VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

PRODUCED BY: SUTTON, A. & SHARMA, M.

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- Assessed TTCV vaccine coverage using data from sub-Saharan Africa Demographic Health Surveys

2 Key considerations for the development of novel mRNA candidate vaccines in LMICs: A WHO/MPP mRNA Technology Transfer Programme meeting report.

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- Summarized meeting session discussions among key stakeholders in the WHO/MPP mRNA Technology Transfer Programme

3 Impact and cost-effectiveness of measles vaccination through microarray patches in 70 low-income and middle-income countries: mathematical modelling and early-stage economic evaluation.

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- Assessed the impact of integrating MR-MAPs into existing vaccination programs

4 Resilience in childhood vaccination: analysing delivery system responses to shocks in Lebanon.

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- Analyzed the vaccine delivery system responses to shock events in Lebanon using a qualitative system dynamics approach

5 High-resolution geospatial mapping of zero-dose and under-immunized children following Nigeria's 2021 multiple indicator cluster survey/national immunization coverage survey (MICS/NICS).

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- Predicted zero-dose and under-immunized children at the local government area (LGA) level in Nigeria using geospatial mapping methods

6 Construction of an indicator framework for vaccine inclusion in public health programs: A Delphi-entropy method study.

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- Discussed the development of an indicator framework for vaccine inclusion at the national, provincial, municipal, and district/county levels in China

7 Task-Shifting Immunization Activities to Community Health Workers: A Mixed-Method Cross-Sectional Study in Sahel Region, Burkina Faso.

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- Evaluated a program developed to improve immunization activities in an area of Burkina Faso suffering frequent disruptions to the health care system due to terrorist attacks that involved task-shifting of immunization activities to CHWs

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- Detailed review of the burden of mother-to-child transmission of hepatitis B virus in sub-Saharan Africa

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- Reported trends in World Health Organization and UNICEF immunization coverage estimates at global, regional, and national levels through 2022

10 Introducing seasonal influenza vaccine in Bhutan: Country experience and achievements.

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- Detailed the successful introduction of influenza vaccination in Bhutan in 2019

11 Estimating the global impact of rotavirus vaccines on child mortality.

{Abstract & START Commentary} {Full Article}

- Estimated rotavirus deaths prevented by vaccination over the period 2006-2019 in 186 countries using a proportionate outcomes model

12 Progress Toward Measles and Rubella Elimination - Indonesia, 2013-2022.

{Abstract & START Commentary} {Full Article}

- Described Indonesia's progress toward measles and rubella elimination before and after the COVID-19 pandemic

13 Engagement of community health workers to improve immunization coverage through addressing inequities and enhancing data quality and use is a feasible and effective approach: An implementation study in Uganda.

{Abstract & START Commentary} {Full Article}

- Reported findings from a randomized control trial investigating effectiveness of using community health workers to obtain quality and reliable data that can be used for planning and evidence-based response actions

14 Global regulatory reforms to promote equitable vaccine access in the next pandemic.

{Abstract & START Commentary} {Full Article}

- Used case studies of three successful programs to highlight key lessons learned to facilitate future vaccine development to meet the needs of LMICs

15 Post-epidemic health system recovery: A comparative case study analysis of routine immunization programs in the Republics of Haiti and Liberia.

{Abstract & START Commentary} {Full Article}

- Discussed facilitators and barriers to routine immunization program recovery following major epidemics using Haiti and Liberia as example cases

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Details of Articles

1. Prevalence and determinants of two or more doses of tetanus toxoid-containing vaccine immunization among pregnant women in sub-Saharan Africa: Evidence from recent demographic and health survey data.

Tamir T, Kassie A, Zegeye A.

Vaccine. 2023 Nov 28;41(49):7428-7434.

PubMed ID: 37949753

ABSTRACT

INTRODUCTION: Tetanus is a major public health problem in low and middle income countries including in sub-Saharan Africa. Tetanus toxoid vaccine immunization during pregnancy is a global strategy against mortality due to maternal and neonatal tetanus. Recent data on tetanus toxoid-containing vaccination during pregnancy provides insight to policymakers for better implementation of the vaccine. Hence, this study aimed to determine prevalence and determinants of immunization with tetanus toxoid containing vaccine among pregnant women in sub-Saharan Africa.

METHODS: Secondary analysis of the recent demographic and health survey data was done using a sample of 173,032 pregnant women. Stata 14 statistical software was used for analysis and multilevel logistic regression model was applied to determine associated factors of two or more tetanus toxoid-containing vaccine immunization. P-value less than 0.05 for adjusted odds ratio was used to identify factors significantly associated with the outcome.

RESULT: The prevalence of immunization with two and more doses of tetanus toxoid-containing vaccine in sub-Saharan Africa was found to be 49.8 %. Women's age 36-49, women's education, poor household wealth index, unwanted pregnancy, women's occupation, husband education, and community illiteracy were significantly associated with two or more doses of tetanus toxoid-containing vaccine immunization in sub-Saharan Africa.

CONCLUSION: In sub-Saharan Africa, less than half of pregnant women were immunized with two or more doses of tetanus toxoid-containing vaccine. Women's education and women's employment positively affected immunization with two or more doses of tetanus toxoid-containing vaccine. Women's age group of 36-49 years, unwanted pregnancy, poor household wealth index, husbands having no formal education, and community illiteracy negatively affected receipt of two or more doses of tetanus toxoid-containing vaccine. Therefore, policymakers should take into account the determinants of tetanus toxoid immunization throughout its implementation so as to boost the coverage of tetanus toxoid immunization in sub-Saharan Africa.

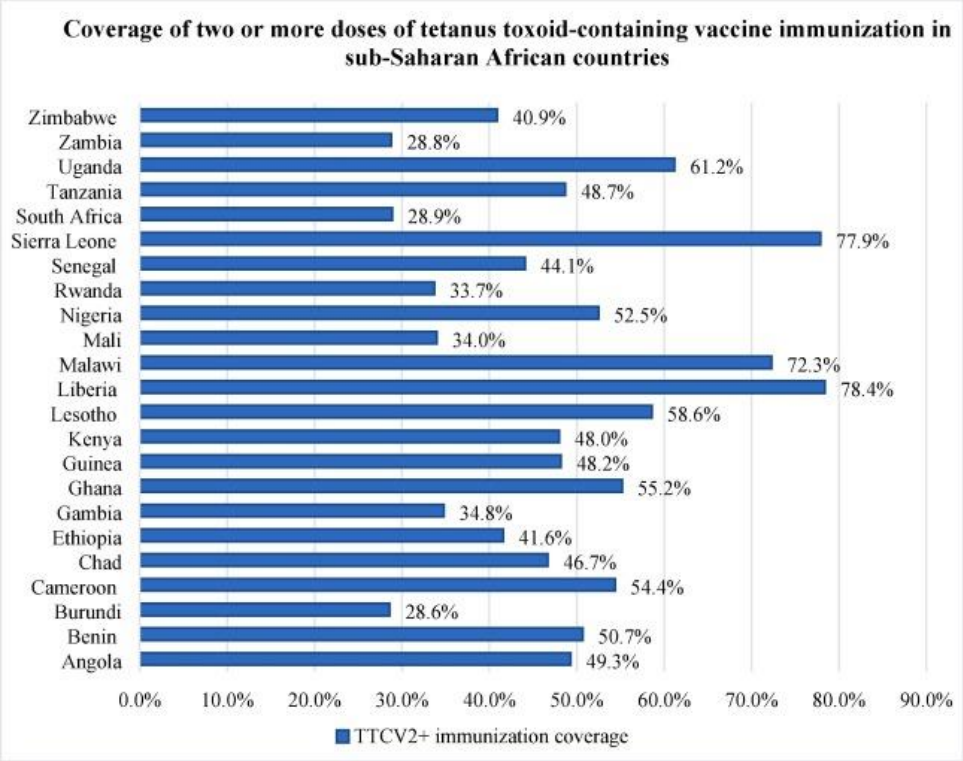
WEB: 10.1016/j.vaccine.2023.11.007

IMPACT FACTOR: 5.5

CITED HALF-LIFE: 7.2

START COMMENTARY

Using data from sub-Saharan Africa Demographic Health Surveys collected between 2014 and 2020, Tamir, et al. found widely varying coverage for two or more doses of tetanus toxoid-containing vaccine (TTCV2+) across countries with less than 30% of pregnant women in Burundi, South Africa, and Zambia having received TTCV2+ while more than 70% of pregnant women in Sierra Leone, Malawi, and Liberia had received at least 2 doses of TTCV. The authors did not find a significant association between number of antenatal care visits (<4 vs 4 or more) or place of delivery (home vs facility birth) and maternal TTCV2+.



