# VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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- 8 Supporting evidence-based rotavirus vaccine introduction decision-making and implementation: Lessons from 8 Gavi-eligible countries.

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- 9 Improving Middle-Income Countries Access to Vaccines. A Blueprint to Overcome Current Challenges.

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- This article discusses the development of a framework by a panel of experts to improve vaccine discovery and development, strengthen regulatory processes, and boost vaccine production, access, and implementation in middle-income countries.
- 10 Missed opportunities: Reducing zero dose children among the urban poor after COVID, Mumbai India, 2022.

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- In this study, health facility visits where providers did not discuss vaccination were highlighted as missed opportunities to increase vaccination of zero dose children under 5 years of age in Mumbai.
- 11 New Vaccine Introductions in WHO African Region between 2000 and 2022.

#### {Abstract & START Commentary} {Full Article}

 This study reports on the significant progress that has been made in the introduction of new vaccines between in the WHO African Region since 2000. 12 Promoting data harmonization to evaluate vaccine hesitancy in LMICs: approach and applications.

#### {Abstract & START Commentary} {Full Article}

- In this article, a new software package is described that can combine spatially misaligned and incompatible datasets, and its use is demonstrated in an analysis of the association between political and geospatial factors and vaccine hesitancy.
- 13 The full value of immunisation against respiratory syncytial virus for infants younger than 1 year: effects beyond prevention of acute respiratory illness.

{Abstract & START Commentary} {Full Article}

- This article summarizes evidence for public health benefits of respiratory syncytial virus vaccination beyond reduction in RSV-associated acute lower respiratory tract infections in infants.
- 14 Progress Toward Measles Elimination Worldwide, 2000-2022.

{Abstract & START Commentary} {Full Article}

 This article provides details about measles elimination progress, finding that immunization coverage had improved in 2022 but had still not returned to prepandemic levels.

**Appendix** 

### **Details of Articles**

Gender analysis of the World Health Organization online learning program on Immunization Agenda 2030.

Nyasulu B, Heidari S, Manna M, Bahl J, Goodman T. Front Glob Womens Health. 2023 Dec 29;4:1230109.

PubMed ID: 38152380

#### **ABSTRACT**

Vaccine-preventable diseases pose a significant threat to children under five globally, creating disparities in immunization coverage. Despite its cost-effectiveness and life-saving potential, immunization faces challenges in achieving equitable coverage. Gender inequalities deeply influence access to healthcare, affecting immunization rates. This study examines the action plans submitted by participants of the World Health Organization's (WHO) IA2030 Scholar Level 1 certification course in 2021. A qualitative analysis was conducted on a subset of 111 action plans that scored above 75%, employing narrative thematic analysis to categorize and explore gender incorporation and identified barriers based on the IA2030 Gender Guide. Among the 111 analyzed action plans, gender considerations were present in almost all plans, underscoring the effectiveness of integrating gender perspectives in the course curriculum. The most frequently cited barriers included low education and health literacy, issues related to accessing quality immunization services, gendered dynamics in decision-making within households, and limited access to resources and mobility, predominantly impacting women. The findings confirm that gender inequalities significantly contribute to suboptimal immunization coverage. An intersectional approach, recognizing diverse social markers impacting immunization, is vital to address disparities effectively. Moreover, the need for gender-sensitive data and deeper understanding of intersectional dynamics was emphasized. The study highlights the importance of gender-transformative interventions, including community engagement and efforts targeting both men and women to enhance immunization coverage. While acknowledging limitations, such as potential biases in peer evaluations and the need for wider inclusivity in gender perspectives, this analysis underscores the significance of mainstreaming gender in immunization capacity-building programs. The integration of gender considerations not only raises awareness but also equips professionals to create more gender-responsive immunization programs. Continuous efforts to incorporate gender perspectives can lead to more effective, equitable, and gender-transformative immunization initiatives at various levels.

WEB: 10.3389/fgwh.2023.1230109

IMPACT FACTOR: N/A CITED HALF-LIFE: N/A

#### START COMMENTARY

The World Health Organization's (WHO) Immunization Agenda 2030 (IA2030) Scholar Level 1 certification course was designed to familiarize individuals involved in national or sub-national immunization planning with the IA2030 priorities and principles. It included a module focused on gender and immunization and highlighted the ways that gender impacts under-immunization throughout the course. Participants were asked to create action plans that would maximize the impact of immunization efforts. Of the 111 action plans created and analyzed for this report, 108 identified gender-related barriers to immunization and included targeted efforts to overcome them. This paper includes a succinct and well-organized summary of study findings related to gender inequality in the introduction.

2. Epidemiology of Meningococcal Disease in Four South American Countries and Rationale of Vaccination in Adolescents from the Region: Position Paper of the Latin American Society of Pediatric Infectious Diseases (SLIPE).

Villena R, Safadi M, Gentile &, Pujadas M, De la Maza V, George S, et al.

Vaccines (Basel). 2023 Dec 25;11(12).

PubMed ID: 38140244

#### **ABSTRACT**

Surveillance of meningococcal disease (MD) is crucial after the implementation of vaccination strategies to monitor their impact on disease burden. Adolescent vaccination could provide direct and indirect protection. Argentina, Brazil, and Chile have introduced meningococcal conjugate vaccines (MCV) into their National Immunization Programs (NIP), while Uruguay has not. Here, we analyze the epidemiology of MD and vaccination experience from these four South American countries to identify needs and plans to improve the current vaccination programs.

**METHODOLOGY:** Descriptive study of MD incidence rates, serogroup distribution, case fatality rates (CFR), and MCV uptakes during the period 2010-2021 in Argentina, Brazil, Chile, and Uruguay. Data were extracted from national surveillance programs, reference laboratories, NIPs, and Pubmed.

**RESULTS:** MD overall incidence from 2010 to 2021 have a decreasing trend in Argentina (0.37 [IQR = 0.20-0.61]), Brazil (0.59 [IQR = 0.54-1.22]), and Chile (0.45 [IQR = 0.40-0.77]), while a significant increase in Uruguay (0.47 [IQR = 0.33-0.69]) was found from 2016 to 2019. During the COVID-19 pandemic, all countries sharply reduced their MD incidence. The highest incidence rates were observed among infants, followed by children 1-4 years of age. No second peak was evident in adolescents. A reduction in serogroup C, W, and Y cases has occurred in Argentina, Brazil, and Chile after introduction of MCV, serogroup B becoming predominant in all four countries. Median CFR was 9.0%, 21%, 19.9%, and 17.9% in Argentina, Brazil, Chile, and Uruguay, respectively. Median uptake of MCV for Argentina and Brazil were 66.6% and 91.0% for priming in infants; 54.7% and 84.5% for booster in toddlers; and 47.5% and 53% for adolescents; while for Chile, 95.6% for toddlers.

