced attributable antibiotic demand by as much as 93.4% among the poorest quintile. Increasing vaccination coverage by an additional 11 percentage points from 2016 levels results in mortality and antibiotic use across wealth quintiles becoming increasingly similar ($p < 0.05$), reducing in health inquities. We project that near-universal vaccine coverage would further reduce inequities in antibiotic demand and may eliminate of outbreak-associated antibiotic use from S. pneumoniae and Hib.

INTERPRETATION: Though vaccination has a complex relationship with antibiotic use because both are modulated by socioeconomic factors, increasing vaccinations for S. pneumoniae and Hib may have a significant impact on reducing antibiotic use and improving health outcomes among the poorest individuals.

FUNDING: The Bill & Melinda Gates Foundation (grant numbers OPP1158136 and OPP1190803).

WEB: 10.1016/j.lansea.2024.100498
IMPACT FACTOR: 5.0
CITED HALF-LIFE: 1.1

START COMMENTARY

While infection from streptococcus pneumoniae and Hib were modeled independently, the model was calibrated to report the incidence and antibiotic use averted from both together. This was considered a useful measure for health systems as both are the cause of pneumonia-like illness. Model parameters and their sources can be found in Supplemental Table 1. Future studies should explicitly model individual streptococcus pneumoniae serotype dynamics as this would provide better understanding of which serotypes cause the most antibiotic use and could determine which serotypes to target in future vaccine formulations.

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7. Routine Vaccination Coverage - Worldwide, 2023.

Jones C, Danovaro-Holliday M, Mwinnyaa G, Gacic-Dobo M, Francis L, Grevendonk J, et al.
MMWR Morb Mortal Wkly Rep. 2024 Oct 31;73(43):978-984.
PubMed ID: 39480752

ABSTRACT

In 2020, the World Health Assembly endorsed the Immunization Agenda 2030 (IA2030), a 10-year strategy to reduce vaccine-preventable disease (VPD)-associated morbidity and mortality. IA2030 goals include improving equitable vaccination coverage, halving the number of unimmunized (zero-dose) children, and increasing the introduction of new and underutilized vaccines. The COVID-19 pandemic disrupted health systems worldwide, hindering years of childhood vaccination achievements and putting global public health goals at risk. This report presents trends in World Health Organization (WHO) and UNICEF routine vaccination coverage estimates through 2023 across the 194 WHO member countries. During 2022-2023, global coverage with the first and third doses of diphtheria-tetanus-pertussis-containing vaccine (DTPcv) (89% and 84%, respectively) and the first dose of measles-containing vaccine (83%) stagnated and remained lower than prepandemic levels. The 31 WHO member countries with fragile, conflict-affected, and vulnerable (FCV) settings include approximately one half of the world's 14.5 million children who did not receive the first DTPcv dose. The introduction of new and underutilized vaccines, such as a second MCV dose in the African Region, has improved countries' overall protection against VPDs. Accelerating country-specific routine immunization and catch-up vaccination programs to reach unvaccinated and incompletely vaccinated children, especially those living in FCV settings, is critical to reducing morbidity and mortality associated with VPDs.

WEB: 10.15585/mmwr.mm7343a4
IMPACT FACTOR: 21.0
CITED HALF-LIFE: 3.6

START COMMENTARY

Although globally the number of children with no measles-containing vaccine (MCV) doses increased between 2020-2023, MCV2 was introduced in 10 African Region countries and MCV2 coverage in that region increased from 33% in 2019 to 49% in 2023. HPV vaccine was introduced in 30 countries between 2020-2023, and global first dose and complete immunization among girls increased during that timeframe from 17% and 13% to 27% and 20%, respectively. Global inactivated poliovirus type 1 (IPV1) vaccine coverage has returned to pre-pandemic levels (83%).

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8. Facilitators and barriers to maternal immunization and strategies to improve uptake in low-income and lower-middle income countries: A systematic review.

Khan T, Malik S, Rafeekh L, Halder S, Desai S, Das Bhattacharya S.