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2. Key considerations for the development of novel mRNA candidate vaccines in LMICs: A WHO/MPP mRNA Technology Transfer Programme meeting report.

Gsell P, Giersing B, Gottlieb S, Wilder-Smith A, Wu L, Friede M.

Vaccine. 2023 Nov 28;41(49):7307-7312.

PubMed ID: 37949751

ABSTRACT

The WHO/MPP mRNA Technology Transfer Programme, initiated in 2021, focuses on establishing mRNA vaccine manufacturing capacity in LMICs. On 17-21 April 2023, Programme partners were convened to review technology transfer progress, discuss sustainability aspects and promote mRNA product development for diseases relevant to LMICs. To help guide product development, this report introduces key considerations for understanding the likelihood of technical and regulatory success and of policy development and procurement for mRNA vaccines to be developed and manufactured in LMICs. The report underscores the potential for LMICs to establish sustainable mRNA R&D pipelines.

WEB: 10.1016/j.vaccine.2023.10.027

IMPACT FACTOR: 5.5

CITED HALF-LIFE: 7.2

START COMMENTARY

This report by Gsell, et al. summarizes discussions from the first in-person meeting of manufacturing and academic research partners, national representatives, and key funders and global experts in vaccine development involved in the World Health Organization and Medicines Patent Pool's mRNA Technology Transfer Programme. The meeting convened to explore some of the key aspects of mRNA vaccine development, highlighting opportunities for manufacturing partners in South Africa, Argentina, Bangladesh, Brazil, Egypt, India, Indonesia, Kenya, Nigeria, Pakistan, Senegal, Serbia, Tunisia, Ukraine, and Vietnam. Included are discussions of the probability of technical and regulatory success (PTRS) and the probability of policy development and procurement (PPDP) for mRNA vaccines for HIV, tuberculosis, malaria, flaviviruses such as dengue and Zika, emerging infectious diseases such as Nipah and Ebola, sexually transmitted infections including HPV and HSV, and viral respiratory diseases such as RSV and influenza.

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3. Impact and cost-effectiveness of measles vaccination through microarray patches in 70 low-income and middle-income countries: mathematical modelling and early-stage economic evaluation.

Fu H, Abbas K, Malvolti S, Gregory C, Ko M, Amorij J, et al.

BMJ Glob Health. 2023 Nov 13;8(11).

PubMed ID: 37949503

ABSTRACT

BACKGROUND: Microarray patches (MAPs) are a promising technology being developed to reduce barriers to vaccine delivery based on needles and syringes (N&S). To address the evidence gap on the public health value of applying this potential technology to immunisation programmes, we evaluated the health impact on measles burden and cost-effectiveness of introducing measles-rubella MAPs (MR-MAPs) in 70 low-income and middle-income countries (LMICs).

METHODS: We used an age-structured dynamic model of measles transmission and vaccination to project measles cases, deaths and disability-adjusted life-years during 2030-2040. Compared with the baseline scenarios with continuing current N&S-based practice, we evaluated the introduction of MR-MAPs under different measles vaccine coverage projections and MR-MAP introduction strategies. Costs were calculated based on the ingredients approach, including direct cost of measles treatment, vaccine procurement and vaccine delivery. Model-based burden and cost estimates were derived for individual countries and country income groups. We compared the incremental cost-effectiveness ratios of introducing MR-MAPs to health opportunity costs.

RESULTS: MR-MAP introduction could prevent 27%-37% of measles burden between 2030 and 2040 in 70 LMICs, compared with the N&S-only immunisation strategy. The largest health impact could be achieved under lower coverage projection and accelerated introduction strategy, with 39 million measles cases averted. Measles treatment cost is a key driver of the net cost of introduction. In countries with a relatively higher income, introducing MR-MAPs could be a cost-saving intervention due to reduced treatment costs. Compared with country-specific health opportunity costs, introducing MR-MAPs would be cost-effective in 16%-81% of LMICs, depending on the MR-MAPs procurement prices and vaccine coverage projections.

CONCLUSIONS: Introducing MR-MAPs in LMICs can be a cost-effective strategy to revitalise measles immunisation programmes with stagnant uptake and reach undervaccinated children. Sustainable introduction and uptake of MR-MAPs has the potential to improve vaccine equity within and between countries and accelerate progress towards measles elimination.

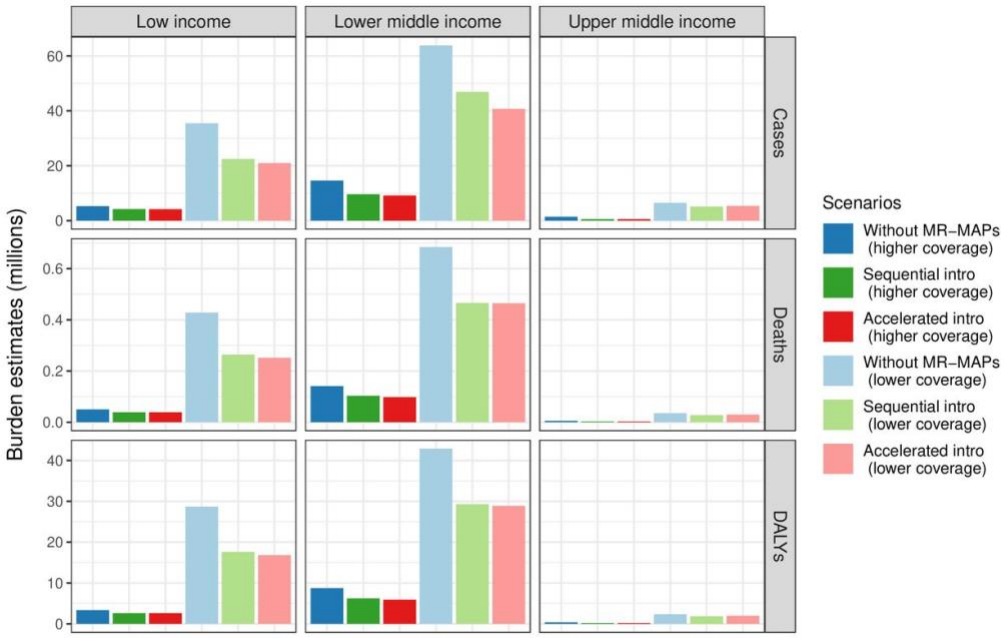
WEB: 10.1136/bmjgh-2023-012204

IMPACT FACTOR: 8.1

CITED HALF-LIFE: 2.7

START COMMENTARY

This study by Fu, et al. used the Dynamic Measles Immunisation Calculation Engine (DynaMICE) to project the impact of integrating measles-rubella micro-array patches (MR-MAP) into existing immunization programs under two coverage and two introduction scenarios. The higher coverage scenario modelled measles-containing vaccine dose 1 (MCV1) and 2 (MCV2) coverage to increase by 0.5-3% per year with supplementary immunization activities (SIAs) taking place very 2-5 years until coverage was greater than 90% while the lower coverage scenario assumed that routine immunization coverage remained constant at the 2019 level with SIAs only reaching 85% of children. Accelerated introduction of MR-MAP prioritized countries with greatest need based on MCV1 coverage. Sequential introduction modelled MR-MAP introduction first occurring in countries with higher measles and rubella burden that also had operational and financial support for new vaccine introduction, followed by introduction of MR-MAP in other countries. The figure below shows cumulative measles cases, deaths, and DALYs in millions over 10 years (2030-2040) under the two coverage and two introduction scenarios by income setting.