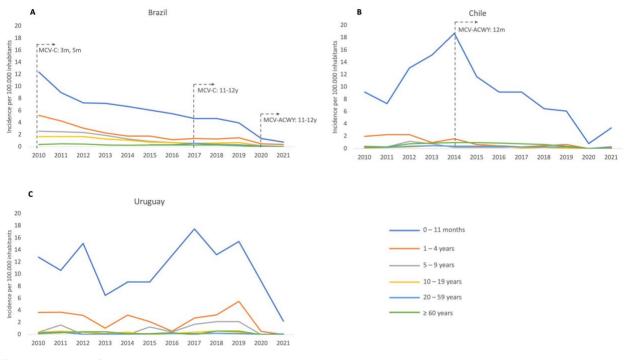
**CONCLUSIONS:** Experience after the implementation of MCV programs in South America was successful, reducing the burden of MD due to the vaccine serogroups. High vaccine uptake and the inclusion of adolescents will be crucial in the post-pandemic period to maintain the protection of the population. The increase in the proportion of serogroup B cases emphasizes the importance of continuous surveillance to guide future vaccination strategies.

WEB: 10.3390/vaccines11121841

IMPACT FACTOR: 7.8 CITED HALF-LIFE: 1.6

#### START COMMENTARY

Argentina, Brazil, Chile, and Uruguay have taken different approaches to reduce meningococcal disease. Argentina, Brazil, and Chile have all introduced meningococcal conjugate vaccines (MCV), but at different times with different serotype coverage (MCV-C, MCV-ACWY) and targeting different age groups. Uruguay has not included MCV in their national immunization program. Figures A, B, and C show the incidence of meningococcal disease by age group in Brazil, Chile, and Uruguay, highlighting the decreased incidence of meningococcal disease in Brazil and Chile after the introduction of MCV, and the additional benefit of vaccinating adolescents observed in Brazil after implementation of adolescent vaccination programs.



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### 3. Recent advances in expression and purification strategies for plant made vaccines.

Venkataraman S, Khan I, Habibi P, Le M, Lippert R, Hefferon K.

Front Plant Sci. 2023 Dec 11;14:1273958.

PubMed ID: 38078091

#### **ABSTRACT**

Plants have been explored as a platform to produce pharmaceutical proteins for over 20 years. Important features such as the cost-effectiveness of production, the ease of scaling up to manufacturing capacity, the lack of cold chain requirements and the ability to produce complex therapeutic proteins which are biologically and functionally identical to their mammalian counterparts, make plants a strong alternative for vaccine production. This review article focuses on both the expression as well as the downstream purification processes for plant made vaccines. Expression strategies including transgenic, transient and cell suspension cultures are outlined, and various plant tissues targeted such as leaves and seeds are described. The principal components used for downstream processing of plant made vaccines are examined. The review concludes with a reflection of the future benefits of plant production platforms for vaccine production.

WEB: 10.3389/fpls.2023.1273958

IMPACT FACTOR: 5.6 CITED HALF-LIFE: 4.6

#### START COMMENTARY

This overview by Venkataraman et al. highlights the potential benefits of plant-based systems for vaccine manufacturing. It includes discussion of specific plants that could be used, and progress made toward their use in vaccine production. One example provided is Medicago Inc.'s use of plant transient expression systems in developing their vaccine candidate for SARS-Cov-2 that has successfully completed phase 2 clinical trials and received regulatory approval from Health Canada. Return to List of Articles

4. <u>Co-administration with Men-B vaccine increases Rotavirus vaccination coverage: A 5-year regionwide retrospective cohort study (STORM study).</u>

Lo Vecchio A, Scarano S, Palladino R, Del Bene M, Trama U, Affinito G, et al.

Vaccine. 2024 Jan 01;42(2):287-294.

PubMed ID: 38072758

#### **ABSTRACT**

**INTRODUCTION:** In Italy Rotavirus vaccination (RVV) is provided free of charge from 2018, however, the coverage is scattered and suboptimal. The narrow time frame to complete the schedule is a barrier to uptake, and co-administration with other vaccines may potentially increase the coverage. Although the co-administration of RV vaccine and Meningococcal Group B vaccine (MenB) is not included in the product labels, we aimed at studying its impact on RVV coverage.

**METHODS:** This Surveillance study on Timing and cOverage of Rotavirus and MenB vaccine coadministration (STORM study) used the Regional Vaccination Registry to collect data about children born in Campania Region between January 2016 and December 2020, and receiving vaccines scheduled in the first year of life.

**RESULTS:** Among the 224,110 children enrolled, 60,614 (27.0%) completed the RVV schedule, with a vaccination rate that increased over time from 1.15% in 2016 to 56.92% in 2020. The first and last dose of RVV schedule were administered beyond the recommended time in 6% of the study population, respectively. Co-administration of RV vaccine with MenB vaccine increased from 0.7 % in 2016 to 46.85 % in 2020. Children receiving RV/MenB vaccines concomitantly had a significantly higher chance of completing the RV schedule compared to those receiving RVV alone during a specific appointment (94.78 % vs 72.26 %, Prevalence Ratio -PR- 1.275, 95 %CI 1.245-1.295p < 0.00001). The positive driving effect of RV/MenB co-administration was more evident for children receiving pentavalent (PR 1.288) than monovalent RVV (PR 1.115) which was confirmed when adjusted for confounding variables (i.e., year of vaccination, local district, gender).

**CONCLUSIONS:** Although still far from the target, RVV coverage has increased in recent years in Campania Region. Co-administration with MenB vaccine may aid in increasing RVV coverage, especially for pentavalent RVV. Further safety data are needed to support co-administration as a key tool to increase coverage.