Hum Vaccin Immunother. 2024 Oct 30;20(1):2411823.

PubMed ID: 3947317139558759

ABSTRACT

Maternal immunization (MI) is an emerging strategy to combat infant mortality in low-income (LIC) and lower-middle income countries (LMIC). We conducted a systematic review to identify the facilitators and barriers to MI and strategies that improve uptake in LICs and LMICs. We searched PubMed, Cochrane Library, and Scopus for quantitative, qualitative, and mixed-methods studies published in English from January 1, 2011, to October 31, 2021, from all LICs and LMICs. Data was appraised using the Mixed Methods Appraisal Tool. 55 studies were included. The major barriers were low knowledge and concern of vaccine safety among pregnant women and healthcare providers (HCP). HCP's recommendation, maternal knowledge, vaccine confidence and ≥4 antenatal care (ANC) visits facilitated uptake. The key strategies encompassed health financing, reminders, intersectoral coordination, integration, community engagement, capacity building, and education. Community-based delivery models were effective. Tailored programs are needed to improve ANC access, and educate pregnant women and HCPs.

WEB: 10.1080/21645515.2024.2411823

IMPACT FACTOR: 4.1

CITED HALF-LIFE: 4.1

START COMMENTARY

Key factors influencing maternal immunization in low- and lower-middle income countries were identified and categorized according to the socioeconomic model (Figure 3). Policy level facilitators included government recommendation, available data on disease burden and vaccine safety, and low vaccine costs. Strategies that strengthen maternal immunization studies were identified in 12 studies (Figure 4). Included studies were conducted in 26 countries, but few studies were from conflict areas or included refugee populations. Most studies focused on tetanus toxoid and influenza vaccines (32 and 13 studies, respectively).

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9. Financing immunisation in Kenya: examining bottlenecks in health sector planning and budgeting at the decentralised level.

Adjagba A, Oguta J, Akoth C, Wambiya E, Nonvignon J, Jackson D.

Cost Eff Resour Alloc. 2024 Nov 01;22(1):76.

PubMed ID: 39472992

ABSTRACT

BACKGROUND: Decentralisation has increasingly been adopted by countries as an important health sector reform aimed at increasing community participation in decision making while enhancing swift response at decentralised levels, to accelerate the attainment of health system goals. Kenya adopted a devolved system of government where health services delivery became a function of the 47 semi-autonomous county governments with planning and budgeting functions practised at both levels of government. This study sought to explore challenges facing health sector planning and budgeting and how they affect immunisation service delivery at the county level.

METHODS: Data were collected through 77 in-depth interviews of senior county department of health officials across 15 counties in Kenya. We applied an inductive thematic approach in analysing the qualitative data using NVIVO software.

FINDINGS: The study found a lack of alignment between planning and budgeting processes, with planning being more inclusive compared to budgeting. Inadequate capacity in conducting planning and budgeting and political interference were reported to hinder the processes. Limited budget allocations and delayed and untimely disbursement of funds were reported to affect execution of health and immunisation budgets. Low prioritisation of preventive health interventions like immunisation due to their perceived intangibility influenced resource allocation to the programs.

CONCLUSION: The findings highlight the need for effective strategies to align planning and budgeting processes, increased technical support to counties to enhance the requisite capacity, and efforts to improve budget execution to improve budget credibility. Counties should plan to increase their funding commitment toward immunisation to ensure sustainability of the program as Kenya transitions from GAVI support.

WEB: 10.1186/s12962-024-00581-w

IMPACT FACTOR: 1.7

CITED HALF-LIFE: 5.0

START COMMENTARY

In Kenya, vaccine procurement is the managed by the national government, so immunization programs are generally perceived as national programs. However, vaccine delivery funding is the responsibility of the individual counties. County health officials indicated that the immunization program is often ignored in local planning and budgeting because results are not attributed to the county and are not tangible or immediately apparent. Funding is more often allocated to structures and facilities that can be seen by a politician's constituents even though funding may not be available to staff or supply the facility.