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4. Resilience in childhood vaccination: analysing delivery system responses to shocks in Lebanon.

Ismail S, Tomoaia-Cotisel A, Noubani A, Fouad F, Bell S, Borghi J, et al.

BMJ Glob Health. 2023 Nov 08;8(11).

PubMed ID: 37931939

ABSTRACT

INTRODUCTION: Despite rapidly growing academic and policy interest in health system resilience, the empirical literature on this topic remains small and focused on macrolevel effects arising from single shocks. To better understand health system responses to multiple shocks, we conducted an in-depth case study using qualitative system dynamics. We focused on routine childhood vaccination delivery in Lebanon in the context of at least three shocks overlapping to varying degrees in space and time: large-scale refugee arrivals from neighbouring Syria; COVID-19; and an economic crisis.

METHODS: Semistructured interviews were performed with 38 stakeholders working at different levels in the system. Interview transcripts were analysed using purposive text analysis to generate individual stakeholder causal loop diagrams (CLDs) mapping out relationships between system variables contributing to changes in coverage for routine antigens over time. These were then combined using a stepwise process to produce an aggregated CLD. The aggregated CLD was validated using a reserve set of interview transcripts.

RESULTS: Various system responses to shocks were identified, including demand promotion measures such as scaling-up community engagement activities and policy changes to reduce the cost of vaccination to service users, and supply side responses including donor funding mobilisation, diversification of service delivery models and cold chain strengthening. Some systemic changes were introduced-particularly in response to refugee arrivals-including task-shifting to nurse-led vaccine administration. Potentially transformative change was seen in the integration of private sector clinics to support vaccination delivery and depended on both demand side and supply side changes. Some resilience-promoting measures introduced following earlier shocks paradoxically increased vulnerability to later ones.

CONCLUSION: Flexibility in financing and human resource allocation appear key for system resilience regardless of the shock. System dynamics offers a promising method for ex ante modelling of ostensibly resilience-strengthening interventions under different shock scenarios, to identify-and safeguard against-unintended consequences.

WEB: 10.1136/bmjgh-2023-012399

IMPACT FACTOR: 8.1

CITED HALF-LIFE: 2.7

START COMMENTARY

Ismail, et al. classified responses to health system shocks as either absorptive, in which the shock is accommodated using existing system structures and pathways; adaptive, in which structures and pathways change in response to the shock; or transformative, in which systems are fundamentally and deliberately altered and strengthened in response to shock, increasing resilience against future shocks. They emphasized the importance of long-term transformative changes to increase system resilience such as task-shifting to nurse-led vaccine administration over short-term technical absorptive and adaptive responses such as introduction of solar fridges to increase cold chain capacity. They noted that short-term responses can ultimately increase system vulnerability, which occurred with the solar fridges as they required imported replacement parts that were difficult to source in later shock events.

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5. High-resolution geospatial mapping of zero-dose and under-immunized children following Nigeria's 2021 multiple indicator cluster survey/national immunization coverage survey (MICS/NICS).

Jean Baptiste A, Wagai J, Hahné S, Adeniran A, Koko R, de Vos S, et al.

J Infect Dis. 2023 Nov 06.

PubMed ID: 37930309

ABSTRACT

BACKGROUND: The "zero-dose" children are those without any routine vaccination or lacking the first dose of the diphtheria-tetanus-pertussis-containing vaccine. As per 2022 WHO/UNICEF estimates, globally, Nigeria has the highest number of zero-dose with over 2.3 million unvaccinated.

METHODS: We used data from the 2021 Nigeria Multiple Indicator Cluster Survey - National Immunisation Coverage Survey to identify zero-dose and under-immunized children. Geospatial modelling techniques were employed to determine the prevalence of zero-dose children and predict risk areas with under-immunized at a high resolution of 1x1 km.

RESULTS: Both zero-dose and under-immunized children are more prevalent in socially deprived groups. Univariate and multivariate Bayesian analyses showed positive correlations between the prevalence of zero-dose and under-immunized children with factors like stunting, contraceptive prevalence, and literacy. The prevalence of zero-dose and under-immunized children varies significantly by region and ethnicity, with higher rates observed in the country's northern parts. Significant heterogeneity in the distribution of under-vaccinated children was observed.

CONCLUSIONS: Nigeria needs to enhance its immunization system and coverage. Geospatial modelling can help deliver vaccines effectively to underserved communities. By adopting this approach, countries can ensure equitable vaccine access and contribute to global vaccination objectives.

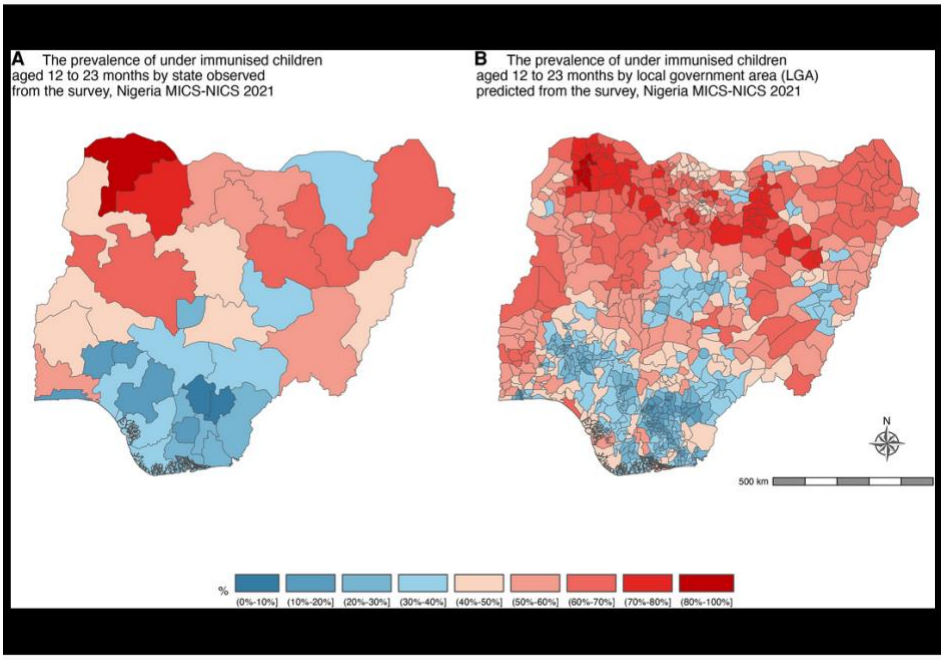
WEB: 10.1093/infdis/jiad476
IMPACT FACTOR: 6.4
CITED HALF-LIFE: 9.5

START COMMENTARY

Jean Baptiste, et al. used data from the Nigeria Multiple Indicator Cluster Survey – National Immunisation Coverage Survey (MICS/NICS) and covariates informed by previous work on immunization geospatial analysis to predict prevalence of zero-dose and under-immunized children at the local government area (LGA) level in Nigeria. Zero-dose children were defined as those aged

12 to 23 months who did not receive any DTP doses, while under-immunized children were defined as those who were missing the third dose of the DTP vaccine. As seen in Figure 1, this granularity can inform vaccine delivery programs as areas of focus are highlighted in the LGA model that were not apparent in the observed state-level results.

Figure 1.



Maps of Nigeria display data from the 2021 Multiple Indicator Cluster Survey/National Immunization Coverage Survey (MICS/NICS). *A* and *B*, Maps illustrate the observed and predicted prevalence of underimmunized children aged 12 to 23 months within Nigeria's states and local government areas. Underimmunized children are those who missed the third dose of the diphtheria, tetanus, and pertussis–containing vaccine.