WEB: 10.1016/j.vaccine.2023.12.003

IMPACT FACTOR: 5.5 CITED HALF-LIFE: 7.2

#### START COMMENTARY

In late 2019, after reviewing evidence about the immunogenicity and safety of co-administration of vaccines, the Regional Health Bureau in Campania Italy authorized the co-administration of rotavirus vaccine (RV) and any other vaccine as a strategy to increase RV uptake. This study by Lo Vecchio et al. examines the impact on RV coverage of co-administering RV with meningococcal group B (MenB) vaccine. Of note, among those who received the first rotavirus vaccine, more than 83% completed the series, and that proportion remained stable across all 5 years of the study, suggesting that if co-administering vaccines increases the number of children receiving the first vaccine, it is likely that an increase in full vaccination for RV will result. Authors note that only 0.15% of children in the region received no vaccines, suggesting that incomplete or missing RV was not due to overall vaccine hesitancy.

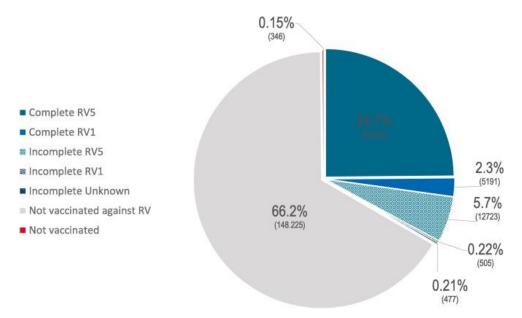


Fig. 2. Rotavirus Vaccine uptake in children living in Campania Region between 2016 and 2020. The figure shows the percentage of children who received a complete or incomplete RV immunization schedule, according to single RV vaccines, and those who were not vaccinated against RV or did not receive any vaccination.

# 5. <u>Understanding household-level risk factors for zero dose immunization in 82 low- and middle-income countries.</u>

Farrenkopf B, Zhou X, Shet A, Olayinka F, Carr K, Patenaude B, et al.

PLoS One. 2023 Dec 16;18(12):e0287459.

PubMed ID: 38060516

#### **ABSTRACT**

**INTRODUCTION:** In 2021, an estimated 18 million children did not receive a single dose of routine vaccinations and constitute the population known as zero dose children. There is growing momentum and investment in reaching zero dose children and addressing the gross inequity in the reach of immunization services. To effectively do so, there is an urgent need to characterize more deeply the population of zero dose children and the barriers they face in accessing routine immunization services.

**METHODS:** We utilized the most recent DHS and MICS data spanning 2011 to 2020 from low, lower-middle, and upper-middle income countries. Zero dose status was defined as children aged 12-23 months who had not received any doses of BCG, DTP-containing, polio, and measles-containing vaccines. We estimated the prevalence of zero-dose children in the entire study sample, by country income level, and by region, and characterized the zero dose population by household-level factors. Multivariate logistic regressions were used to determine the household-level sociodemographic and health care access factors associated with zero dose immunization status. To pool multicountry data, we adjusted the original survey weights according to the country's population of children 12-23 months of age. To contextualize our findings, we utilized United Nations Population Division birth cohort data to estimate the study population as a proportion of the global and country income group populations.

**RESULTS:** We included a total of 82 countries in our univariate analyses and 68 countries in our multivariate model. Overall, 7.5% of the study population were zero dose children. More than half (51.9%) of this population was concentrated in African countries. Zero dose children were predominantly situated in rural areas (75.8%) and in households in the lowest two wealth quintiles (62.7%) and were born to mothers who completed fewer than four antenatal care (ANC) visits (66.5%) and had home births (58.5%). Yet, surprisingly, a considerable proportion of zero dose children's mothers did receive appropriate care during pregnancy (33.5% of zero dose children have mothers who received at least 4 ANC visits). When controlled for other factors, children had three times the odds (OR = 3.00, 95% CI: 2.72, 3.30) of being zero dose if their mother had not received any tetanus injections, 2.46 times the odds (95% CI: 2.21, 2.74) of being zero dose if their mother had not received any ANC visits, and had nearly twice the odds (OR = 1.87, 95% CI: 1.70, 2.05) of

being zero dose if their mother had a home delivery, compared to children of mothers who received at least 2 tetanus injections, received at least 4 ANC visits, and had a facility delivery, respectively.

**DISCUSSION:** A lack of access to maternal health care was a strong risk factor of zero dose status and highlights important opportunities to improve the quality and integration of maternal and child health programs. Additionally, because a substantial proportion of zero dose children and their mothers do receive appropriate care, approaches to reach zero dose children should incorporate mitigating missed opportunities for vaccination.

WEB: 10.1371/journal.pone.0287459

IMPACT FACTOR: 3.7 CITED HALF-LIFE: 7.3

#### START COMMENTARY

In 20 of the 82 countries included in the analysis, more than 10% of children 12 to 23 months meet the definition for zero-dose children, which is defined in this study as not having received any dose of BCG, DTP, polio, or measles vaccine. Figure 2 shows proportion of children with zero dose by country. Table 1 provides the proportion of children 12 to 23 months that are zero dose by demographic and health system characteristics, both globally and by country income.

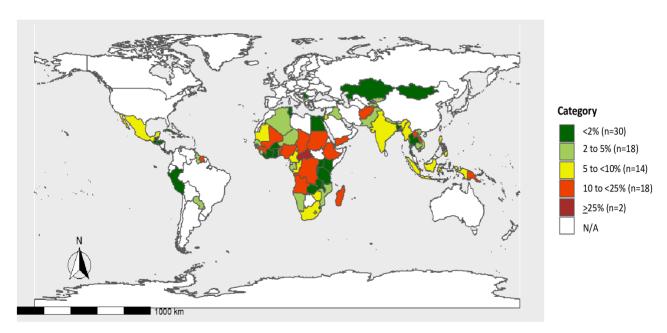


Figure 2. Distribution of zero dose prevalence by country

### 6. Progress in Immunization Safety Monitoring - Worldwide, 2020-2022.

Blau E, Balakrishnan M, Sköld H, Santhana Gopala Krishnan R, Lundquist P, Pal S, et al. *MMWR Morb Mortal Wkly Rep.* 2023 Dec 20;72(49):1321-1326.