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10. The effect of Plasmodium falciparum exposure and maternal anti-circumsporozoite protein antibodies on responses to RTS,S/AS01E vaccination in infants and children: an ancillary observational immunological study to a phase 3, randomised clinical trial.

Macià D, Campo J, Jairoce C, Mpina M, Sorgho H, Dosoo D, et al.

Lancet Infect Dis. 2024 Oct 26.

PubMed ID: 39461358

ABSTRACT

BACKGROUND: The RTS,S/AS01E malaria vaccine showed lower antibody response and protective efficacy in infants aged 6-12 weeks compared with children aged 5-17 months (for whom this vaccine is recommended). We aimed to study the effect of previous Plasmodium falciparum exposure on the antibody responses to RTS,S/AS01E vaccination in infants and children, and the mediating effect of baseline (including maternal) anti-circumsporozoite protein (CSP) antibodies.

METHODS: In this observational study, we included children and infants from six African countries (Burkina Faso, Gabon, Ghana, Kenya, Mozambique, and Tanzania) enrolled in the MAL067 immunology ancillary study of the RTS,S/AS01E phase 3 clinical trial from March 27, 2009, to Jan 21, 2011. We used comparator-vaccinated infants and children to identify antibody-based signatures of previous P falciparum exposure, which were later applied to RTS,S/AS01E-vaccinated infants and children. In these participants, we explored the relationship between vaccine antibody immunoglobulin G (IgG) responses measured by ELISA and pre-vaccination serological markers of malaria exposure by assessing the IgG levels against 1000 P falciparum antigens using partial proteome microarrays.

FINDINGS: We included 718 comparator-vaccinated infants (348 [48%]) and children (370 [52%]) and 606 RTS,S/AS01E-vaccinated infants (329 [54%]) and children (277 [46%]). Anti-CSP IgG responses to primary vaccination did not correlate with a baseline signature of previous exposure in children, suggesting that prior P falciparum exposure does not significantly affect antibody immunogenicity in children (Pearson's r=-0·02 [95% CI -0·13 to 0·10]). By contrast, high P falciparum exposure signature levels at the time of vaccination in infants, presumably driven by maternally transferred antibodies and declining within the initial 6-12 months of life, correlated with reduced RTS,S/AS01E responses (r=-0·17 [-0·27 to -0·06]). This negative correlation was stronger for anti-CSP IgG than for the exposure signature or any other more immunogenic blood stage P falciparum antigens (r=-0·42 [-0·50 to -0·33]), persisted after adjustment by baseline levels of the exposure signature (semi-partial correlation r=-0·44 [-0·55 to -0·33]), and involved antibodies to the central NANP region (r=-0·39 [-0·49 to -0·28]) but not the C-terminal region (r=0·02 [-0·10 to 0·15]) of CSP. The negative effect of maternal anti-CSP IgG in infants did not appear to be confounded by other malaria transmission-dependent variables.

INTERPRETATION: Interference between passive immunity and vaccine response is clinically significant and might affect the implementation of next-generation CSP-based vaccines for young infants and mothers as well as passive immunisation with human monoclonal antibodies.

FUNDING: US National Institutes of Health, National Institute of Allergy and Infectious Diseases; PATH-Malaria Vaccine Initiative; Spanish Ministerio de Economía y Competitividad (Instituto de Salud Carlos III), European Regional Development Fund and European Social Fund; Fundación Ramón Areces; Spanish Ministry of Science and Innovation; and Generalitat de Catalunya (CERCA Program).

WEB: 10.1016/S1473-3099(24)00527-9
IMPACT FACTOR: 36.4
CITED HALF-LIFE: 4.4

START COMMENTARY

Interference of maternal anti-CSP IgG antibodies in vaccinated infants rather than malaria exposure was responsible for reduced immunogenicity of the RTS,S/AS01E in children younger than 5 months. Infants with very low or undetected maternal antibodies had vaccine responses similar to those of older children. The negative correlation between high maternal anti-CSP IgG at baseline and low vaccine immunogenicity was observed through 18 months post- primary vaccination in those immunized at 2 months of age. The impact was still noted after a booster dose, suggesting that maternal antibody interference with primary vaccination also influenced response to booster doses.