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6. Construction of an indicator framework for vaccine inclusion in public health programs: A Delphi-entropy method study.

Wang Q, Dai P, Jia M, Jiang M, Li J, Yang W, et al.

Hum Vaccin Immunother. 2023 Nov 02;19(3):2272539.

PubMed ID: 37905961

ABSTRACT

Governments must decide which vaccine priority to include in their public health programs. Using the modified Delphi and entropy method, we developed an indicator framework for vaccine inclusion at the national, provincial, municipal, and district/county levels, each containing three dimensions. In total, 4 primary indicators, 17 secondary indicators, and 45 tertiary indicators were selected, covering vaccine-preventable diseases, candidate vaccines, and social drivers of the supply and demand sides. From a subjective perspective, there was no significant weighting difference in the primary and secondary indicators at all administrative levels. “Vaccine-preventable diseases” as a primary indicator had the greatest weight in the peer group, of which “Health burden” had the highest weight among the secondary indicators. From the objective perspective, the social drivers on the supply and demand sides of the primary indicators accounted for 65% and higher. Among the secondary indicators, “the characteristics of the candidate vaccine” and “vaccine-related policies on the supply side” held 8% of weights or more at both national and provincial levels. “Demographic characteristics” held the highest weight at the municipal (13.50) and district/county (15.45) level. This study indicates that China needs different considerations when using WHO-recommended vaccines at the national, provincial, municipal, and district/county levels. In addition, this study highlights that behavioral and social drivers are important indicators that need to be considered for decision-making. This framework provides a tool for policymakers to determine the inclusion priority of candidate vaccines.

WEB: 10.1080/21645515.2023.2272539

IMPACT FACTOR: 4.8

CITED HALF-LIFE: 3.9

START COMMENTARY

Wang, et al. worked with experts of vaccine policy, disease control, and vaccine production and sales as well as academics from areas throughout China to develop an indicator framework for vaccine inclusion decisions for China’s National Immunization Program (NIP). They argue that a common framework for such decisions is needed as several vaccines recommended by WHO for inclusion in national vaccine programs such as pneumococcal conjugate vaccine, Hib vaccine, and influenza vaccine have not yet been included in China’s NIP. They state that a process should be

developed for deciding which vaccines to prioritize. The flowchart for constructing the indicator framework can be found in Figure 1 and includes a literature review to decide preliminary indicators to include followed by two rounds of expert consultations and framework revisions. The framework highlighted commonalities and differences in priorities at different administrative levels.

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7. Task-Shifting Immunization Activities to Community Health Workers: A Mixed-Method Cross-Sectional Study in Sahel Region, Burkina Faso.

Ouédraogo H, Kabore Y, Sawadogo A, Bakouan M, Sawadogo N, Mano M, et al.

Glob Health Sci Pract. 2023 Nov 02;11(5).

PubMed ID: 37903579

ABSTRACT

INTRODUCTION: Faced with the frequent disruptions to the health care system and provision of immunization services caused by terrorist attacks that began in 2015, the Sahel region in Burkina Faso initiated resilience strategies, including the task-shifting of immunization activities to community health workers (CHWs). This strategy was designed to involve more CHWs in the vaccination delivery process and ultimately to improve the performance of the health care system.

STRATEGY DEVELOPMENT AND IMPLEMENTATION: The task-shifting strategy began as a pilot in Djibo health district in 2019 and then extended to all 4 districts of the Sahel region. CHWs included both personnel recruited through the Ministry of Health and Public Hygiene processes at the national level and other community members who support the operation of health facilities. They were trained on standardized immunization modules and provided with vaccines by functional health facilities teams. Implementation initiated with the administration of oral antigens by CHWs. Subsequently, their service delivery was expanded to include injectable vaccines in the context of the worsening terrorist attacks and the urgent need to protect the health of local populations affected by the security and humanitarian crisis.

STRATEGY EVALUATION: The intervention was evaluated through an internal programmatic review conducted as a descriptive cross-sectional study implemented from August 1 to October 28, 2022, in the Sahel region, including a survey in Dori health district. CHWs involved in implementing the strategy were considered for interviews. Performance indicators for all antigens have shown an upward trend since the strategy's inception in 2019.

CONCLUSION: The task-shifting of immunization activities to CHWs has been implemented successfully in a region seriously affected by terrorism-related insecurity. It holds the promise of maintaining or even improving performance if institutionalized and scaled up while improving the monitoring of adverse events following immunization by the CHWs.

WEB: 10.9745/GHSP-D-23-00044

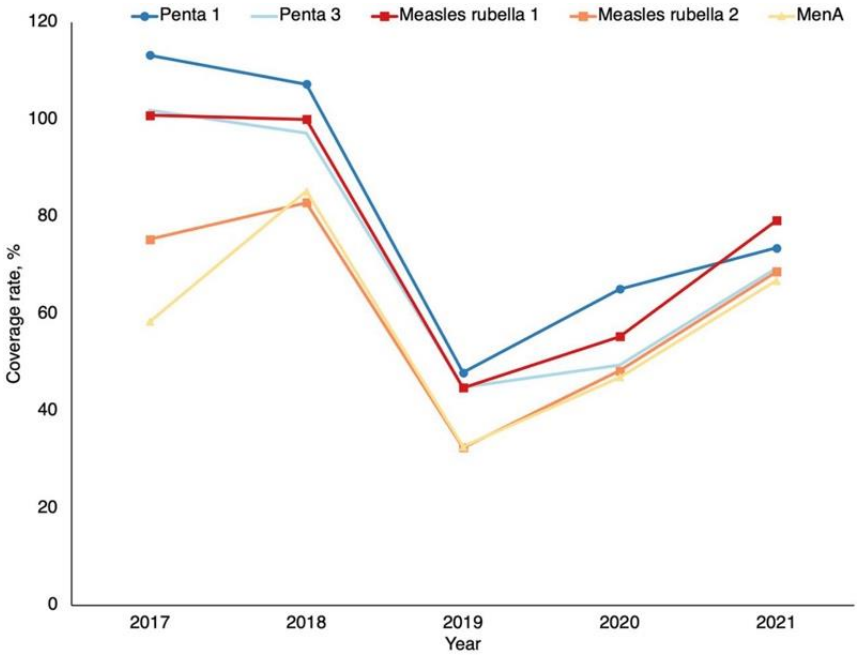
IMPACT FACTOR: 4.0

CITED HALF-LIFE: 4.5

START COMMENTARY

This study by Ouédraogo, et al. detailed the development of a health system resilience strategy to shift vaccination efforts to community health workers (CHWs) in insecure areas of Burkina Faso. Authors found that shifting immunization activities to CHWs in the Sahel region resulted in more than 6000 children receiving vaccinations after the implementation of the pilot program in 2019 (Figure 2). CHWs were trained in administering vaccines, biomedical waste management, and data management, and were given a monthly stipend of $34/month (USD). The authors provided recommendations for improvement based on their program evaluation, which included increasing financial motivation of CHWs as the current stipend often does not cover even transportation for immunization activities, providing refresher training and supervision, strengthening the cold chain, providing better resources for waste management, and strengthening resources for adverse event surveillance.

Figure 2: Evolution of Vaccination Coverage of the Sahel Region, Burkina Faso, 2017-2021



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8. Weak Adoption and Performance of Hepatitis B Birth-Dose Vaccination Programs in Africa: Time to Consider Systems Complexity?-A Scoping Review.

Solomon-Rakiep T, Olivier J, Amponsah-Dacosta E.

Trop Med Infect Dis. 2023 Oct 29;8(10).

