VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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JUNE 2024

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{Abstract & START Commentary} {Full Article}

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{Abstract & START Commentary} {Full Article}

- Implementation and delivery strategies for malaria vaccines in sub-Saharan African countries were assessed through analysis of available national malaria policies and guidelines.

13 Comparison of Wealth-Related Inequality in Tetanus Vaccination Coverage before and during Pregnancy: A Cross-Sectional Analysis of 72 Low- and Middle-Income Countries.

{Abstract & START Commentary} {Full Article}

- Inequalities in maternal tetanus toxoid containing vaccination (TTCV) coverage before and during pregnancy, and at birth were analyzed for 72 low- and middle-income countries using data from the Demographic and Health Survey or Multiple Indicator Cluster Survey from 2013-2022.

14 Prevalence of and factors associated with zero-dose and under-immunized children in selected areas of Bangladesh: Findings from Lot Quality Assurance Sampling Survey.

{Abstract & START Commentary} {Full Article}

- The factors associated with children being zero-dose (ZD) or under-immunized (UI) were examined in selected geographical locations in Bangladesh with a high prevalence of ZD and UI children.

15 Safety and immunogenicity of the Euvichol-S oral cholera vaccine for prevention of Vibrio cholerae O1 infection in Nepal: an observer-blind, active-controlled, randomised, non-inferiority, phase 3 trial.

{Abstract & START Commentary} {Full Article}

- The safety and immunogenicity of the Euvichol-S cholera vaccine was compared with the Shanchol cholera vaccine in this non-inferiority trial in Nepal.

Appendix

Details of Articles

1. Perceptions of yellow fever emergency mass vaccinations among vulnerable groups in Uganda: A qualitative study.

Huebl L, Nnyombi A, Kihumuro A, Lukwago D, Walakira E, Kutalek R.

PLoS Negl Trop Dis. 2024 May 23;18(5):e0012173.
PubMed ID: 38739650

ABSTRACT

BACKGROUND: Yellow fever (YF), a mosquito-borne viral hemorrhagic fever, is endemic in Uganda and causes frequent outbreaks. A total of 1.6 million people were vaccinated during emergency mass immunization campaigns in 2011 and 2016. This study explored local perceptions of YF emergency mass immunization among vulnerable groups to inform future vaccination campaigns.

METHODOLOGY: In this qualitative study, we conducted 43 semi-structured interviews, 4 focus group discussions, and 10 expert interviews with 76 participants. Data were collected in six affected districts with emergency mass vaccination. We included vulnerable groups (people ≥ 65 years and pregnant women) who are typically excluded from YF vaccination except during mass immunization. Data analysis was conducted using grounded theory. Inductive coding was utilized, progressing through open, axial, and selective coding.

PRINCIPAL FINDINGS: Participants relied on community sources for information about the YF mass vaccination. Information was disseminated door-to-door, in community spaces, during religious gatherings, and on the radio. However, most respondents had no knowledge of the vaccine, and it was unclear to them whether a booster dose was required. In addition, the simultaneous presidential election during the mass vaccination campaign led to suspicion and resistance to vaccination. The lack of reliable and trustworthy information and the politicization of vaccination campaigns reinforced mistrust of YF vaccines.

CONCLUSIONS/SIGNIFICANCE: People in remote areas affected by YF outbreaks rely on community sources of information. We therefore recommend improving health education, communication, and engagement through respected and trusted community members. Vaccination campaigns can never be seen as detached from political systems and power relations.

WEB: 10.1371/journal.pntd.0012173
IMPACT FACTOR: 3.8
CITED HALF-LIFE: 5.9

START COMMENTARY

The authors queried vaccinated individuals about the information they received during two yellow fever (YF) mass immunization campaigns in Uganda. They found that access to information differed depending on where participants lived, with those in rural areas relying heavily on local health care workers and peers for information as they did not have access to information from radio or electronic communication. Some participants were motivated by receiving an expensive vaccination for free that was required for travel. The importance of political factors was highlighted by interviewees sharing that some opposition members did not want to carry YF vaccination cards because they were yellow, a color associated with the ruling party. While reasons for vaccine refusal could not be determined because only vaccinated individuals were included in the study, it was noted that there was heightened suspicion of the YF vaccination campaign in one community as it was the first time adults were being targeted in a mass vaccination campaign, communication about the purpose of the campaign was not sufficient, and it was conducted soon after a mass polio campaign had been completed among children, leading to rumors that the purpose of the YF campaign was to harm community members.

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2. "I'll take them another day": A qualitative study exploring the socio-behavioral complexities of childhood vaccination in urban poor settlements.

Gichuki J, Ngoye B, Wafula F.

PLoS One. 2024 May 13;19(5):e0303215.

PubMed ID: 38739597

ABSTRACT

Despite improvement over recent decades, childhood vaccination uptake remains a concern across countries. The World Health Organization observed that over 25 million children missed out on one or more vaccines in 2021, with urban poor and other marginalized groups being the most affected. Given the higher risk of disease transmission and vaccine-preventable diseases (VPD) outbreaks across densely populated urban slums, identifying effective interventions to improve childhood vaccination in this vulnerable population is crucial. This study explored the behavioral and social factors influencing childhood vaccination uptake in urban informal settlements in Nairobi, Kenya. A grounded theory approach was employed to develop a theoretical account of the socio-behavioral determinants of childhood vaccination. Five focus group discussions (FGDs) were conducted with purposively sampled caregivers of children under five years of age residing in informal settlements. The Theory of Planned Behavior guided the structuring of the FGD questions. An iterative process was used to analyze and identify emerging themes. Thirty-nine caregivers (median age 29 years) participated in the FGDs. From the analysis, four main thematic categories were derived. These included attitude factors such as perceived vaccine benefits, cultural beliefs, and emotional factors including parental love. Additionally, subjective norms, like fear of social judgment, and perceived behavioral control factors, such as self-control and gender-based influences, were identified. Furthermore, a number of practical factors, including the cost of vaccines and healthcare providers attitude, also affected the uptake of vaccination. Various social, behavioral, cultural, and contextual factors influence caregiver vaccination decisions in urban poor settings. Community-derived and context-specific approaches that address the complex interaction between socio-behavioral and other contextual factors need to be tested and applied to improve the timely uptake of childhood vaccinations among marginalized populations.