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11. An evaluation of the surveillance system for monitoring and reporting adverse events following immunization in Kebbi State, Northern Nigeria: a mixed method approach.

Omoleke S, de Kiev L.

BMC Public Health. 2024 Oct 22;24(1):2906.

PubMed ID: 39434046

ABSTRACT

INTRODUCTION: Despite the benefits of periodic evaluation of the vaccine safety surveillance system, no formal assessment, to our knowledge, has been conducted in Nigeria. Hence, this study evaluated the surveillance system for adverse events following immunization (AEFI) to ascertain the system's functionality to inform vaccine safety considerations and guide communication strategies for demand generation.

MATERIALS AND METHODS: The study employed a mixed-method approach. Survey questionnaires were administered to 274 routine immunization service providers in Kebbi State, Northern Nigeria, and data were analyzed descriptively using SPSS. In this study, 10 Key Informant Interviews and two Focus Group Discussions were conducted with senior officers and managers at sub-national and national levels within the immunization and surveillance landscape in Nigeria. The interview recordings were cleaned minimally, transcribed, and manually analyzed thematically. Finally, methodological triangulation was done to improve research rigor and provide a better understanding of the phenomena under investigation.

RESULTS: Of the respondents, 201(73.4%) reported that the surveillance system can inform vaccine safety considerations while 170(62%) reported that the AEFI surveillance system can determine the magnitude of AEFI within the population. Further, 173(63%) reported that the surveillance system can provide timely feedback about causality assessment. However, 158(58%) of the respondents stated that the surveillance system is competent in informing communication strategies to improve immunization demand. Triangulation was done which showed dissonance in AEFI surveillance and vaccine safety considerations but partial agreement in immunization demand generation. Further, AEFI surveillance system attributes' triangulation revealed agreements (convergence) on simplicity and timeliness; partial agreements on acceptability, data quality, sensitivity, flexibility, and completeness; dissonance on representativeness and silence on stability, indicating a sub-optimal performance of the AEFI surveillance system in the study setting. Finally, the study unearthed some underlying health system factors impeding the AEFI surveillance system from fully fulfilling its objectives.

CONCLUSION: The AEFI surveillance system in Northern Nigeria is well established but functioning sub-optimally. Based on the study findings, the capacity to provide information on vaccine safety

exists but it is not robust enough to generate sufficient and convincing vaccine safety data and guide communication strategies for vaccine demand generation, especially for new vaccines and those under emergency authorization use.

WEB: 10.1186/s12889-024-20356-5
IMPACT FACTOR: 3.5
CITED HALF-LIFE: 5.4

START COMMENTARY

Nearly all routine immunization service providers surveyed reported that the case definition for adverse events following immunization (AEFI) was simple to understand and that the surveillance system allows easy recording and timely data reporting (Table 2). Reasons suggested for poor documentation included workload, lack of understanding of the relevance of the data collected, lack of feedback or recognition, and time required to complete reports. There was consensus among interviewees that delayed detection, reporting, and transmission of AEFI data to the next administrative level was common and limited the usefulness of the current AEFI surveillance system.

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12. Effect of 10-valent pneumococcal conjugate vaccine on trends of pneumococcal meningitis in children under five years, Uganda, 2003-2022.

Nuwamanya Y, Ampeire I, Baganizi M, Atugonza R, Nsubuga F, Kwesiga B, et al.

BMC Infect Dis. 2024 Oct 22;24(1):1187.

PubMed ID: 39434021

ABSTRACT

BACKGROUND: Pneumococcal meningitis, a vaccine-preventable disease caused by Streptococcus pneumoniae (Spn) is the leading bacterial meningitis in under five children. In April 2014, Uganda introduced routine immunization with 10-valent Pneumococcal Conjugate Vaccine (PCV10) for infants. The target coverage for herd immunity is ≥ 90% with three doses (PCV10-dose 3). We assessed the effect of PCV10 introduction and coverage on the trends of pneumococcal meningitis in under five children.