PubMed ID: 37888602

ABSTRACT

The persistent burden of chronic hepatitis B among ≤5-year-old children in Africa suggests missed opportunities for controlling mother-to-child transmission (MTCT) of the hepatitis B virus (HBV). This scoping review maps the evidence base on the risk of HBV MTCT, the status of HBV MTCT mitigation strategies including hepatitis B birth-dose vaccination, and the role of systems complexity on the suboptimal adoption and performance of hepatitis B birth-dose vaccination programs in Africa. Overall, 88 peer-reviewed and grey literature sources published between 2000-2022 were included in this review. The growing evidence base consistently argues for a heightened risk of HBV MTCT amidst the HIV co-epidemic in the region. Without universal HBV screening programs integrated within broader antenatal care services, current selective hepatitis B birth-dose vaccination is unlikely to effectively interrupt HBV MTCT. We underscore critical health systems-related barriers to universal adoption and optimal performance of hepatitis B birth-dose vaccination programs in the region. To better conceptualize the role of complexity and system-wide effects on the observed performance of the program, we propose an adapted systems-based logic model. Ultimately, exploring contextualized complex systems approaches to scaling-up universal hepatitis B birth-dose vaccination programs should form an integral part of the regional research agenda.

WEB: 10.3390/tropicalmed8100474

IMPACT FACTOR: 2.9

CITED HALF-LIFE: 2.8

START COMMENTARY

In this detailed scoping review of the burden of mother-to-child transmission (MTCT) of hepatitis B virus (HBV) in sub-Saharan Africa, Solomon-Rakiep et al. provide evidence for hepatitis B birth-dose vaccines as the most effective strategy to prevent MTCT of hepatitis B due to its cost-effectiveness and effectiveness in preventing vertical transmission. The article discusses barriers to implementation of a birth-dose vaccination programs at the national level, including difficulty in delivering a vaccine dose within 24 hours of birth in geographically remote areas and to children born outside medical facilities. The authors propose a systems-based logic model for assessing the complexity within programs, found in Figure 5.

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9. Routine Vaccination Coverage - Worldwide, 2022.

Kaur G, Danovaro-Holliday M, Mwinnyaa G, Gacic-Dobo M, Francis L, Grevendonk J, et al.
MMWR Morb Mortal Wkly Rep. 2023 Oct 30;72(43):1155-1161.
PubMed ID: 37883326

ABSTRACT

In 2020, the World Health Assembly endorsed the Immunization Agenda 2030 (IA2030), the 2021-2030 global strategy that envisions a world where everyone, everywhere, at every age, fully benefits from vaccines. This report reviews trends in World Health Organization and UNICEF immunization coverage estimates at global, regional, and national levels through 2022 and documents progress toward improving coverage with respect to the IA2030 strategy, which aims to reduce the number of children who have not received the first dose of a diphtheria-tetanus-pertussis-containing vaccine (DTPcv1) worldwide by 50% and to increase coverage with 3 diphtheria-tetanus-pertussis-containing vaccine doses (DTPcv3) to 90%. Worldwide, coverage ≥1 dose of DTPcv1 increased from 86% in 2021 to 89% in 2022 but remained below the 90% coverage achieved in 2019. Estimated DTPcv3 coverage increased from 81% in 2021 to 84% in 2022 but also remained below the 2019 coverage of 86%. Worldwide in 2022, 14.3 million children were not vaccinated with DTPcv1, a 21% decrease from 18.1 million in 2021, but an 11% increase from 12.9 million in 2019. Most children (84%) who did not receive DTPcv1 in 2022 lived in low- and lower-middle-income countries. COVID-19 pandemic-associated immunization recovery occurred in 2022 at the global level, but progress was unevenly distributed, especially among low-income countries. Urgent action is needed to provide incompletely vaccinated children with catch-up vaccinations that were missed during the pandemic, restore national vaccination coverage to prepandemic levels, strengthen immunization programs to build resiliency to withstand future unforeseen public health events, and further improve coverage to protect children from vaccine-preventable diseases.

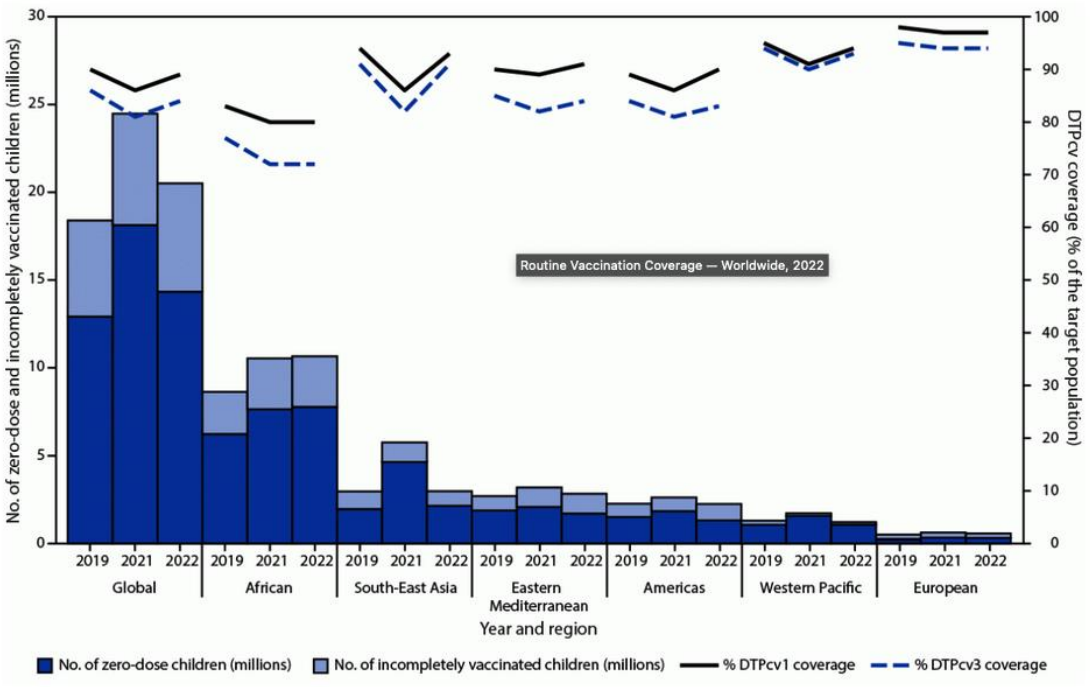
WEB: 10.15585/mmwr.mm7243a1
IMPACT FACTOR: 33.9
CITED HALF-LIFE: 2.7

START COMMENTARY

Figure 1 below shows the estimated number of zero-dose and incompletely vaccinated children globally and by World Health Organization region in 2019, 2020, and 2022. All regions except the African region had improved diphtheria-tetanus-pertussis-containing vaccine coverage in 2022 over 2020, but coverage remained below 2019 levels. Authors note that while a similar number of children

were vaccinated in 2022 and 2019 in some low- and middle-income countries, the 2022 birth cohort is substantially larger.

Figure 1: Estimated number of zero-dose (dark blue) and incompletely vaccinated (light blue) children and estimated coverage with first (solid) and third dose (dashed) of diphtheria-tetanus-pertussis-containing vaccine, by World Health Organization Region



Abbreviations: DTPcv1 = first dose of diphtheria-tetanus-pertussis-containing vaccine; DTPcv3 = third dose of diphtheria-tetanus-pertussis-containing vaccine.

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10. Introducing seasonal influenza vaccine in Bhutan: Country experience and achievements.

Wangchuk S, Prabhakaran A, Dhakal G, Zangmo C, Gharpure R, Dawa T, et al.

Vaccine. 2023 Nov 22;41(48):7259-7264.