WEB: 10.1371/journal.pone.0303215

IMPACT FACTOR: 3.7

CITED HALF-LIFE: 7.3

START COMMENTARY

Participating caregivers were identified and recruited by community health volunteers guided by research objectives to include individuals with a range of perspectives and experiences and included

caregivers with children who were up to date on vaccinations and those with delayed vaccination. Identified themes and subthemes are found in Table 2. All interviewees had basic knowledge of the ability of vaccinations to prevent disease. One barrier to timely vaccination expressed by caregivers was fear that providers would judge them for their children being poorly dressed or underweight, highlighting the need for positive interactions with health care workers to increase vaccination rates.
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3. Incomplete immunization uptake and associated factors among children aged 12-23 months in sub-Saharan African countries; multilevel analysis evidenced from latest demography and health survey data, 2023.

Tsegaw T, Alemaw H, Wale Y, Nigatu S, Birhan T, Taddese A.

Ital J Pediatr. 2024 May 12;50(1):96.

PubMed ID: 38735946

ABSTRACT

BACKGROUND: In 1974, the World Health Organization (WHO) established the Expanded Program on Immunization to control vaccine-preventable diseases, saving millions of lives annually. However, the coverage of basic vaccines recommended by the WHO in Africa was only 75%, which fell short of the goal of 90% by 2015. To formulate effective policies and implementation programs to reduce incomplete vaccination rates, it is important to conduct a study to determine the factors contributing to incomplete immunization among children aged 12-23 months.

METHODS: The study was conducted in 16 sub-Saharan African countries, using data extracted from the latest DHS data. It was a community-based cross-sectional survey that used two-stage stratified probability sampling sample designs. The vaccination coverage was assessed using vaccination cards and mother recalls. Multilevel multivariable logistic regression was used to determine the extent of incomplete immunization and the individual and community-level factors associated with partial immunization among children aged 12-23 months. Variables with a p-value less than 0.05 were considered statistically significant predictors of incomplete immunization.

RESULT: A total of 35, 193 weighted samples were used to determine the pooled prevalence of partial immunization. The pooled prevalence of incomplete immunization was 36.06%. In the final model factors significantly associated were: being uneducated mother(AOR:1.75;95%CI:1.48,2.05), being an unemployed mother (AOR:1.16;95%CI:1.09,1.23), no history of family planning utilization (AOR: 1.71; 95% CI: 1.61, 1.84), non-antenatal care (AOR: 1.79; 95% CI: 1.58, 2.04), non-postnatal care (AOR: 1.25; 95%CI: 1.17, 1.35), rural residence(AOR:1.50;95%CI:1.37,1.63), home delivery (AOR: 2.04; 95%CI:1.89, 2.21), having children more than five (AOR: 1.56; 95%CI: 1.13, 2.17), and non-utilization of health insurance (AOR: 1.74; 95%CI: 1.48, 2.05).

CONCLUSION: The pooled prevalence of incomplete immunization was found to be high in this investigation. Based on the findings of the study we recommended that policymakers and stakeholders prioritize enhancing prenatal and postnatal care, contraception, and reducing home birth rates to minimize the rate of incomplete immunization.

WEB: 10.1186/s13052-024-01642-9

IMPACT FACTOR: 3.6

CITED HALF-LIFE: 4.1

START COMMENTARY

In this study, children were considered fully immunized if they had received one dose of BCG vaccine, three doses of DPT vaccine, three doses of polio vaccine, and one dose of measles-containing vaccine by the age of 12 months. Individual factors evaluated were age, marital status, education level, and employment status of the mother, family socioeconomic status, antenatal care, place of delivery, parity, and use of family planning. Community factors evaluated were place of residence and media exposure. Variation in immunization rates was high within and between countries. Accessing antenatal and postnatal healthcare was associated with higher immunization rates among children.

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4. Urgent considerations for booster vaccination strategies against Ebola virus disease.

Adriaensen W, Oostvogels S, Levy Y, Leigh B, Kavunga-Membo H, Watson-Jones D.

Lancet Infect Dis. 2024 May 11.

PubMed ID: 38734010

ABSTRACT

With two endorsed and prophylactic vaccines against Zaire ebolavirus (referred to hereafter as EBOV), the number of individuals vaccinated against EBOV worldwide is estimated to range between 500 000 and 1 000 000 individuals, increasing with every renewed EBOV threat and vaccination campaign. Therefore, re-exposure of previously vaccinated health-care workers, and possibly community members, could become more frequent. In the absence of long-term data on vaccine efficacy and duration of protection, we urgently need to understand revaccination strategies that could maximise the level of protection. In this Personal View, we highlight the scarcity of available evidence to guide revaccination recommendations for the accumulating groups of previously vaccinated communities or front-line health-care workers that could be redeployed or re-exposed in the next EBOV outbreak(s). This evidence base is crucial to identify optimal target populations and the frequency of booster doses, and guide vaccine interchangeability (especially in settings with limited or unpredictable vaccine supplies), while preventing vaccine mistrust, equity concerns, and exclusion of vulnerable populations. We discuss five priority gaps (to whom, when, and how frequently, to provide booster doses; long-term correlates and thresholds of protection; the effect of vector-directed immunity and viral variant protection; comparative research in mix-and-match schedules; and implementation concerns) that should be urgently tackled to adapt the initial EBOV prophylactic vaccination strategies considering potential booster dose vaccinations.

WEB: 10.1016/S1473-3099(24)00210-X

IMPACT FACTOR: 56.3

CITED HALF-LIFE: 3.7

START COMMENTARY

Adriaensen et al. provide an overview of gaps in understanding of ebolavirus prophylactic vaccine long-term efficacy and discuss considerations for future vaccine strategies. They provide a brief description of the two vaccines that have been licensed and highlight two ongoing studies – EBO-BOOST trial and PREVAC-UP study - that will provide information on the durability of immune response and booster timing. Given that choice of booster vaccine may be dependent which vaccine is available, they call for research into the safety and immunogenicity of mixed-dose schedules.

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5. Probable extinction of influenza B/Yamagata and its public health implications: a systematic literature review and assessment of global surveillance databases.

Caini S, Meijer A, Nunes M, Henaff L, Zounon M, Boudewijns B, et al.

Lancet Microbe. 2024 May 10.

PubMed ID: 38729197

ABSTRACT

Early after the start of the COVID-19 pandemic, the detection of influenza B/Yamagata cases decreased globally. Given the potential public health implications of this decline, in this Review, we systematically analysed data on influenza B/Yamagata virus circulation (for 2020-23) from multiple complementary sources of information. We identified relevant articles published in PubMed and Embase, and data from the FluNet, Global Initiative on Sharing All Influenza Data, and GenBank databases, webpages of respiratory virus surveillance systems from countries worldwide, and the Global Influenza Hospital Surveillance Network. A progressive decline of influenza B/Yamagata detections was reported across all sources, in absolute terms (total number of cases), as positivity rate, and as a proportion of influenza B detections. Sporadically reported influenza B/Yamagata cases since March, 2020 were mostly vaccine-derived, attributed to data entry errors, or have yet to be definitively confirmed. The likelihood of extinction necessitates a rapid response in terms of reassessing the composition of influenza vaccines, enhanced surveillance for B/Yamagata, and a possible change in the biosafety level when handling B/Yamagata viruses in laboratories.