METHODS: We analyzed laboratory-confirmed pediatric bacterial meningitis (PBM) data at two high-volume WHO-accredited sentinel surveillance hospitals in Kampala City and Gulu District, from 2003 to 2022. We used confirmed cases to estimate the minimum incidence of pneumococcal meningitis in the host districts and calculated annual incidence of pneumococcal meningitis per one million populations, and the proportion of confirmed PBM attributable to Spn. We divided the study period into 2003-2013 (pre-PCV10) and 2014-2022 (post-PCV10), and conducted interrupted time series analysis using autoregressive integrated moving average models for the effect of PCV10 on trends of pneumococcal meningitis and PBM attributable to Spn. We analyzed reported PCV10 data in DHIS2 from 2014 to 2022 for annual PCV10-dose 3 coverage.

RESULTS: Among the 534 confirmed PBM cases, 331(62%) were pneumococcal meningitis; 227(69%) from Gulu District and 104(31%) from Kampala City. The majority (95%) of the isolates were not serotyped. The majority (57%) were male and unimmunized (98%); median age = 14(IQR = 6-27) months with most (55%) aged ≥ 12 months. The case-fatality rate was 9%. During Pre-PCV10 period, the overall incidence of pneumococcal meningitis in the host districts increased; slope change = 1.0 (95%CI = 0.99999, 1.00001) but declined in post-PCV10 period (2014-2022) by 92% from 86 cases /1,000,000 in 2014 to 7/1,000,000 in 2022, slope change= -1.00006 (95%CI=-1.00033, -0.99979). Whereas there was an immediate decline in the proportion of confirmed PBM attributable to Spn in the host districts, level change=-1.84611(95%CI=-1.98365,-1.70856), an upward trend was recorded from 2016 to 2022, slope change = 1.0 (95%CI = 0.99997, 1.00003). During 2015-2022, PCV10-dose 3 coverage was largely > 90% for Gulu District and 52-72% for Kampala City.

CONCLUSION: The PCV10 routine immunization program reduced the incidence of pneumococcal meningitis in Kampala City and Gulu District. There was no effect on the confirmed PBM proportionately attributable to Spn. Kampala City persistently recorded PCV10-dose3 coverage < 90%. We recommend enhancing serotyping and periodic nasopharyngeal carriage surveys to ascertain the maximum vaccine effectiveness and monitor Spn serotypes, and strengthening routine immunization in Kampala City.

WEB: 10.1186/s12879-024-10075-y
IMPACT FACTOR: 3.4
CITED HALF-LIFE: 4.9

START COMMENTARY

Only 5% of pediatric bacterial meningitis (PBM)-causing streptococcal pneumococcal (Spn) isolates were serotyped and some years had no serotyped isolates. Increased serotyping rates for Spn PBM isolates are necessary to determine if serotype replacement by non-PCV10 Spn serotypes is causing PBM. Authors recommend a nasopharyngeal carriage survey for Spn to assess the impact of PCV10 in reducing pneumococcal carriage and to assess the distribution of serotypes in the population, which could be used to determine effective PCV vaccine formulations and schedules.
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13. A prospective, multicenter study of hepatitis B birth-dose vaccine with or without hepatitis B immunoglobulin in preventing mother-to-child transmission of hepatitis B virus in Ethiopia.

Arefaine M, Johannessen A, Teklehaymanot T, Mihret A, Alemayehu D, Osman M, et al.
Vaccine. 2024 Oct 19;42(26):126461.
PubMed ID: 39426287

ABSTRACT

BACKGROUND: Historically, mother-to-child transmission (MTCT) of hepatitis B virus (HBV) was considered uncommon in Africa, leading to a reluctant attitude to birth-dose HBV vaccination on the continent. As a randomized trial would be unethical, real-life data are needed to assess the effect of HBV birth-dose vaccine in Africa.