PubMed ID: 38060432

#### **ABSTRACT**

Effective surveillance of adverse events following immunization (AEFIs) primarily relies on the collaboration of two partners: national regulatory authorities (NRAs) and national expanded programs on immunization (EPIs). In December 2020, the World Health Organization (WHO) Global Advisory Committee for Vaccine Safety recommended a new case-based indicator of national capacity to monitor immunization safety: at least one serious AEFI reported per 1 million total population per year. To achieve this indicator, WHO-affiliated countries and territories (WHO countries) rely upon data generated from functional AEFI surveillance systems. This report describes 2020-2022 global, regional, and national progress in use of the newly introduced immunization safety monitoring indicator and progress on joint AEFI reporting from national EPIs and NRAs. Among WHO countries, 51 (24%) of 214 implemented the new indicator in 2020, 111 (52%) of 214 implemented it in 2021, and 92 (43%) of 215 in 2022. In 2020, 41 (19%) WHO countries reported AEFI data jointly from EPIs and NRAs; this increased to 55 (26%) in 2021 and 57 (27%) in 2022. These findings, resulting in part from the intensified support for COVID-19 vaccination, demonstrate that national AEFI surveillance systems increasingly support the timely use and sharing of casebased immunization safety data, but work is still needed to strengthen global vaccine safety monitorina.

WEB: 10.15585/mmwr.mm7249a2

IMPACT FACTOR: 33.9 CITED HALF-LIFE: 2.7

#### START COMMENTARY

In Figure 1, Blau et al. show the number of World Health Organization (WHO)-affiliated countries and territories that have reported suspected serious adverse events following immunization to the WHO's global pharmacovigilance database, (VigiBase). Of note, only 43% of the (92 of 215) WHO countries currently meet the target for the new safety monitor indicator. A limitation of this study is that it relies on reporting to VigiBase, which is voluntary and may not reflect ability to monitor adverse events by the national immunization safety surveillance system within a country.

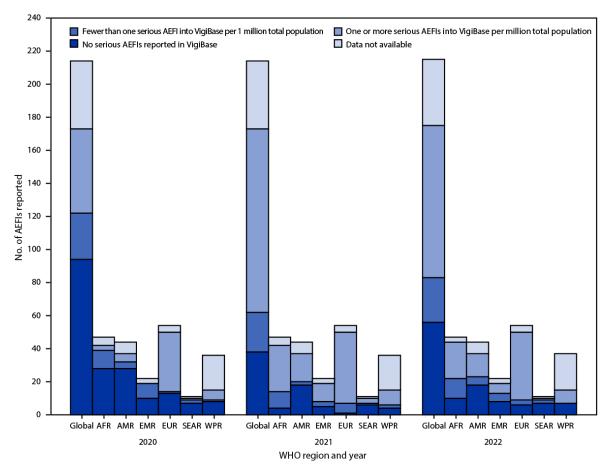


Figure 1. World Health Organization-affiliated countries and territories reporting serious adverse events following immunization into VigiBase, by World Health Organization region – worldwide, 2020-2022

Abbreviations: AEFIs = adverse events following immunization; AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WHO = World Health Organization; WPR = Western Pacific Region.

# 7 Durability of single-dose HPV vaccination in young Kenyan women: randomized controlled trial 3-year results.

Barnabas R, Brown E, Onono M, Bukusi E, Njoroge B, Winer R, et al.

Nat Med. 2023 Dec 16;29(12):3224-3232.

PubMed ID: 38049621

#### **ABSTRACT**

Cervical cancer burden is high where prophylactic vaccination and screening coverage are low. We demonstrated in a multicenter randomized, double-blind, controlled trial that single-dose human papillomavirus (HPV) vaccination had high vaccine efficacy (VE) against persistent infection at 18 months in Kenyan women. Here, we report findings of this trial through 3 years of follow-up. Overall, 2,275 healthy women aged 15-20 years were recruited and randomly assigned to receive bivalent (n = 760), nonavalent (n = 758) or control (n = 757) vaccine. The primary outcome was incidentpersistent vaccine type-specific cervical HPV infection. The primary evaluation was superiority analysis in the modified intention-to-treat (mITT) HPV 16/18 and HPV 16/18/31/33/45/52/58 cohorts. The trial met its prespecified end points of vaccine type-specific persistent HPV infection. A total of 75 incident-persistent infections were detected in the HPV 16/18 mITT cohort: 2 in the bivalent group, 1 in the nonavalent group and 72 in the control group. Nonavalent VE was 98.8% (95% CI 91.3-99.8%, P < 0.0001) and bivalent VE was 97.5% (95% CI 90.0-99.4%, P < 0.0001). Overall, 89 persistent infections were detected in the HPV 16/18/31/33/45/52/58 mITT cohort: 5 in the nonavalent group and 84 in the control group; nonavalent VE was 95.5% (95% CI 89.0-98.2%, P < 0.0001). There were no vaccine-related severe adverse events. Three years after vaccination, single-dose HPV vaccination was highly efficacious, safe and conferred durable protection. ClinicalTrials.gov no. NCT03675256.

WEB: 10.1038/s41591-023-02658-0

IMPACT FACTOR: 82.9 CITED HALF-LIFE: 5.7

#### START COMMENTARY

This study by Barnabas et al. was conducted at three clinic sites within the Kenya Medical Research Institute to test the efficacy of single dose bivalent or nonavalent HPV vaccines. The outcome of interest was incident-persistent HPV infection, defined as high-risk vaccine-type-specific HPV detected at two consecutive visits at least 4 months apart. Cumulative incidence curves by vaccine group can be found in Figure 2. Results after three years of follow-up add to evidence from trials in

Costa Rica, India, and Tanzania that support the efficacy and durability of single-dose HPV vaccination. This study did not include individuals with HIV.

# 8. Supporting evidence-based rotavirus vaccine introduction decision-making and implementation: Lessons from 8 Gavi-eligible countries.

Jennings M, Sauer M, Manchester C, Soeters H, Shimp L, Hyde T, et al.

Vaccine. 2023 Dec 21;42(1):8-16.

PubMed ID: 38042696

#### **ABSTRACT**

Despite the 2009 World Health Organization recommendation that all countries introduce rotavirus vaccines (RVV) into their national immunization programs, just 81 countries had introduced RVV by the end of 2015, leaving millions of children at risk for rotavirus morbidity and mortality. In response, the Rotavirus Accelerated Vaccine Introduction Network (RAVIN) was established in 2016 to provide support to eight Gavi-eligible countries that had yet to make an RVV introduction decision and/or had requested technical assistance with RVV preparations: Afghanistan, Bangladesh, Benin, Cambodia, Democratic Republic of Congo, Lao People's Democratic Republic, Myanmar, and Nepal. During 2016-2020, RAVIN worked with country governments and partners to support evidence-based immunization decision-making, RVV introduction preparation and implementation, and multilateral coordination. By the September 2020 program close-out, five of the eight RAVIN focus countries successfully introduced RVV into their routine childhood immunization programs. We report on the RAVIN approach, describe how the project responded collectively to an evolving RVV product landscape, synthesize common characteristics of the RAVIN country experiences, highlight key lessons learned, and outline the unfinished agenda to inform future new vaccine introduction efforts by countries and global partners.