WEB: 10.1016/S2666-5247(24)00066-1

IMPACT FACTOR: 38.2

CITED HALF-LIFE: 1.6

START COMMENTARY

Due to current evidence of low viral circulation of B/Yamagata influenza cases, Caini et al. call for the investigation of all identified B/Yamagata influenza cases to determine whether they are vaccine-derived as the result of live attenuated influenza vaccination or if they are wild-type. They also suggest that a greater proportion of influenza B virus cases undergo genomic sequencing to determine their lineage (B/Victoria or B/Yamagata). A key limitation of this study is that regions of southeast Asia and Africa are under-represented in the available data, and these areas tend to have a higher circulation of influenza B.

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6. Measles Vaccine Coverage and Disease Outbreaks: A Systematic Review of the Early Impact of COVID-19 in Low and Lower-Middle Income Countries.

Packham A, Taylor A, Karangwa M, Sherry E, Muvunyi C, Green C.

Int J Public Health. 2024 May 10;69:1606997.

PubMed ID: 38725903

ABSTRACT

Objectives: We aimed to evaluate changes to measles-containing vaccine (MCV) provision and subsequent measles disease cases in low- and lower-middle income countries (LICs, LMICs) in relation to the COVID-19 pandemic. Methods: A systematic search was conducted of MEDLINE, OVID EMBASE and PubMed records. Primary quantitative and qualitative research studies published from January 2020 were included if they reported on COVID-19 impact on MCV provision and/or measles outbreak rates within LICs and LMICs. Results: 45 studies were included. The change in MCV1 vaccination coverage in national and international regions ranged -13% to +44.4% from pre-COVID time periods. In local regions, the median MCV1 and overall EPI rate changed by -23.3% and -28.5% respectively. Median MCV2 rate was disproportionally impacted in local areas during COVID-interruption time-periods (-48.2%) with ongoing disruption in early-recovery time-periods (-17.7%). 8.9% of studies reported on vaccination status of confirmed measles cases; from these, 71%-91% had received no MCV dose. Conclusion: MCV vaccination coverage experienced ongoing disruption during the recovery periods after initial COVID-19 disruption. Vaccination in local area datasets notably experienced longer-term disruption compared to nationally reported figures.

WEB: 10.3389/ijph.2024.1606997

IMPACT FACTOR: 4.6

CITED HALF-LIFE: 6.0

START COMMENTARY

This study found that the impact of the COVID-19 pandemic on measles outbreaks and measles vaccine coverage varied widely by country. While some results were described for time periods designated as pre-COVID, COVID-interruption, early-recovery, and late-recovery time periods, these time periods were not defined consistently in the articles included in the review (Supplementary Appendix S5), making it difficult to draw any conclusions about time periods based on reported results. Successful methods used to improve measles vaccination coverage during the pandemic was mentioned, including Nepal's use of triangulated surveillance data of simultaneous outbreaks of COVID-19 and measles to guide a vaccination campaign.

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7. Acceptability of an Incentivized Peer Referral Intervention to Address COVID-19 Vaccine Hesitancy Among Adults in Yopougon-Est, Côte d'Ivoire.

Thanel K, Pedersen B, Albert Y, Ouattara M, Gbeke D, Ranebennur V, et al.

Glob Health Sci Pract. 2024 May 09.

PubMed ID: 38724197

ABSTRACT

INTRODUCTION: Vaccine hesitancy persists as a barrier to vaccine uptake among adults across geographies. We pilot-tested an incentivized peer referral intervention in Yopougon-Est, Côte d'Ivoire, to encourage adults who recently received COVID-19 vaccination to discuss their experiences and motivate family and friends to seek vaccination.

IMPLEMENTATION: From May through June 2023, the intervention operated at 2 vaccination sites, where staff approached individuals immediately after receiving COVID-19 vaccination. Interested vaccine recipients received up to 9 referral coupons to distribute among their social circles, with a small financial incentive (approximately US$3) offered for each person they referred who returned to 1 of the 2 sites for COVID-19 vaccination.

METHODS: We collected data on numbers of people vaccinated and coupons returned. Qualitative interviews were conducted with 40 referred vaccine recipients and 7 public health officials.

RESULTS: During the 6-week intervention, 450 newly vaccinated individuals were offered the opportunity to enroll, with 197 opting to distribute coupons. Nearly half (45%) of these peer mobilizers who distributed coupons referred at least 1 person who subsequently came in for vaccination, and most of this subset had 2 or more completed referrals. Qualitative findings revealed that coupons served as effective reminders, sparking discussions within social networks and prompting vaccine-seeking behavior. According to the referred vaccine recipients, hearing about their peers' vaccination experience influenced uptake. Vaccine recipients and public health officials found the small referral incentive acceptable. Officials noted the intervention's potential utility and cost effectiveness, suggesting possible sustainability.

CONCLUSION: This incentivized peer referral intervention, capitalizing on peer networks and social norms, holds promise for increasing vaccine uptake in Yopougon-Est and potentially in other vaccination contexts globally. Practitioners can leverage the implementation guide and training materials we developed to replicate the intervention at larger scale and assess impact on vaccination trends.

WEB: 10.9745/GHSP-D-23-00468

IMPACT FACTOR: 4.0

CITED HALF-LIFE: 4.5

START COMMENTARY

Overall, 399 individuals came to the clinics with coupons during the 8-week trial. Figure 4 is a diagram of intervention participation and vaccination referral coupons that were returned. By the fourth week, more individuals who came to the clinic for the COVID-19 vaccine were referred by peers than came independently. Among the referred peers, more than 1/3 were receiving their first dose of the vaccine. Authors note that this type of intervention may be especially effective for vaccination programs targeting adults such as influenza and human papillomavirus vaccination programs.

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8. Genotypic analysis of RTS,S/AS01E malaria vaccine efficacy against parasite infection as a function of dosage regimen and baseline malaria infection status in children aged 5-17 months in Ghana and Kenya: a longitudinal phase 2b randomised controlled trial.

Juraska M, Early A, Li L, Schaffner S, Lievens M, Khorgade A, et al.