METHODS: A multicenter, prospective, observational study of hepatitis B surface antigen (HBsAg)-positive pregnant women and their infants was carried out in Ethiopia, from January 2019 to May 2021. Pregnant women were screened for HBsAg and HIV as part of routine antenatal care and/or delivery, and HBsAg-positive HIV-negative pregnant women were included in the study. HBV birth-dose vaccine and hepatitis B immunoglobulin (HBIg) were recommended but not all newborns received it as it was not national policy. All infants, however, received the pentavalent HBV vaccine at 6, 10, and 14 weeks of age. Vaccination status was confirmed from delivery ward charts and infant vaccination certificates. Infants were tested for HBsAg at 9 months of age and a positive result was taken as evidence of MTCT.

FINDINGS: Of 290 HBsAg-positive pregnant women, 168 mother/infant pairs returned for their 9-month follow-up visit and were included in this analysis. Two of 112 (1.8 %) infants who received birth-dose vaccine with HBIg, and 2 of 23 (8.7 %) who received birth-dose vaccine alone were HBsAg positive at nine months of age, compared to 8 of 33 (24.2 %) who received neither vaccine nor HBIg at birth (p = 0.002). High maternal viral load (>200,000 IU/ml; adjusted odds ratio [AOR] 10.4; 95 % confidence interval [CI] 1.2-92.1) and not receiving HBV birth-dose vaccine nor HBIg (AOR 29.2; 95 % CI 4.0-211.3) were independent predictors of MTCT.

INTERPRETATION: Birth-dose HBV vaccine with or without HBIg significantly reduced the risk of MTCT of HBV in Ethiopia. Improved coverage of birth-dose HBV vaccine should be an urgent priority.

WEB: 10.1016/j.vaccine.2024.126461
IMPACT FACTOR: 4.5
CITED HALF-LIFE: 7.9

START COMMENTARY

The risk of mother to child transmission (MTCT) was lower, but not significantly so, in infants receiving birth-dose hepatitis B vaccine and hepatitis B immunoglobin when compared to those receiving only the birth dose vaccine. Larger studies are needed as the lack of statistical significance may have been due to low numbers in the birth dose only group. Limitations include lack of whole genome testing to verify that HBV transmission was the result of MTCT and loss to follow-up due to COVID-19 restrictions.

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14. Safety of hepatitis E vaccine in pregnancy: an emulated target trial following a mass reactive vaccination campaign in Bentiu internally displaced persons camp, South Sudan.

Nesbitt R, Azman A, Asilaza V, Edwards J, Gitahi P, Nkemenang P, et al.

Lancet Glob Health. 2024 Oct 18;12(11):e1881-e1890.
PubMed ID: 39424575

ABSTRACT

BACKGROUND: Epidemic forms of hepatitis E cause high mortality among pregnant people, with case fatality risks over 30% and adverse fetal outcomes. In 2022, the first mass reactive vaccination campaign against hepatitis E was conducted in South Sudan with the HEV239 vaccine. We aimed to assess whether vaccination against hepatitis E in pregnancy increases the risk of fetal loss in a cohort of vaccinated and unvaccinated pregnant people.

METHODS: In this emulated target trial, an exhaustive pregnancy census was conducted in Bentiu internally displaced persons camp after the second of three vaccination rounds. Women and girls aged 14-45 years with no current jaundice or acute illness were eligible for participation. Individuals who consented were revisited 28 days after their delivery date to document the pregnancy outcome. We used an emulated target trial framework to address biases inherent in observational studies. We matched vaccinated to unvaccinated participants on age, gestational age, and vaccination propensity score and estimated cumulative incidence functions for fetal loss in vaccinated compared to unvaccinated women in a competing risks framework using the Aalen-Johansen estimator.

FINDINGS: Between May 16 and June 30, 2022, 3421 participants were enrolled and followed up for inclusion in analysis. Among 2741 women who had a pregnancy outcome after the start of the vaccination campaign, 67 (2·4%) were vaccinated before conception, 2036 (74·3%) were vaccinated during pregnancy, and 638 (23·2%) were not vaccinated. Among the 2407 women retained in the matched analyses, the cumulative risk of fetal loss among individuals vaccinated during pregnancy was 7·2% (95% CI 5·6-8·7) compared with 6·1% (3·7-9·2) among unvaccinated individuals, implying a risk ratio of 1·2 (95% CI 0·7-1·9).