PubMed ID: 37866993

ABSTRACT

Bhutan successfully introduced multiple vaccines since the establishment of the Vaccine Preventable Disease Program in 1979. Surveillance and subsequent introduction of influenza vaccination became a public health priority for the Ministry of Health following the influenza A(H1N1)pdm09 pandemic. Sentinel surveillance for influenza in Bhutan began in 2008, and a study of severe acute respiratory infection was conducted in 2017, which found the highest influenza burden in children aged <5 years and adults ≥50 years. Following review of surveillance and burden of disease data, the National Technical Advisory Group presented recommendations to Bhutan's Ministry of Health which approved influenza vaccine introduction for all five high-risk groups in the country. Upon the official launch of the program in June 2018, the Vaccine Preventable Disease Program began planning, budgeting, and procurement processes with technical and financial support from the Partnership for Influenza Vaccine Introduction, the United States Centers for Disease Control and Prevention, the Bhutan Health Trust Fund, and the World Health Organization. Influenza vaccination for high-risk groups was integrated into Bhutan's routine immunization services in all health care facilities beginning in November 2019 and vaccinated all populations in 2020 in response to the COVID-19 pandemic. Coverage levels between 2019 and 2022 were highest in children aged 6-24 months (62.5%-96.9%) and lowest in pregnant women (47.7%-62.5%). Bhutan maintained high coverage levels despite the COVID-19 pandemic by continued provision of influenza vaccine services at health centers during lockdowns, conducting communication and sensitization efforts, and using catch-up campaigns. Bhutan's experience with introducing and scaling up the influenza vaccine program contributed to the country's capacity to rapidly deploy its COVID-19 vaccination program in 2021.

WEB: 10.1016/j.vaccine.2023.10.053

IMPACT FACTOR: 5.5

CITED HALF-LIFE: 7.2

START COMMENTARY

In the first year of influenza vaccination introduction in Bhutan, more than 90% of individuals with chronic medical conditions and children 6-24 months of age received the vaccine; nearly 80% of health care workers and persons 65 years and older also received the vaccine. Authors attribute

success of the influenza vaccine program to the establishment of an influenza surveillance system, strong leadership and political commitment, a robust network of health infrastructure, and community trust in public health immunization services. Challenges identified included difficulty with data collection, inventory reporting, and adverse event reporting, which led to the creation of the Bhutan Vaccine System in 2021.

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11. Estimating the global impact of rotavirus vaccines on child mortality.

Clark A, Mahmud S, Debellut F, Pecenka C, Jit M, Perin J, et al.

Int J Infect Dis. 2023 Dec 04;137:90-97.
PubMed ID: 37863311

ABSTRACT

OBJECTIVES: We estimated the global impact of rotavirus vaccines on deaths among children under five years old by year.

METHODS: We used a proportionate outcomes model with a finely disaggregated age structure to estimate rotavirus deaths prevented by vaccination over the period 2006-2019 in 186 countries. We ran deterministic and probabilistic uncertainty analyses and compared our estimates to surveillance-based estimates in 20 countries.

RESULTS: We estimate that rotavirus vaccines prevented 139,000 under-five rotavirus deaths (95% uncertainty interval 98,000-201,000) in the period 2006-2019. In 2019 alone, rotavirus vaccines prevented 15% (95% uncertainty interval 11-21%) of under-five rotavirus deaths (0.5% of child mortality). Assuming global use of rotavirus vaccines and coverage equivalent to other co-administered vaccines could prevent 37% of under-five rotavirus deaths (1.2% of child mortality). Our estimates were sensitive to the choice of rotavirus mortality burden data and several vaccine impact modeling assumptions. The World Health Organization's recommendation to remove age restrictions in 2012 could have prevented up to 17,000 rotavirus deaths in the period 2013-2019. Our modeled estimates of rotavirus vaccine impact were broadly consistent with estimates from post-vaccination surveillance sites.

CONCLUSION: Rotavirus vaccines have made a valuable contribution to global public health. Enhanced rotavirus mortality prevention strategies are needed in countries with high mortality in under-5-year-old children.

WEB: 10.1016/j.ijid.2023.10.005
IMPACT FACTOR: 8.4
CITED HALF-LIFE: 2.6

START COMMENTARY

Despite the demonstrated impact of live oral rotavirus vaccines on rotavirus gastroenteritis (RVGE) mortality, Clark et al. found that the maximum effect of these vaccines on rotavirus gastroenteritis (RVGE) deaths is likely 40% or lower due to lower vaccine efficacy in LMICs, where most RVGE deaths occur. However, their model does not account for indirect benefits, and authors note a recent

study that estimated a 49% reduction of RVGE mortality in a model that included herd immunity. They stress the importance of continued disease prevention and treatment strategies to supplement vaccine efforts to more fully address RVGE mortality.

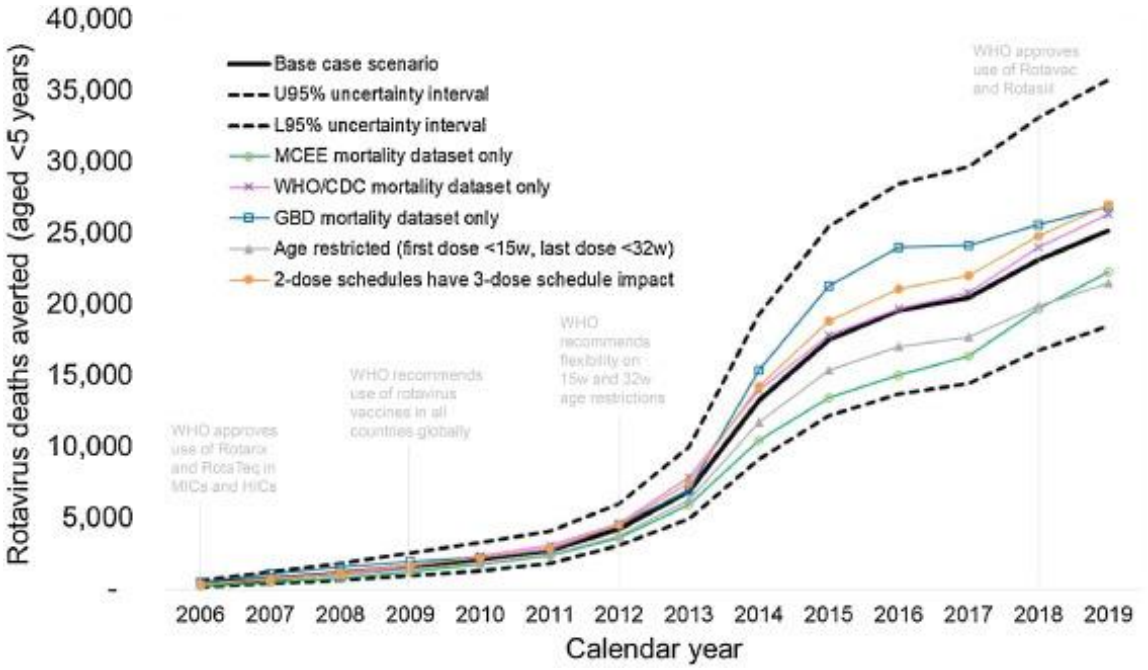

Figure 3: The number of RVGE deaths averted by rotavirus vaccination in 186 countries by year: base case (95% uncertainty interval) and alternative scenarios. Abbreviations: GBD, Global Burden of Disease Study; MCEE, Maternal and Child Epidemiology Estimation Group.
95% uncertainty intervals are based on 100 probabilistic runs per country and include uncertainty in the population aged <5 years, RVGE mortality rates aged <5 years, RVGE age distributions, Rotavirus vaccine coverage, timeliness, efficacy, and waning. Deterministic scenarios are also shown for different mortality datasets, an age-restricted scenario and a scenario with higher impact assuming products with 2-dose schedules are assigned the same impact as products with 3-dose schedules.

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12. Progress Toward Measles and Rubella Elimination - Indonesia, 2013-2022.

Chacko S, Kamal M, Hastuti E, Mildya F, Kelyombar C, Voronika V, et al.