WEB: 10.1016/j.vaccine.2023.11.035

IMPACT FACTOR: 5.5 CITED HALF-LIFE: 7.2

#### START COMMENTARY

Jennings et al. identified core elements from the Rotavirus Accelerated Vaccine Introduction Network (RAVIN) approach (Figure 3) and include technical advocacy for rotavirus vaccine introduction, liaising with country stakeholders to assess needs, summarizing and strengthening the case for investment, supporting Gavi application submission, providing timely in-country technical assistance for introduction planning and implementation, and providing post-introduction support. Throughout the process, multi-country workshops were held to provide opportunities to problem-solve and share experiences. Key lessons learned are summarized in Figure 5.

#### Decision-making

- To effectively support country decision-making and its follow-through, it is essential to monitor shifting political and program priorities and adapt the approach accordingly.
- Countries may not have existing in-country champions for specific vaccines and may require external support to build advocacy capacity.
- Local technical experts are critical partners in supporting evidence-based decision-making and should be engaged early and often, across the vaccine introduction continuum
- Countries do not make public health decisions in traditional silos, and partners are most effective when they can support comprehensive planning and independent decision-making, encompassing both immunization and non-immunization interventions.

#### Introduction preparation and support for implementation

- With targeted support, resources, and planning, RVV (and other new vaccine) introduction is an opportunity to strengthen the overall routine immunization system.
- Use of country- and language-specific training and demand generation materials likely improved vaccine implementation and acceptance.
- Flexibility in implementation plan and strategy is needed in the face of emerging health priorities.

#### Multilateral coordination

- An independent, coordinated group of partners can help mitigate the demands on countries and global partners by triaging and prioritizing needs and serving as an intermediary expediter.
- Expanded partner consortia must work within and in alignment with the expected and routine pathways of engagement with countries leadership and multilateral agencies, making early, regular, and ongoing communication and coordination crucial.
- Rapidly identifying and addressing emerging barriers to vaccine decision-making and financing often requires a comprehensive and creative solution to mitigate undue influence of partner or personal politics on these decisions.
- Targeted, time-limited initiatives may help facilitate successful new vaccine introduction by supplementing core EPI program initiatives and staff facing competing priorities and constrained resources

Figure 5. Lessons learned from RAVIN support for RV decision-making and introduction

# 9. Improving Middle-Income Countries Access to Vaccines. A Blueprint to Overcome Current Challenges.

Espinal C, Becerra-Posada F, Torres J. *Ann Glob Health.* 2023 Dec 06;89(1):80.

PubMed ID: 38025920

#### **ABSTRACT**

The Global Health Consortium at Florida International University developed an end-to-end solution framework based on the input of a diverse panel of experts from middle-income country (MIC) government agencies, public health think tanks, academia, and nonprofit organizations to identify mechanisms to help MIC governments and stakeholders increase access to novel vaccines for infectious diseases. The resultant layout can be deployed to improve vaccine discovery and development, strengthen regulatory processes, and boost vaccine production, access, and implementation. Mechanisms include policies and incentives MIC governments can use to stimulate vaccine investment and activity, as well as actions government agencies can take together with other stakeholders to coordinate efforts or build capabilities. Through a series of individual virtual interviews, we engaged diverse experts from MIC government agencies, public health think tanks, academia, and nonprofit organizations who understand the vaccine ecosystem, immunization policies, and population health financing at global, regional, and country levels. Responses were mapped, and in-depth questions were prepared for a group virtual discussion. This paper is the result of such a group discussion. The panel identified clear opportunities for MICs to improve locally-driven innovations and future access to novel vaccines. It proposes a solution framework for countries considering investing in vaccine research and development and innovation to use as a guide to evaluate the steps they could take to improve such an environment and incentivize innovation in vaccine development. It is hoped that this end-to-end solution framework will become a key resource to help MICs strengthen policies and take more actions to make such improvements.

WEB: 10.5334/aogh.4151 IMPACT FACTOR: 2.9 CITED HALF-LIFE: 3.8

#### START COMMENTARY

Barriers limiting middle-income countries (MICs) identified by panel experts include financial and economic constraints, lack of political will due to focus on short-term results, over-reliance on multinational corporations and global actors, and competition from other health priorities. Gaps in

research and development capabilities, both real and perceived, are also limiting. Table 3 shows the solution framework that was developed with suggested actions for governments of MICs.

# 10. Missed opportunities: Reducing zero dose children among the urban poor after COVID, Mumbai India, 2022.

Vashi M, Watkins M.

Vaccine. 2023 Dec 18;42(1):59-63.

PubMed ID: 38016846

#### **ABSTRACT**

Reaching urban poor populations poses challenges for equitable immunization coverage. Furthermore, COVID disrupted routine immunization services. In Mumbai, India, first dose diphtheria tetanus pertussis containing vaccine (DTPCV1) coverage dropped from 88% (2019) to 76% (2021). We identified and characterized 125 zero-dose (those without DTPCV1) migrant children in urban Mumbai in October 2022. Almost half were born elsewhere than Mumbai; 53% resided at their present location for less than a year. More than half were 12-59 months of age, well-beyond the age for first routine childhood immunizations. Three of four zero dose children had received birth dose vaccination in the hospital; but failed to receive DTPCV1. Vaccine hesitancy, awareness gaps and operational issues were common reasons for non-vaccination. Despite frequent visits to health facilities for illness, only a third of facility staff asked or advised parents about vaccination. Missed opportunities were much more common in private than government facilities. For the vast majority (88%), residential sites were included in local routine immunization micro-plans and distances to immunization sites were short (less than 1 km for 94% of families). However, planned session frequency was inadequate half of the time. Expanded efforts to reach migrant urban poor children are needed to ensure vaccine equity.

WEB: 10.1016/j.vaccine.2023.11.027

IMPACT FACTOR: 5.5 CITED HALF-LIFE: 7.2

#### START COMMENTARY

Vashi and Watkins defined zero dose children as those who had received no doses of diphtheria, tetanus, pertussis-containing vaccine (DTPCV). Zero dose children 4 months to 5 years of age were identified by immunization field monitors doing house-to-house routine immunization monitoring, which used a random selection of houses within a defined area in Mumbai. In-person interviews were conducted to ascertain reasons for lack of immunization and parents were asked about health facility visits for the child to assess missed opportunities for vaccination. Parents were asked about vaccination in only 40 of the 109 health visits (37%) indicating a missed opportunity to provide

parents with information and access to vaccination for their children. Authors followed up with 96 of the 125 children in January 2023, and found that 58% of them had received their first dose of DTPCV in the time since their study interview.