Lancet Infect Dis. 2024 May 09.

PubMed ID: 38723650

ABSTRACT

BACKGROUND: The first licensed malaria vaccine, RTS,S/AS01E, confers moderate protection against symptomatic disease. Because many malaria infections are asymptomatic, we conducted a large-scale longitudinal parasite genotyping study of samples from a clinical trial exploring how vaccine dosing regimen affects vaccine efficacy.

METHODS: Between Sept 28, 2017, and Sept 25, 2018, 1500 children aged 5-17 months were randomly assigned (1:1:1:1:1) to receive four different RTS,S/AS01E regimens or a rabies control vaccine in a phase 2b open-label clinical trial in Ghana and Kenya. Participants in the four RTS,S groups received two full doses at month 0 and month 1 and either full doses at month 2 and month 20 (group R012-20); full doses at month 2, month 14, month 26, and month 38 (group R012-14); fractional doses at month 2, month 14, month 26, and month 38 (group Fx012-14; early fourth dose); or fractional doses at month 7, month 20, and month 32 (group Fx017-20; delayed third dose). We evaluated the time to the first new genotypically detected infection and the total number of new infections during two follow-up periods (12 months and 20 months) in more than 36 000 dried blood spot specimens from 1500 participants. To study vaccine effects on time to the first new infection, we defined vaccine efficacy as one minus the hazard ratio (HR; RTS,S vs control) of the first new infection. We performed a post-hoc analysis of vaccine efficacy based on malaria infection status at first vaccination and force of infection by month 2. This trial (MAL-095) is registered with ClinicalTrials.gov, NCT03281291.

FINDINGS: We observed significant and similar vaccine efficacy (25-43%; 95% CI union 9-53) against first new infection for all four RTS,S/AS01E regimens across both follow-up periods (12 months and 20 months). Each RTS,S/AS01E regimen significantly reduced the mean number of new infections in the 20-month follow-up period by 1·1-1·6 infections (95% CI union 0·6-2·1). Vaccine efficacy against first new infection was significantly higher in participants who were infected with malaria (68%; 95% CI 50-80) than in those who were uninfected (37%; 23-48) at the first vaccination (p=0·0053).

INTERPRETATION: All tested dosing regimens blocked some infections to a similar degree. Improved vaccine efficacy in participants infected during vaccination could suggest new strategies for highly efficacious malaria vaccine development and implementation.

FUNDING: GlaxoSmithKline Biologicals SA, PATH, Bill & Melinda Gates Foundation, and the German Federal Ministry of Education and Research.

WEB: 10.1016/S1473-3099(24)00179-8
IMPACT FACTOR: 56.3
CITED HALF-LIFE: 3.7

START COMMENTARY

While Juraska et al. found that all dosage regimens are efficacious and none is superior for the follow-up period overall, they note that genotypic outcomes suggest that a fractional dose regimen could be less protective than full dose regimens offered on the same schedule. Figure 3 shows the cumulative distribution function and vaccine effect on the mean number of new genotypic infections among vaccine groups and the control group and figure 4 shows the complexity of first new genotypic infections among the various vaccine groups when compared to the control group. Based on their findings, authors suggest future studies include genotype outcomes and that immune assays be used to gain an understand the mechanisms behind the protective effect.

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9. Identifying factors that can be used to assess a country's readiness to deploy a new vaccine or improve uptake of an underutilised vaccine: a scoping review.

Bhatt A, Monk V, Bhatti A, Eiden A, Hermany L, Hansen N, et al.

BMJ Open. 2024 May 08;14(5):e080370.
PubMed ID: 38719292

ABSTRACT

OBJECTIVES: Identifying whether a country is ready to deploy a new vaccine or improve uptake of an existing vaccine requires knowledge of a diverse range of interdependent, context-specific factors. This scoping review aims to identify common themes that emerge across articles, which include tools or guidance that can be used to establish whether a country is ready to deploy a new vaccine or increase uptake of an underutilised vaccine.

DESIGN: Scoping review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews guidelines.

DATA SOURCES: Embase, CINAHL, Cochrane Library, Google Scholar, MEDLINE, PsycINFO and Web of Science were searched for articles published until 9 September 2023. Relevant articles were also identified through expert opinion.

ELIGIBILITY CRITERIA: Articles published in any year or language that included tools or guidance to identify factors that influence a country's readiness to deploy a new or underutilised vaccine.

DATA EXTRACTION AND SYNTHESIS: Two independent reviewers screened records and performed data extraction. Findings were synthesised by conducting a thematic analysis.

RESULTS: 38 articles met our inclusion criteria; these documents were created using methodologies including expert review panels and Delphi surveys and varied in terms of content and context-of-use. 12 common themes were identified relevant to a country's readiness to deploy a new or underutilised vaccine. These themes were as follows: (1) legal, political and professional consensus; (2) sociocultural factors and communication; (3) policy, guidelines and regulations; (4) financing; (5) vaccine characteristics and supply logistics; (6) programme planning; (7) programme monitoring and evaluation; (8) sustainable and integrated healthcare provision; (9) safety surveillance and reporting; (10) disease burden and characteristics; (11) vaccination equity and (12) human resources and training of professionals.

CONCLUSIONS: This information has the potential to form the basis of a globally applicable evidence-based vaccine readiness assessment tool that can inform policy and immunisation programme decision-makers.

WEB: 10.1136/bmjopen-2023-080370

IMPACT FACTOR: 2.9

CITED HALF-LIFE: 4.0

START COMMENTARY

Although only two of the included documents included all twelve themes identified by Bhat et al. as critical for successful deployment of a new vaccine or increased uptake of an underutilized vaccine, each theme was identified in more than half of the documents. A full list of themes and subthemes that were identified can be found in Box 1.The most prominent theme identified was sociocultural factors and communication, which was identified in nearly all included documents, highlighting the importance of community engagement and culturally informed communication plans.

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10. Contribution of vaccination to improved survival and health: modelling 50 years of the Expanded Programme on Immunization.

Shattock A, Johnson H, Sim S, Carter A, Lambach P, Hutubessy R, et al.

Lancet. 2024 May 25;403(10441):2307-2316.

PubMed ID: 38705159

ABSTRACT

BACKGROUND: WHO, as requested by its member states, launched the Expanded Programme on Immunization (EPI) in 1974 to make life-saving vaccines available to all globally. To mark the 50-year anniversary of EPI, we sought to quantify the public health impact of vaccination globally since the programme's inception.