INTERPRETATION: No evidence of increased risk of fetal loss was found among individuals vaccinated during pregnancy.

FUNDING: Médecins Sans Frontières.

WEB: 10.1016/S2214-109X(24)00321-8
IMPACT FACTOR: 20.0
CITED HALF-LIFE: 4.3

START COMMENTARY

In a subanalysis of participants vaccinated in early pregnancy (<90 days gestation) vs matched controls, there was no evidence of increased risk for miscarriage (RR: 0.9, 95%CI: 0.5-1.9). However, pregnancy loss was determined through self-report, and early pregnancy loss is sometimes missed, so there may be an effect of vaccination on early miscarriage that was not detected by this study. There was no difference found in risk of fetal loss among those vaccinated prior to pregnancy and unvaccinated individuals.

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15. Update on Vaccine-Derived Poliovirus Outbreaks - Worldwide, January 2023-June 2024.

Namageyo-Funa A, Greene S, Henderson E, Traoré M, Shaukat S, Bigouette J, et al.

MMWR Morb Mortal Wkly Rep. 2024 Oct 17;73(41):909-916.

PubMed ID: 39418214

ABSTRACT

Circulating vaccine-derived polioviruses (cVDPVs) can emerge and lead to outbreaks of paralytic polio as well as asymptomatic transmission in communities with a high percentage of undervaccinated children. Using data from the World Health Organization Polio Information System and Global Polio Laboratory Network, this report describes global polio outbreaks due to cVDPVs during January 2023-June 2024 and updates previous reports. During the reporting period, 74 cVDPV outbreaks were detected in 39 countries or areas (countries), predominantly in Africa. Among these 74 cVDPV outbreaks, 47 (64%) were new outbreaks, detected in 30 (77%) of the 39 countries. Three countries reported cVDPV type 1 (cVDPV1) outbreaks and 38 countries reported cVDPV type 2 (cVDPV2) outbreaks; two of these countries reported cocirculating cVDPV1 and cVDPV2. In the 38 countries with cVDPV2 transmission, 70 distinct outbreaks were reported. In 15 countries, cVDPV transmission has lasted >1 year into 2024. In Nigeria and Somalia, both countries with security-compromised areas, persistent cVDPV2 transmission has spread to neighboring countries. Delayed implementation of outbreak response campaigns and low-quality campaigns have resulted in further international spread. Countries can control cVDPV outbreaks with timely allocation of resources to implement prompt, high-quality responses after outbreak confirmation. Stopping all cVDPV transmission requires effectively increasing population immunity by overcoming barriers to reaching children.

WEB: 10.15585/mmwr.mm7341a1

IMPACT FACTOR: 21.0

CITED HALF-LIFE: 3.6

START COMMENTARY

The World Health Organization (WHO) has recommended use of novel oral poliovirus vaccine type 2 (nOPV2) since 2021 because it has less risk of reversion to neurovirulence than other available OPV2 vaccines. However, nOPV2 was linked to 29 outbreaks of circulating vaccine-derived poliovirus 2 (cVDPV2) in 19 countries, causing 113 acute flaccid paralysis (AFP) cases in 14 countries. Outbreaks in 5 countries were only detected in environmental surveillance with no identified cases of AFP. No new countries have reported cVDPV1 emergences or outbreaks since 2022.