### New Vaccine Introductions in WHO African Region between 2000 and 2022.

Iwu-Jaja C, Iwu C, Jaca A, Wiysonge C. *Vaccines (Basel)*. 2023 Dec 14;11(11).

PubMed ID: 38006054

#### **ABSTRACT**

Significant progress has been made in vaccine development worldwide. This study examined the WHO African Region's vaccine introduction trends from 2000 to 2022, excluding COVID-19 vaccines. We extracted data on vaccine introductions from the WHO/UNICEF joint reporting form for 17 vaccines. We examined the frequency and percentages of vaccine introductions from 2000 to 2022, as well as between two specific time periods (2000-2010 and 2011-2022). We analysed Gavi eligible and ineligible countries separately and used a Chi-squared test to determine if vaccine introductions differed significantly. Three vaccines have been introduced in all 47 countries within the region: hepatitis B (HepB), Haemophilus influenzae type b (Hib), and inactivated polio vaccine (IPV). Between 2011 and 2022, HepB, Hib, IPV, the second dose of measles-containing vaccine (MCV2), and pneumococcal conjugate vaccine (PCV) were the five most frequently introduced vaccines. Hepatitis A vaccine has only been introduced in Mauritius, while Japanese encephalitis vaccine has not been introduced in any African country. Between 2000-2010 and 2011-2022, a statistically significant rise in the number of vaccine introductions was noted (p < 0.001) with a significant positive association between Gavi eligibility and vaccine introductions (p < 0.001). Significant progress has been made in the introduction of new vaccines between 2000 and 2022 in the WHO African Region, with notable introductions between 2011 and 2022. Commitments from countries, and establishing the infrastructure required for effective implementation, remain crucial.

WEB: 10.3390/vaccines11111722

IMPACT FACTOR: 7.8 CITED HALF-LIFE: 1.6

#### START COMMENTARY

Iwu-Jaja et al. detail information about vaccines introduced in the World Health Organization (WHO) African Region between 2000 and 2022. They found no significant disparities between Gavi and non-Gavi countries in introduction of new and underutilized vaccines. Figure 2 provides details of the timing of vaccine introduction and number of countries that have introduced specific vaccines.

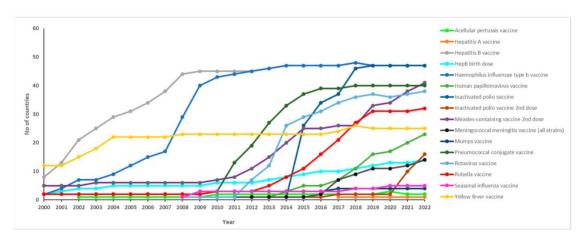


Figure 2. Trends in new vaccine introduction per year in the WHO African Region from 2000 to 2022.

# 12. Promoting data harmonization to evaluate vaccine hesitancy in LMICs: approach and applications.

Rego R, Zhukov Y, Reneau K, Pienta A, Rice K, Brady P, et al.

BMC Med Res Methodol. 2023 Nov 27;23(1):278.

PubMed ID: 38001442

#### **ABSTRACT**

**BACKGROUND:** Factors influencing the health of populations are subjects of interdisciplinary study. However, datasets relevant to public health often lack interdisciplinary breath. It is difficult to combine data on health outcomes with datasets on potentially important contextual factors, like political violence or development, due to incompatible levels of geographic support; differing data formats and structures; differences in sampling procedures and wording; and the stability of temporal trends. We present a computational package to combine spatially misaligned datasets, and provide an illustrative analysis of multi-dimensional factors in health outcomes.

**METHODS:** We rely on a new software toolkit, Sub-National Geospatial Data Archive (SUNGEO), to combine data across disciplinary domains and demonstrate a use case on vaccine hesitancy in Low and Middle-Income Countries (LMICs). We use data from the World Bank's High Frequency Phone Surveys (HFPS) from Kenya, Indonesia, and Malawi. We curate and combine these surveys with data on political violence, elections, economic development, and other contextual factors, using SUNGEO. We then develop a stochastic model to analyze the integrated data and evaluate 1) the stability of vaccination preferences in all three countries over time, and 2) the association between local contextual factors and vaccination preferences.

**RESULTS:** In all three countries, vaccine-acceptance is more persistent than vaccine-hesitancy from round to round: the long-run probability of staying vaccine-acceptant (hesitant) was 0.96 (0.65) in Indonesia, 0.89 (0.21) in Kenya, and 0.76 (0.40) in Malawi. However, vaccine acceptance was significantly less durable in areas exposed to political violence, with percentage point differences (ppd) in vaccine acceptance of -10 (Indonesia), -5 (Kenya), and -64 (Malawi). In Indonesia and Kenya, although not Malawi, vaccine acceptance was also significantly less durable in locations without competitive elections (-19 and -6 ppd, respectively) and in locations with more limited transportation infrastructure (-11 and -8 ppd).

**CONCLUSION:** With SUNGEO, researchers can combine spatially misaligned and incompatible datasets. As an illustrative example, we find that vaccination hesitancy is correlated with political violence, electoral uncompetitiveness and limited access to public goods, consistent with past results that vaccination hesitancy is associated with government distrust.

WEB: 10.1186/s12874-023-02088-z

IMPACT FACTOR: 4.0 CITED HALF-LIFE: 8.5

#### START COMMENTARY

Rego et al. introduce a new software toolkit: Sub-National Geospatial Data Archive (SUNGEO), which facilitates combining data from public health surveys with other data such as geopolitical or economic which often have incompatible formats. It includes an open-source software package in R to process user-supplied data and will merge it with pre-loaded geo-referenced data for analysis. It also includes an archiving tool to allow users to contribute data to the repository. The authors provide an example of utilizing this software to analyze contextual effects of violence, electoral competitiveness, and development on vaccine hesitancy. An overview of the SUNGEO system can be found in Figure 1.