METHODS: In this modelling study, we used a suite of mathematical and statistical models to estimate the global and regional public health impact of 50 years of vaccination against 14 pathogens in EPI. For the modelled pathogens, we considered coverage of all routine and supplementary vaccines delivered since 1974 and estimated the mortality and morbidity averted for each age cohort relative to a hypothetical scenario of no historical vaccination. We then used these modelled outcomes to estimate the contribution of vaccination to globally declining infant and child mortality rates over this period.

FINDINGS: Since 1974, vaccination has averted 154 million deaths, including 146 million among children younger than 5 years of whom 101 million were infants younger than 1 year. For every death averted, 66 years of full health were gained on average, translating to 10·2 billion years of full health gained. We estimate that vaccination has accounted for 40% of the observed decline in global infant mortality, 52% in the African region. In 2024, a child younger than 10 years is 40% more likely to survive to their next birthday relative to a hypothetical scenario of no historical vaccination. Increased survival probability is observed even well into late adulthood.

INTERPRETATION: Since 1974 substantial gains in childhood survival have occurred in every global region. We estimate that EPI has provided the single greatest contribution to improved infant survival over the past 50 years. In the context of strengthening primary health care, our results show that equitable universal access to immunisation remains crucial to sustain health gains and continue to save future lives from preventable infectious mortality.

FUNDING: WHO.

WEB: 10.1016/S0140-6736(24)00850-X

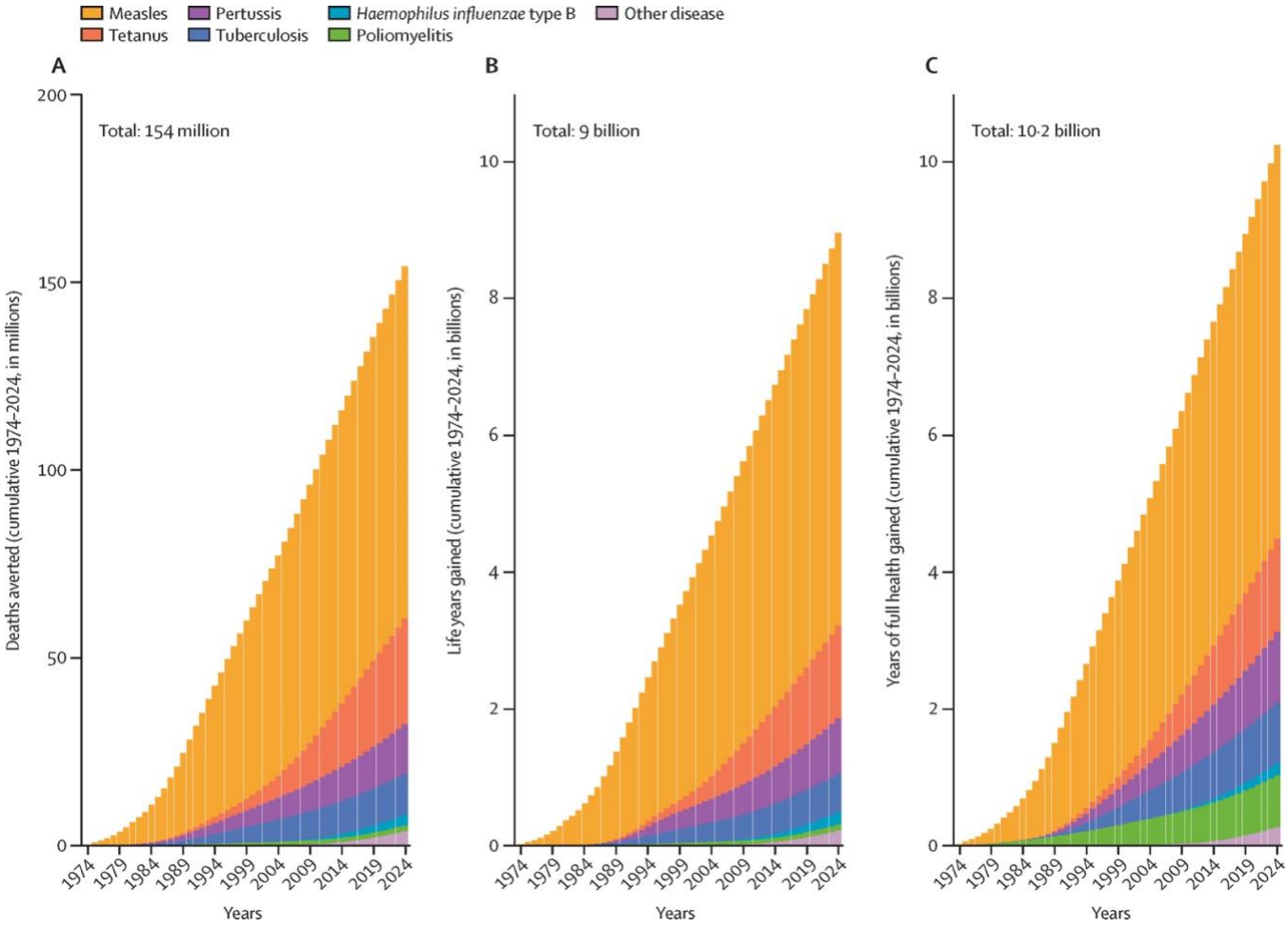
IMPACT FACTOR: 168.9

CITED HALF-LIFE: 6.9

START COMMENTARY

Figure 1 shows cumulative deaths averted, years of life saved, and years of full health gained due to vaccination. The impact of measles vaccination, seen in yellow, accounts for the greatest number of deaths averted (93.7 million), the most life years gained (5.7 billion), and the most years of full health gained (5.8 billion). The Eastern Mediterranean and African regions have seen the largest gains in life course survival probability due to vaccines over the last 50 years while the European region has seen the lowest absolute gains due to vaccines.

Figure 1: Deaths averted, years of life saved, and years of full health gained due to vaccination



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11. Exploring landscape of measles vaccination coverage: A step towards measles elimination goal in India.

Dhalaria P, Kumar P, Verma A, Priyadarshini P, Kumar Singh A, Tripathi B, et al.

Vaccine. 2024 Jun 05;42(17):3637-3646.
PubMed ID: 38704248

ABSTRACT

INTRODUCTION: Measles remains a critical public health concern causing significant morbidity and mortality globally. Despite the success of measles vaccination programs, challenges persist, particularly in India. This study investigates dose-wise measles vaccination coverage and explores gaps in immunization focusing on zero-dose, one-dose, and two-dose coverage among children aged 24-35 months.