MMWR Morb Mortal Wkly Rep. 2023 Oct 25;72(42):1134-1139.
PubMed ID: 3785668137917555

ABSTRACT

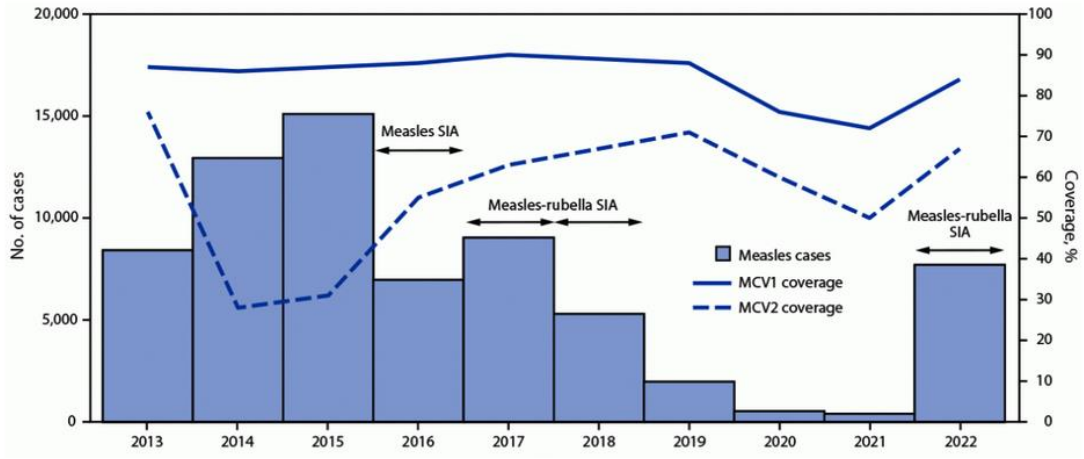
In 2019, Indonesia and the other countries in the World Health Organization South-East Asia Region adopted the goal of measles and rubella elimination by 2023. This report describes Indonesia's progress toward measles and rubella elimination during 2013-2022. During this period, coverage with a first dose of measles-containing vaccine (MCV) decreased from 87% to 84%, and coverage with a second MCV dose decreased from 76% to 67%. After rubella vaccine was introduced in 2017, coverage with the first dose of rubella-containing vaccine increased approximately fivefold, from 15% in 2017 to 84% in 2022. During 2013-2021, annual reported measles incidence decreased by 95%, from 33.2 to 1.4 cases per million population; reported rubella incidence decreased 89%, from 9.3 to 1.0 cases per million population. However, a large surge in measles and rubella cases occurred in 2022, with a reported measles incidence of 29 cases per million and a reported rubella incidence of 3 per million, primarily related to disruption in immunization services caused by the COVID-19 pandemic. In 2022, approximately 26 million children (an estimated 73% of the target population) received a combined measles- and rubella-containing vaccine during supplementary immunization activities completed in 32 provinces. Progress toward measles and rubella elimination in Indonesia has been made; however, continued and urgent efforts are needed to restore routine immunization services that were adversely affected by the COVID-19 pandemic and close immunity gaps to accelerate progress toward measles and rubella elimination.

WEB: 10.15585/mmwr.mm7242a2
IMPACT FACTOR: 33.9
CITED HALF-LIFE: 2.7

START COMMENTARY

In addition to reporting increased measles and rubella cases in 2022, Chacko, et al. note that only 43% of specimens collected from suspected cases in Indonesia were tested within 4 days of receipt by the laboratory and 30% of laboratory results were submitted to the immunization program more than 4 days after specimen receipt; this lag in testing and reporting could delay public health response to measles cases. Of the patients with laboratory-confirmed or epidemiologically linked measles cases, 88% had not received a measles-containing vaccine or had an unknown vaccination history.

Figure 1 shows the number of reported measles cases, estimated percentage of children who received their first (MCV1) and second (MCV2) dose of measles-containing vaccine, and timing of supplementary immunization activities (SIAs) by year in Indonesia.



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13. Engagement of community health workers to improve immunization coverage through addressing inequities and enhancing data quality and use is a feasible and effective approach: An implementation study in Uganda.

Bakkabulindi P, Ampeire I, Ayebale L, Mubiri P, Feletto M, Muhumuza S.

PLoS One. 2023 Oct 24;18(10):e0292053.

PubMed ID: 37856451

ABSTRACT

BACKGROUND: Uganda, like many other developing countries, faces the challenges of unreliable estimates for its immunization target population. Strengthening immunization data quality and its use for improving immunization program performance are critical steps toward improving coverage and equity of immunization programs. The goal of this study was to determine the effectiveness of using community health workers (CHWs) to obtain quality and reliable data that can be used for planning and evidence-based response actions.

METHODS: An implementation study in which 5 health facilities were stratified and randomized in two groups to (i) receive a package of interventions including monthly health unit immunization data audit meetings, and defaulter tracking and linkage and (ii) to serve as a control group was conducted between July and September 2020. Immunization coverage of infants in both arms was determined by a review of records three months before and after the study interventions. In addition, key informant and in-depth interviews were conducted among facility-based health workers and CHWs respectively, at the endline to explore the feasibility of the interventions.

RESULTS: Overall, a total of 2,048 children under one year eligible for immunization were registered in Bukabooli sub-county by CHWs as compared to the estimated district population of 1,889 children representing a moderate variance of 8.4%. The study further showed that it is feasible to use CHWs to track and link defaulters to points of immunization services as more than two-thirds (68%) of the children defaulting returned for catch-up immunization services. At the endline, immunization coverage for the Oral Polio Vaccine third dose; Rotavirus vaccine second dose; Pneumococcal Conjugate Vaccine third dose increased in both the intervention and control health facilities. There was a decrease in coverage for the Measles-Rubella vaccine decreased in the intervention health facilities and a decrease in Bacillus Calmette-Guérin vaccine coverage in the control facilities. Difference in difference analysis demonstrated that the intervention caused a significant 35.1% increase in coverage of Bacillus Calmette-Guérin vaccine (CI 9.00-61.19; $p<0.05$)). The intervention facilities had a 17.9% increase in DTP3 coverage compared to the control facilities (CI: 1.69-34.1) while for MR, OPV3, and Rota2 antigens, there was no significant effect of the intervention.

CONCLUSION: The use of CHWs to obtain reliable population estimates is feasible and can be useful in areas with consistently poor immunization coverage to estimate the target population. Facilitating monthly health unit immunization data audit meetings to identify, track, and link defaulters to immunization services is effective in increasing immunization coverage and equity.

WEB: 10.1371/journal.pone.0292053
IMPACT FACTOR: 3.7
CITED HALF-LIFE: 7.3

START COMMENTARY

Bakkabulindi, et al. found that benefits of house-to-house registration reported by community health workers (CHWs) in key informant interviews included the opportunity it gave them to get to know their community better. This face-to-face contact allowed CHWs to identify vaccine hesitant households and children who had missed immunizations, died, relocated, or were critically ill. They also reported that home visits allowed them to reach hard-to-reach households, improving outreach to vulnerable populations. Those in the intervention group reported that monthly meetings provided opportunities to discuss how to communicate with families and provided an opportunity to track which children had caught up on vaccines since the last home visit and which children were still under-immunized, allowing for appropriate follow-up by the CHW.

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14. Global regulatory reforms to promote equitable vaccine access in the next pandemic.

Mahoney R, Hotez P, Bottazzi M.

PLOS Glob Public Health. 2023 Oct 21;3(10):e0002482.

PubMed ID: 37851688

ABSTRACT

There is broad consensus that the global response to the Covid-19 pandemic was inadequate, leading to unacceptable levels of avoidable morbidity and mortality. Three strategic missteps led to the lack of equitable vaccine access: The heavy reliance on commercial vaccine manufacturers in high-income countries (HICs) versus low- and middle-income countries (LMICs); the emergence of vaccine nationalism restricting and delaying the supply of vaccines to LMICs; and an inadequate support or recognition for LMIC national regulatory authorities. To avoid these inequities in a future pandemic, we focus on three successful vaccine development and technology transfer case studies-the Hepatitis B vaccine produced in South Korea in the 1980s; the Meningitis A vaccine for Africa led by Program for Appropriate Technologies in Health (PATH) and the World Health Organization (WHO) in the 2000s; and a recombinant SARS CoV-2 protein-based vaccine technology from the Texas Children's Hospital transferred to India and to Indonesia. In addition to expanding support for academic or non-profit product development partnerships, our analysis finds that an essential step is the strengthening of selected LMIC regulatory systems to become Stringent Regulatory Authorities (SRAs), together with a re-prioritization of the WHO Prequalification (PQ) system to ensure early vaccine availability in LMICs especially during pandemics. Advancing LMIC National Regulatory Authorities (NRAs) to Stringent Regulatory Authorities (SRAs) status will require substantial resources, but the benefits for future pandemic control and for health in LMIC would be immense. We call on the WHO, United Nation (UN) agencies and SRAs, to collaborate and implement a comprehensive roadmap to support LMIC regulators to achieve stringent status by 2030.