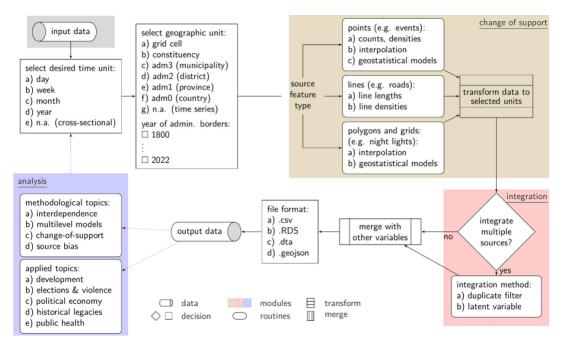


Figure 1. Overview of the SUNGEO system

13. The full value of immunisation against respiratory syncytial virus for infants younger than 1 year: effects beyond prevention of acute respiratory illness.

Feikin D, Karron R, Saha S, Sparrow E, Srikantiah P, Weinberger D, et al.

Lancet Infect Dis. 2023 Dec 14.

PubMed ID: 38000374

#### **ABSTRACT**

Respiratory syncytial virus (RSV) is a leading cause of severe respiratory illness and death among children worldwide, particularly in children younger than 6 months and in low-income and middleincome countries. Feasible and cost-effective interventions to prevent RSV disease are not yet widely available, although two new products aimed at preventing RSV disease-long-acting monoclonal antibodies and maternal vaccines-have been licensed within the past 2 years. The primary target of these products is reduction of the substantial burden of RSV-associated acute lower respiratory tract infections (LRTI) in infants younger than 1 year. However, other important public health benefits might also accrue with the prevention of RSV-associated LRTI during the first year of life. Mounting evidence shows that preventing RSV-associated LRTI in infants younger than 1 year could prevent secondary pneumonia caused by other pathogens, reduce recurrent hospitalisations due to other respiratory diseases in later childhood, decrease all-cause infant mortality, ameliorate the burden of respiratory diseases on health-care systems, reduce inappropriate antibiotic use, and possibly improve lung health beyond infancy. We herein review current evidence and suggest approaches to better assess the magnitude of these potential secondary effects of RSV prevention, which, if proven substantial, are likely to be relevant to policy makers in many countries as they consider the use of these new products.

WEB: 10.1016/S1473-3099(23)00568-6

IMPACT FACTOR: 56.3 CITED HALF-LIFE: 3.7

#### START COMMENTARY

Feikin et al. summarize the evidence for public health benefits of respiratory syncytial virus (RSV) vaccination beyond reduction in RSV-associated acute lower respiratory tract infections in infants (Figure 1). In Table 2, the authors list potential outcomes of RSV disease prevention with the level of pre-licensure evidence, certainty of the effect of RSV prevention on that outcome, and amount of time it would take for the effect to be demonstrated after the RSV vaccine implementation. They discuss study designs to investigate secondary outcomes, positing that settings with clearly defined RSV seasons would be ideal to measure impact, and that it would be necessary for the study to extend through multiple RSV seasons as the severity may differ from year to year.

### 14 Progress Toward Measles Elimination - Worldwide, 2000-2022.

Minta A, Ferrari M, Antoni S, Portnoy A, Sbarra A, Lambert B, et al. *MMWR Morb Mortal Wkly Rep.* 2023 Nov 20;72(46):1262-1268.

PubMed ID: 37971951

#### **ABSTRACT**

Measles is a highly contagious, vaccine-preventable disease that requires high population immunity for transmission to be interrupted. All six World Health Organization regions have committed to eliminating measles; however, no region has achieved and sustained measles elimination. This report describes measles elimination progress during 2000-2022. During 2000-2019, estimated coverage worldwide with the first dose of measles-containing vaccine (MCV) increased from 72% to 86%, then declined to 81% in 2021 during the COVID-19 pandemic, representing the lowest coverage since 2008. In 2022, first-dose MCV coverage increased to 83%. Only one half (72) of 144 countries reporting measles cases achieved the measles surveillance indicator target of two or more discarded cases per 100,000 population in 2022. During 2021-2022, estimated measles cases increased 18%, from 7,802,000 to 9,232,300, and the number of countries experiencing large or disruptive outbreaks increased from 22 to 37. Estimated measles deaths increased 43% during 2021-2022, from 95,000 to 136,200. Nonetheless, an estimated 57 million measles deaths were averted by vaccination during 2000-2022. In 2022, measles vaccination coverage and global surveillance showed some recovery from the COVID-19 pandemic setbacks; however, coverage declined in low-income countries, and globally, years of suboptimal immunization coverage left millions of children unprotected. Urgent reversal of coverage setbacks experienced during the COVID-19 pandemic can be accomplished by renewing efforts to vaccinate all children with 2 MCV doses and strengthening surveillance, thereby preventing outbreaks and accelerating progress toward measles elimination.

WEB: 10.15585/mmwr.mm7246a3

IMPACT FACTOR: 33.9 CITED HALF-LIFE: 2.7

#### START COMMENTARY

Immunization coverage had improved in 2022 but had still not achieved 2019 prepandemic levels, with only 65 countries reporting >95% coverage for the first dose of measles containing vaccine (MCV1). Coverage for the second dose of measles containing vaccine (MCV2) was 74% in 2022, and six countries had added MCV2 to their immunization program. However, authors estimate that 21.9 million children had not receive any dose of MCV, leaving them susceptible to measles

infection. While 83 countries had achieved or maintained measles elimination by the end of 2022, no WHO region had achieved and sustained measles elimination, and no African Region country had eliminated measles.