DATA SOURCES AND METHODOLOGY: The National Family Health Survey 2019-21 (NFHS-5) served as the data source and the study analyzed information from 43,864 children aged 24-35 months. Sociodemographic variables such as birth order, wealth quintile, gender, social group, religion, residence, mother education, delivery-related factors, and media exposure were considered. Statistical analysis involved weighted estimates, chi-square tests, and multivariate multinomial logistic regression.

RESULTS: The study revealed that challenges persist in achieving optimal measles vaccination coverage. Analysis by sociodemographic factors highlighted disparities in coverage, with variations in zero dose prevalence across states and districts. The percentage of zero-dose children was significantly higher, with 11.5% of children in India remaining to receive any measles vaccination. Factors influencing vaccine coverage include birth order, age, wealth quintile, social group, religion, residence, maternal education, place of delivery, media exposure, and mode of delivery. The findings from the spatial analysis show the clustering of zero-dose children is high in the northeastern states of India.

DISCUSSION: Measles zero-dose children pose a significant obstacle to achieving elimination goals. Spatial analysis identifies clusters of unvaccinated populations guiding targeted interventions. The study aligns with global initiatives such as the Immunization Agenda 2030 emphasizing equitable vaccine access and discusses how India can tailor its strategies to achieve the goal. Lessons from polio eradication efforts inform strategies for measles elimination, stressing the importance of high-quality data and surveillance. The study underscores the urgency of addressing last-mile measles vaccination gaps in India. Spatially targeted interventions informed by sociodemographic factors can enhance immunization coverage. Achieving measles elimination requires sustained efforts and leveraging lessons from successful vaccination campaigns. The study

findings have the potential to contribute to informed decision-making, supporting India's roadmap for the measles and rubella elimination goal.

WEB: 10.1016/j.vaccine.2024.04.075
IMPACT FACTOR: 5.5
CITED HALF-LIFE: 7.2

START COMMENTARY

Dhalaria et al. found no significant differences in zero-dose prevalence based on sex or rural vs urban place of residence. Zero-dose was defined as having received no doses of measles-containing vaccine. Children who were 4th or higher birth order, those from the poorer wealth quintile, and those with mothers who had less education were more likely to be zero-dose. In addition to the 11.5% of children who had not received any measles vaccines nationwide, an additional 30% were partially vaccinated, having received only one of the two recommended doses. More than 30% of children were zero-dose in twenty-six districts, while some clusters of districts had low zero-dose prevalence (Figure 2).

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12. Policy uptake and implementation of the RTS,S/AS01 malaria vaccine in sub-Saharan African countries: status 2 years following the WHO recommendation.

Osoro C, Ochodo E, Kwambai T, Otieno J, Were L, Sagam C, et al.

BMJ Glob Health. 2024 Apr 30;9(4).

PubMed ID: 38688566

ABSTRACT

In October 2021, the WHO recommended the world's first malaria vaccine-RTS,S/AS01-to prevent malaria in children living in areas with moderate-to-high transmission in sub-Saharan Africa (SSA). A second malaria vaccine, R21/Matrix-M, was recommended for use in October 2023 and added to the WHO list of prequalified vaccines in December 2023. This study analysis assessed the country status of implementation and delivery strategies for RTS,S/AS01 by searching websites for national malaria policies, guidelines and related documents. Direct contact with individuals working in malaria programmes was made to obtain documents not publicly available. 10 countries had documents with information relating to malaria vaccine implementation, 7 referencing RTS,S/AS01 and 3 (Burkina Faso, Kenya and Nigeria) referencing RTS,S/AS01 and R21/Matrix-M. Five other countries reported plans for malaria vaccine roll-out without specifying which vaccine. Ghana, Kenya and Malawi, which piloted RTS,S/AS01, have now integrated the vaccine into routine immunisation services. Cameroon and Burkina Faso are the first countries outside the pilot countries to incorporate the vaccine into national immunisation services. Uganda plans a phased RTS,S/AS01 introduction, while Guinea plans to first pilot RTS,S/AS01 in five districts. The RTS,S/AS01 schedule varied by country, with the first dose administered at 5 or 6 months in all countries but the fourth dose at either 18, 22 or 24 months. SSA countries have shown widespread interest in rolling out the malaria vaccine, the Global Alliance for Vaccines and Immunization having approved financial support for 20 of 30 countries which applied as of March 2024. Limited availability of RTS,S/AS01 means that some approved countries will not receive the required doses. Vaccine availability and equity must be addressed even as R21/Matrix-M becomes available.

WEB: 10.1136/bmjgh-2023-014719
IMPACT FACTOR: 8.1
CITED HALF-LIFE: 2.7

START COMMENTARY

While there is widespread interest in introducing the malaria vaccine into national immunization programs, only 18 million doses of RTS,S/AS01 will be available between 2023 and 2025, and only 6 million doses of R21/Matrix-M vaccine are currently available, although Serum Institute projects production of 100-200 million doses annually in the future. Vaccine availability is a key concern as

demand will outweigh supply for at least the next few years. Gavi proposes to distribute available vaccines to countries with areas of high malaria parasite prevalence and high under-five all-cause mortality rates, while the World Health Organization has developed a framework for vaccine allocation which includes considerations for need, health impact, inclusiveness, and also considers of health system structure and function when making allocation decisions.

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13. Comparison of Wealth-Related Inequality in Tetanus Vaccination Coverage before and during Pregnancy: A Cross-Sectional Analysis of 72 Low- and Middle-Income Countries.

Johns N, Blumenberg C, Kirkby K, Allorant A, Costa F, Danovaro-Holliday M, et al.

Vaccines (Basel). 2024 May 18;12(4).

PubMed ID: 38675813

ABSTRACT

Immunization of pregnant women against tetanus is a key strategy for reducing tetanus morbidity and mortality while also achieving the goal of maternal and neonatal tetanus elimination. Despite substantial progress in improving newborn protection from tetanus at birth through maternal immunization, umbilical cord practices and sterilized and safe deliveries, inequitable gaps in protection remain. Notably, an infant's tetanus protection at birth is comprised of immunization received by the mother during and before the pregnancy (e.g., through childhood vaccination, booster doses, mass vaccination campaigns, or during prior pregnancies). In this work, we examine wealth-related inequalities in maternal tetanus toxoid containing vaccination coverage before pregnancy, during pregnancy, and at birth for 72 low- and middle-income countries with a recent Demographic and Health Survey or Multiple Indicator Cluster Survey (between 2013 and 2022). We summarize coverage levels and absolute and relative inequalities at each time point; compare the relative contributions of inequalities before and during pregnancy to inequalities at birth; and examine associations between inequalities and coverage levels. We present the findings for countries individually and on aggregate, by World Bank country income grouping, as well as by maternal and neonatal tetanus elimination status, finding that most of the inequality in tetanus immunization coverage at birth is introduced during pregnancy. Inequalities in coverage during pregnancy are most pronounced in low- and lower-middle-income countries, and even more so in countries which have not achieved maternal and neonatal tetanus elimination. These findings suggest that pregnancy is a key time of opportunity for equity-oriented interventions to improve maternal tetanus immunization coverage.