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Additional Articles of Interest

1 Lot quality assurance sampling for coverage evaluation of a new vaccine: A pilot study. {Full Article}
2 Global vaccination against hepatitis E virus: position paper from the ESGVH-ESCMID. {Full Article}
3 DECENTRALIZED IMMUNIZATION MONITORING: LESSONS LEARNED FROM FOUR STATES - NIGERIA. {Full Article}
4 New pedagogical tools for vaccine education: preparing future healthcare workers for the next pandemic. {Full Article}
5 A highly immunogenic UVC inactivated Sabin based polio vaccine. {Full Article}
6 Machine learning algorithms for prediction of measles one vaccination dropout among 12-23 months children in Ethiopia. {Full Article}
7 Report from the World Health Organization's immunization and vaccines-related implementation research advisory committee (IVIR-AC) meeting, virtual gathering, 10-13 September 2024. {Full Article}
8 Assessing yellow fever outbreak potential and implications for vaccine strategy. {Full Article}
9 Trends of the second measles vaccine (MCV2) over time after its launch as part of routine immunization in Nigeria: a brief research report. {Full Article}
10 Immunization in women's lives: present and future. {Full Article}
11 Leveraging single-dose human papillomavirus vaccination dose-efficiency to attain cervical cancer elimination in resource-constrained settings. {Full Article}
12 Acceptability of single-dose HPV vaccination schedule among health-care professionals in Kenya: a mixed-methods study. {Full Article}
13 Inequalities in measles immunization coverage among two-year-olds in Sierra Leone, 2008-2019. {Full Article}
14 Towards contextualized complex systems approaches to scaling-up hepatitis B birth-dose vaccination in the African region: a qualitative systematic review. {Full Article}
15 AI based predictive acceptability model for effective vaccine delivery in healthcare systems. {Full Article}
16 The Surge in Human Papillomavirus Vaccine Rejection in Nigeria. {Full Article}
17 Multi-level determinants of timely routine childhood vaccinations in The Gambia: Findings from a nationwide analysis. {Full Article}
18 Burden of Lassa fever disease in pregnant women and children and options for prevention. {Full Article}
19 Cost of integrated immunization campaigns in Nigeria and Sierra Leone: bottom-up costing studies. {Full Article}

20 RTS, S malaria vaccination among children aged 24-59 months in the Sunyani Municipality, Ghana; 2023. {Full Article}

21 Knowledge and acceptability of the human papillomavirus vaccine and associated factors among adolescent girls in public primary schools in Dessie Town, South Wollo, Northeast Ethiopia, 2020: A cross-sectional study. {Full Article}

22 Chikungunya vaccine development, challenges, and pathway toward public health impact. {Full Article}

23 Navigating vaccine procurement and financing challenges in Cameroon: Insights and recommendations from a mixed-methods study (2015-2020). {Full Article}

24 Identifying the zero-dose and under-immunized children in Bangladesh: Approaches and experiences. {Full Article}

25 Improving the last mile delivery of vaccines through an informed push model: Experiences, opportunities and costs based on an implementation study in a rural district in Uganda. {Full Article}

26 Prevalence of caregiver hesitancy for vaccinations in children and its associated factors: A systematic review and meta-analysis. {Full Article}

27 Estimating Influenza Illnesses Averted by Year-Round and Seasonal Campaign Vaccination for Young Children, Kenya. {Full Article}

28 Advancing Immunization in Africa: Overcoming Challenges to Achieve the 2030 Global Immunization Targets. {Full Article}

29 Health Facility Capacity and Health-care Worker Knowledge, Attitudes, and Practices of Hepatitis B Vaccine Birth-dose and Maternal Tetanus-Diphtheria Vaccine Administration in Nigeria: A Baseline Assessment. {Full Article}

30 Factors influencing vaccination up-take among nomadic population in four regions of Ghana: a qualitative study. {Full Article}

31 Political engagement: a key pillar in revitalisation of polio and routine immunisation programmes in the Democratic Republic of the Congo. {Full Article}

32 Modelling the spatial variability and uncertainty for under-vaccination and zero-dose children in fragile settings. {Full Article}

33 Assessments of effectiveness of technologies utilizations in VIHSCM among selected health facilities in Tanzania mainland. {Full Article}

Appendix

The literature search for the December 2024 Vaccine Delivery Research Digest was conducted on November 23, 2024. We searched English language articles indexed by the US National Library of Medicine and published between October 15, 2024 and November 14, 2024. The search resulted in 552 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 2024/10/15:2024/11/14[Date - Publication]