### **Additional Articles of Interest**

- 1 Mapping the Cognitive Biases Related to Vaccination: A Scoping Review of the Literature. {Full Article}
- 2 The Acceptability of Pharmacy-Based HPV Vaccination in Western Kenya among Pharmacy Clients and Providers. {Full Article}
- 3 Acceptance of and Adherence to a Four-Dose RTS,S/AS01 Schedule: Findings from a Longitudinal Qualitative Evaluation Study for the Malaria Vaccine Implementation Programme. {Full Article}
- 4 A Systematic Review of Vaccination Guidance for Humanitarian Responses. (Full Article)
- 5 Bioinformatics Analysis of Global Diversity in Meningococcal Vaccine Antigens over the Past 10 Years: Vaccine Efficacy Prognosis. {Full Article}
- 6 Integrated Immunization Information System in Indonesia: Prototype Design Using Quantitative and Qualitative Data. {Full Article}
- 7 Closing the pneumococcal conjugate vaccine (PCV) introduction gap: an archetype analysis of last-mile countries. {Full Article}
- 8 Institutional trust is a distinct construct related to vaccine hesitancy and refusal. {Full Article}
- 9 Despite misinformation, low trust, and conflict in Somalia, high demand for vaccines and a negative endorsement effect of non-state authorities. {Full Article}
- 10 Testing a vaccine candidate against Hepatitis C virus designed by combinatorial optimization. {Full Article}
- 11 Epidemic forecast and preparedness for explosive-cerebrospinal meningitis outbreak in Nigeria using the preventive vaccination strategy. {Full Article}
- 12 Childhood immunization uptake determinants in Kinshasa, Democratic Republic of the Congo: ordered regressions to assess timely infant vaccines administered at birth and 6-weeks. {Full Article}
- 13 Interventions for improving coverage of childhood immunisation in low- and middle-income countries. {Full Article}
- 14 Meningococcal Disease in the Post-COVID-19 Era: A Time to Prepare. {Full Article}
- 15 State policies increase vaccination by shaping social norms. {Full Article}
- 16 13-Valent pneumococcal conjugate vaccines vaccination innovative strategy in Weifang City, China: a case study. {Full Article}
- 17 Designing the global vaccine supply chain: balancing intellectual property rights with post COVID-19 vaccine equity. {Full Article}
- 18 Factors associated with vaccine adherence among an underserved population: the adult Travellers in Nouvelle-Aquitaine, France. {Full Article}

- 19 Accelerating Pneumococcal Conjugate Vaccine introductions in Indonesia: key learnings from 2017 to 2022. {Full Article}
- 20 Evaluating effective measles vaccine coverage in the Malaysian population accounting for between-dose correlation and vaccine efficacy. {Full Article}
- 21 Extracting factors associated with vaccination from Twitter data and mapping to behavioral models. {Full Article}
- 22 Bayesian safety surveillance with adaptive bias correction. {Full Article}
- 23 Resilience of routine childhood immunization services in two counties in Kenya in the face of the COVID-19 pandemic. {Full Article}
- 24 Routine childhood immunization in Sub-Saharan Africa: addressing parental vaccine hesitancy. {Full Article}
- 25 Adding new childhood vaccines to China's National Immunization Program: evidence, benefits, and priorities. {Full Article}
- 26 Missed opportunities for vaccination at point of care and their impact on coverage and urbanrural coverage inequity in the Gambia. {Full Article}
- 27 Health system barriers to timely routine measles vaccinations in rural southwest China: a qualitative study on the perspectives of township vaccination professionals and village doctors. {Full Article}
- 28 A circulating vaccine-derived poliovirus type 2 outbreak in a chronic conflict setting: a descriptive epidemiological study in South Sudan 2020 to 2021. {Full Article}
- 29 Strengthening immunization programs through innovative sub-national public-private partnerships in selected provinces in the Democratic Republic of the Congo. {Full Article}
- 30 Caregiver acceptance of malaria vaccination for children under 5 years of age and associated factors: cross-sectional household survey, Guinea and Sierra Leone, 2022. {Full Article}
- 31 Geospatial vaccine misinformation risk on social media: Online insights from an English/Spanish natural language processing (NLP) analysis of vaccine-related tweets. {Full Article}
- 32 RTS,S/AS01 malaria vaccine pilot implementation in western Kenya: a qualitative longitudinal study to understand immunisation barriers and optimise uptake. {Full Article}
- 33 Cost-effectiveness analysis of typhoid vaccination in Lao PDR. {Full Article}
- 34 A mixed integer programming model for vaccine pricing within a group purchasing organization. {Full Article}
- 35 Thinking outside of the [cold] box: implementing a human-centered design approach to understand barriers and craft solutions to cold chain equipment maintenance in Niger. {Full Article}
- 36 Development of a composite scoring system to rank communities at high risk of zero-dose children in Cameroon: A geospatial analysis. {Full Article}

- 37 Assessment of vaccine management performance in health facilities of Mwanza Region, Tanzania: a cross-sectional study. {Full Article}
- 38 Digital Personal Health Coaching Platform for Promoting Human Papillomavirus Infection Vaccinations and Cancer Prevention: Knowledge Graph-Based Recommendation System. } {Full Article}
- 39 Enhancing Pharmacovigilance in Côte d'Ivoire: Impact of GSK's Training and Mentoring Pilot Project in the Abidjan Region. {Full Article}
- 40 An assessment of the effectiveness of an electronic wristband in improving routine immunization timeliness and reducing drop-out. {Full Article}
- 41 Commodifying Vaccines to Curtail Antibiotic Resistance Impact in Malaria Endemic Countries. {Full Article}

## **Appendix**

The literature search for the January 2024 Vaccine Delivery Research Digest was conducted on December 30, 2023. We searched English language articles indexed by the US National Library of Medicine and published between November 15, 2023 and December 14, 2023. The search resulted in 609 items.

#### **SEARCH TERMS**

(((((vaccine[tiab] OR vaccines[tiab] OR vaccination[tiab] OR immunization[tiab] OR immunisation[tiab] OR vaccine[mesh] OR immunization[mesh]) AND (logistics[tiab] OR supply[tiab] OR "supply chain"[tiab] OR implementation[tiab] OR expenditures[tiab] OR financing[tiab] OR economics[tiab] OR "Cost effectiveness"[tiab] OR coverage[tiab] OR attitudes[tiab] OR belief[tiab] OR beliefs[tiab] OR refusal[tiab] OR "Procurement"[tiab] OR timeliness[tiab] OR systems[tiab])) OR ("vaccine delivery"[tiab]) OR "vaccination refusal"[MeSH Terms] OR "immunization programs"[MeSH Terms] OR "zero dose"[tiab] OR "unvaccinated children"[tiab] OR "gavi"[tiab])) NOT ("in vitro"[tiab] OR "immune response"[tiab] OR gene[tiab] OR chemistry[tiab] OR genotox\*[tiab] OR sequencing[tiab] OR nanoparticle\*[tiab] OR bacteriophage[tiab] OR exome[tiab] OR exogenous[tiab] OR electropor\*[tiab] OR "systems biology"[tiab] OR "animal model"[tiab] OR cattle[tiab] OR sheep[tiab] OR goat[tiab] OR rat[tiab] OR pig[tiab] OR mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR rodent[tiab] OR fish[tiab])) AND (English[LA]) ("2023/15/11"[PDAT] : "2023/14/12"[PDAT]))