WEB: 10.3390/vaccines12040431

IMPACT FACTOR: 7.8

CITED HALF-LIFE: 1.6

START COMMENTARY

Johns et al. found that protection at birth (PAB) against tetanus for mothers and infants was primarily derived from tetanus toxoid-containing vaccines (TTCVs) delivered during pregnancy rather than through childhood vaccination programs in 66 of the 72 of low- and middle-income countries (LMICs) included in this study. During pregnancy, wealth-related inequalities in TTCV receipt increased for

half of these countries, which was likely due in part to unequal access to antenatal care. Programs that provide support for antenatal care are suggested, with an example given of the Safe Delivery Incentive Programme in Nepal that provided reimbursement for travel costs for delivery and free delivery care for all Nepali women, which resulted in increased prenatal care, tetanus vaccine uptake, and reduced wealth-related inequalities in TTCV receipt during pregnancy.

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14. Prevalence of and factors associated with zero-dose and under-immunized children in selected areas of Bangladesh: Findings from Lot Quality Assurance Sampling Survey.

Das H, Jannat Z, Fatema K, Momo J, Ali M, Alam N, et al.

Vaccine. 2024 Apr 27;42(13):3247-3256.
PubMed ID: 38627143

ABSTRACT

BACKGROUND: In the era of Gavi's 5.0 vision of "leaving no one behind with immunization", childhood routine vaccination in missed communities is considered as a priority concern. Despite having a success story at the national level, low uptake of immunization is still persistent in selected pocket areas of Bangladesh. However, prevalence and the associated factors of zero-dose (ZD) and under-immunization (UI) are still unknown at those geo-pockets of Bangladesh. Thus, the study aims to report and identify the factors associated with ZD and UI in selected geographical locations.

METHODS: This study used data from a Lot Quality Assurance Sampling (LQAS) survey where 504 households from 18 clusters of four hard to reach (HTR) and one urban slum were included. Caregivers of children aged 4.5 to 23 months were interviewed. Three outcome variables- ZD, UI and ZD/UI were considered and several related attributes were considered as independent variables. Data were analyzed through bivariate analysis, binary logistic regression and dominance analysis.

RESULTS: Overall, 32% of the children were either ZD (8%) or UI (26%) in the selected areas. The adjusted odds of ZD/UI for urban slum and haor (wetlands) areas were 5.62 and 3.61 respectively considering coastal areas as reference. However, distance of nearest EPI center, availability of EPI card, age of caregivers, education and occupation of mother and number of earning members in household were influential factors for ZD/UI. According to dominance analysis, availability of EPI card can explain the most of the variation of ZD/UI in this study.

CONCLUSION: The study findings highlight the high prevalence ZD/UI in certain geo-pockets of the country. It provided a powerful insight of current situation and associated factors in regards to ZD/UI in the country which will help policy-makers and programme managers in designing programmes to reduce missed communities in Bangladesh.

WEB: 10.1016/j.vaccine.2024.04.018
IMPACT FACTOR: 5.5
CITED HALF-LIFE: 7.2

START COMMENTARY

In discussing potential reasons for the reduced likelihood of being zero-dose or under-immunized (ZD/UI) among children who had an EPI card available, Das et al. mention that possession of accurate health documents can be considered a proxy for access to health facilities and positive perception of vaccination. After availability of the EPI card, distance from an EPI center and maternal education level were the most influential factors, with children living closer to an EPI center and with mothers with higher levels of education being more likely to have received vaccines.

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15. Safety and immunogenicity of the Euvichol-S oral cholera vaccine for prevention of Vibrio cholerae O1 infection in Nepal: an observer-blind, active-controlled, randomised, non-inferiority, phase 3 trial.

Song K, Chapagain R, Tamrakar D, Shrestha R, Kanodia P, Chaudhary S, et al.

Lancet Glob Health. 2024 Apr 15;12(5):e826-e837.

PubMed ID: 38614631

ABSTRACT

BACKGROUND: In October, 2017, WHO launched a strategy to eliminate cholera by 2030. A primary challenge in meeting this goal is the limited global supply capacity of oral cholera vaccine and the worsening of cholera outbreaks since 2021. To help address the current shortage of oral cholera vaccine, a WHO prequalified oral cholera vaccine, Euvichol-Plus was reformulated by reducing the number of components and inactivation methods. We aimed to evaluate the immunogenicity and safety of Euvichol-S (EuBiologics, Seoul, South Korea) compared with an active control vaccine, Shanchol (Sanofi Healthcare India, Telangana, India) in participants of various ages in Nepal.

METHODS: We did an observer-blind, active-controlled, randomised, non-inferiority, phase 3 trial at four hospitals in Nepal. Eligible participants were healthy individuals aged 1-40 years without a history of cholera vaccination. Individuals with a history of hypersensitivity reactions to other preventive vaccines, severe chronic disease, previous cholera vaccination, receipt of blood or blood-derived products in the past 3 months or other vaccine within 4 weeks before enrolment, and pregnant or lactating women were excluded. Participants were randomly assigned (1:1:1:1) by block randomisation (block sizes of two, four, six, or eight) to one of four groups (groups A-D); groups C and D were stratified by age (1-5, 6-17, and 18-40 years). Participants in groups A-C were assigned to receive two 1·5 mL doses of Euvichol-S (three different lots) and participants in group D were assigned to receive the active control vaccine, Shanchol. All participants and site staff (with the exception of those who prepared and administered the study vaccines) were masked to group assignment. The primary immunogenicity endpoint was non-inferiority of immunogenicity of Euvichol-S (group C) versus Shanchol (group D) at 2 weeks after the second vaccine dose, measured by the seroconversion rate, defined as the proportion of participants who had achieved seroconversion (defined as ≥four-fold increase in V cholerae O1 Inaba and Ogawa titres compared with baseline). The primary immunogenicity endpoint was assessed in the per-protocol analysis set, which included all participants who received all their planned vaccine administrations, had no important protocol deviations, and who provided blood samples for all immunogenicity assessments. The primary safety endpoint was the number of solicited adverse events, unsolicited adverse events, and serious adverse events after each vaccine dose in all ages and each age stratum, assessed in

all participants who received at least one dose of the Euvichol-S or Shanchol. Non-inferiority of Euvichol-S compared with Shanchol was shown if the lower limit of the 95% CI for the difference between the seroconversion rates in Euvichol-S group C versus Shanchol group D was above the predefined non-inferiority margin of -10%. The trial was registered at ClinicalTrials.gov, NCT04760236.

FINDINGS: Between Oct 6, 2021, and Jan 19, 2022, 2529 healthy participants (1261 [49·9%] males; 1268 [50·1%] females), were randomly assigned to group A (n=330; Euvichol-S lot number ES-2002), group B (n=331; Euvichol-S ES-2003), group C (n=934; Euvichol-S ES-2004]), or group D (n=934; Shanchol). Non-inferiority of Euvichol-S versus Shanchol in seroconversion rate for both serotypes at 2 weeks after the second dose was confirmed in all ages (difference in seroconversion rate for V cholerae O1 Inaba -0·00 [95% CI -1·86 to 1·86]; for V cholerae O1 Ogawa -1·62 [-4·80 to 1·56]). Treatment-emergent adverse events were reported in 244 (9·7%) of 2529 participants in the safety analysis set, with a total of 403 events; 247 events were reported among 151 (9·5%) of 1595 Euvichol-S recipients and 156 events among 93 (10·0%) of 934 Shanchol recipients. Pyrexia was the most common adverse event in both groups (57 events among 56 [3·5%] of 1595 Euvichol-S recipients and 37 events among 35 [3·7%] of 934 Shanchol recipients). No serious adverse events were deemed to be vaccine-related.

INTERPRETATION: A two-dose regimen of Euvichol-S vaccine was non-inferior to the active control vaccine, Shanchol, in terms of seroconversion rates 2 weeks after the second dose. The simplified formulation and production requirements of the Euvichol-S vaccine have the potential to increase the supply of oral cholera vaccine and reduce the gap between the current oral cholera vaccine supply and demand.

FUNDING: The Bill & Melinda Gates Foundation.

WEB: 10.1016/S2214-109X(24)00059-7
IMPACT FACTOR: 34.3
CITED HALF-LIFE: 3.6

START COMMENTARY

While overall results for immunogenicity met the threshold for non-inferiority, results at 2 weeks after the second dose did not meet the non-inferiority margin for participants in either of the groups comprised of children under age 18 years. Authors were unable to offer possible reasons for this, so further study in these age groups should be conducted. Figure 1 provides details of the trial groups while Table 2 provides seroconversion rates of antibodies against *Vibrio cholerae* O1 Inaba and O1 Ogawa for the groups.

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Additional Articles of Interest

1 Second dose of measles-containing vaccine coverage and associated factors among children aged 24-36 months in Gondar city, Central Gondar, Northwest Ethiopia, 2023. {Full Article}
2 Determinants of second-dose measles vaccination dropout in Ethiopia: A community-based matched case-control study. {Full Article}
3 Coverage and determinants of second-dose measles vaccination among under-five children in East Africa countries: a systematic review and meta-analysis. {Full Article}
4 Role of rotavirus vaccine in reducing diarrheal episodes in infants visiting private primary health care clinics in Karachi, Pakistan: A mixed-methods study. {Full Article}
5 Vaccine hesitancy and trust in sub-Saharan Africa. {Full Article}
6 Enhancing vaccination uptake through community engagement: evidence from China. {Full Article}
7 Hesitancy towards R21/Matrix-M malaria vaccine among Ghanaian parents and attitudes towards immunizing non-eligible children: a cross-sectional survey. {Full Article}
8 Evaluation of a single-dose HPV vaccine strategy for promoting vaccine, health, and gender equity. {Full Article}
9 The Role of Scientific Research in Human Papillomavirus Vaccine Discussions on Twitter: Social Network Analysis. {Full Article}
10 Decentralization and immunization program in a single-party state: the case of the Lao People's Democratic Republic. {Full Article}
11 Is the African Vaccine Manufacturing Accelerator a decoupling mechanism? {Full Article}
12 "It's My Moral Responsibility to Protect Others!" Examining the Effects of Moral Framing and Message Format on Influenza Vaccination Attitude and Intention. {Full Article}
13 Knowledge, attitudes, practices and prevalence of hepatitis B and C and hepatitis B vaccination coverage among public sector healthcare workers in Cambodia. {Full Article}
14 fim3-24/ptxP-3 genotype is associated to whooping cough outbreak in Brazilian Midwest: The selection of Bordetella pertussis strains driven by vaccine immunization. {Full Article}
15 Tiered Pricing and Alternative Mechanisms for Equitative Access to Vaccines in Latin America: A Narrative Review of the Literature. {Full Article}
16 COVID-19 Vaccine Hesitancy and Associated Oral Cholera Vaccine Hesitancy in a Cholera-Endemic Country: A Community-Based Cross-Sectional Study in the Democratic Republic of Congo. {Full Article}
17 Using a Dynamic Model to Estimate the Cost-Effectiveness of HPV Vaccination in Iran. {Full Article}
18 Cost-effectiveness analysis of single-dose or 2-dose of bivalent, quadrivalent, or nonavalent HPV vaccine in a low/middle-income country setting. {Full Article}

19 Low vaccine coverage and varicella outbreaks in Brazil - 2019-2022. {Full Article}

20 Willingness and hesitancy towards the governmental free human papillomavirus vaccination among parents of eligible adolescent girls in Shenzhen, Southern China. {Full Article}

21 Factors associated with hepatitis B vaccination in Laos: findings from the multiple indicator cluster surveys in 2011/12 and 2017. {Full Article}

22 Malaria vaccine acceptance among next of kin of children under 5 years of age in Gulu, northern Uganda in 2023: a community-based study. {Full Article}

23 Age-specific prevalence of IgG against measles/rubella and the impact of routine and supplementary immunization activities: A multistage random cluster sampling study with mathematical modelling. {Full Article}

24 Uptake of Human Papilloma Virus vaccine among young women living in fishing communities in Wakiso and Mukono districts, Uganda. {Full Article}

25 Knowledge and trust of mothers regarding childhood vaccination in Rwanda. {Full Article}

26 Factors associated with malaria vaccine uptake in Nsanje district, Malawi. {Full Article}

Appendix

The literature search for the June 2024 Vaccine Delivery Research Digest was conducted on May 19, 2024. We searched English language articles indexed by the US National Library of Medicine and published between April 15, 2024 and May 14, 2024. The search resulted in 460 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 2024/04/15:2024/05/14[Date - Publication]