WEB: 10.1371/journal.pgph.0002482

IMPACT FACTOR: N/A

CITED HALF-LIFE: N/A

START COMMENTARY

Mahoney, et al. identified three key lessons from the three case studies included in this article for future vaccine development to meet the needs of LMICs. The first is use of expertise and resources from academic-based or non-profit organizations. The second is direct technology transfer in a non-proprietary manner to country vaccine manufacturers in developing countries to enable the production of low-price vaccines. The third is the need to strengthen national and international

regulatory systems to accelerate approval of vaccines for human use in the country where the vaccine is manufactured and in other developing countries. They found that the biggest obstacle was the type of national regulatory framework available for each LMIC manufacturer and the hurdles of obtaining WHO Prequalification from the World Health Organization.

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15. Post-epidemic health system recovery: A comparative case study analysis of routine immunization programs in the Republics of Haiti and Liberia.

Ravi S, Potter C, Paina L, Merritt M.

PLoS One. 2023 Oct 23;18(10):e0292793.

PubMed ID: 37847680

ABSTRACT

Large-scale epidemics in resource-constrained settings disrupt delivery of core health services, such as routine immunization. Rebuilding and strengthening routine immunization programs following epidemics is an essential step toward improving vaccine equity and averting future outbreaks. We performed a comparative case study analysis of routine immunization program recovery in Liberia and Haiti following the 2014-16 West Africa Ebola epidemic and 2010s cholera epidemic, respectively. First, we triangulated data between the peer-reviewed and grey literature; in-depth key informant interviews with subject matter experts; and quantitative metrics of population health and health system functioning. We used these data to construct thick descriptive narratives for each case. Finally, we performed a cross-case comparison by applying a thematic matrix based on the Essential Public Health Services framework to each case narrative. In Liberia, post-Ebola routine immunization coverage surpassed pre-epidemic levels, a feat attributable to investments in surveillance, comprehensive risk communication, robust political support for and leadership around immunization, and strong public-sector recovery planning. Recovery efforts in Haiti were fragmented across a broad range of non-governmental agencies. Limitations in funding, workforce development, and community engagement further impeded vaccine uptake. Consequently, Haiti reported significant disparities in subnational immunization coverage following the epidemic. This study suggests that embedding in-country expertise within outbreak response structures, respecting governmental autonomy, aligning post-epidemic recovery plans and policies, and integrating outbreak response assets into robust systems of primary care contribute to higher, more equitable levels of routine immunization coverage in resource-constrained settings recovering from epidemics.

WEB: 10.1371/journal.pone.0292793

IMPACT FACTOR: 3.7

CITED HALF-LIFE: 7.3

START COMMENTARY

Ravi, et al. discussed facilitators and barriers to routine immunization program recovery following major epidemics using Haiti and Liberia as examples. They advise that political leaders and health authorities should focus on long-term planning to ensure alignment between budgets, plans, and routine immunization programs. Leaders should also treat routine immunization and community

health systems as critical national priorities requiring sustained investment and should prioritize strengthening linkages between health system components. They also suggest improving compensation structures and working conditions for the healthcare workforce. The authors state that donors and other stakeholders should incorporate local experts and leadership into their efforts, support and promote country ownership of domestic health programs, and work with political leaders to support long-term budget and policy planning for routine immunization and community health.
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Additional Articles of Interest

1 Reminder design and childhood vaccination coverage. {Full Article}
2 Ethnic inequities in routine childhood vaccinations in England 2006-2021: an observational cohort study using electronic health records. {Full Article}
3 Effect evaluation of rubella knowledge attitudes and practices (KAP) intervention on parents of 0 to 2 year old children in Chongqing, China. {Full Article}
4 The faces behind vaccination: unpacking the attitudes, knowledge, and practices of staff of Cameroon's Expanded program on Immunization. {Full Article}
5 Vaccination compliance of selected childhood immunization programs and the socio-determinant factors in Nigeria. {Full Article}
6 The Brazilian vaccine divide: How some municipalities were left behind in the Covid-19 vaccine coverage. {Full Article}
7 Characterizing attitudes toward maternal RSV vaccines among pregnant and lactating persons in Kenya: Key considerations for demand generation efforts for vaccine acceptance. {Full Article}
8 Vaccination dropout and wealth related inequality among children aged 12-35 months in remote and underserved settings of Ethiopia: a cross-sectional evaluation survey. {Full Article}
9 HPV immunization in Brazil and proposals to increase adherence to vaccination campaigns. {Full Article}
10 Health and economic effects of introducing single-dose or two-dose human papillomavirus vaccination in India. {Full Article}
11 Education components of school vaccine mandates: An environmental scan. {Full Article}
12 Gaps in vaccine management practices during vaccination outreach sessions in rural settings in southwestern Uganda. {Full Article}
13 Attitudes About the Human Papillomavirus Vaccine Among Patients With and Without Cervical Dysplasia. {Full Article}
14 Association between women's experience of domestic violence and childhood vaccination in West Africa: Cross-sectional analysis of Demographic and Health Survey data. {Full Article}
15 "Messengers matter": Assessing the impact of racially concordant care on vaccine hesitation. {Full Article}
16 Prevalence and factors associated with immunization coverage among children under five years in Mohamed Mooge health center, Hargeisa, Somaliland: a cross-sectional study. {Full Article}
17 Implementing the free HPV vaccination for adolescent girls aged below 14 in Shenzhen, Guangdong Province of China: experience, challenges, and lessons. {Full Article}
18 Factors Influencing HPV Vaccine Intentions in Malaysian Men Who Have Sex with Men: A Cross-Sectional Study in Malaysia. {Full Article}

19 Assessment of immunization session practices in primary health care centers in Al-Najaf province. {Full Article}
20 Vaccination coverage of triple viral and poliomyelitis in Brazil, 2011-2021: temporal trend and spatial dependency. {Full Article}
21 Spatial distribution and determinants of tetanus toxoid immunization among pregnant women in Ethiopia using data from Ethiopian demographic and health survey 2016. {Full Article}
22 Barriers to and facilitators of human papillomavirus vaccination in an ethnically diverse group of migrant parents: A qualitative mixed methods study. {Full Article}
23 Age, gender and socioeconomic disparities in human papillomavirus (HPV) awareness and knowledge among Japanese adults after a 7-year suspension of proactive recommendation for the HPV vaccine: A nationally representative cross-sectional survey. {Full Article}
24 Cost-effectiveness analysis of Japanese Encephalitis (JE) vaccination program in Bali Province, Indonesia. {Full Article}
25 Multicomponent Strategy Improves Human Papillomavirus Vaccination Rates Among Adolescents with Sickle Cell Disease. {Full Article}
26 Analysis of the impact of COVID-19 pandemic and response on routine childhood vaccination coverage and equity in Northern Nigeria: a mixed methods study. {Full Article}
27 Understanding multilevel barriers to childhood vaccination uptake among Internally Displaced Populations (IDPs) in Mogadishu, Somalia: a qualitative study. {Full Article}
28 The Impact of Social Media on Vaccination: A Narrative Review. {Full Article}
29 Web-based intervention for improving influenza vaccination in pregnant women: a cost-effectiveness analysis. {Full Article}
30 Accelerating into Immunization Agenda 2030 with momentum from China's successful COVID-19 vaccination campaign during dynamic COVID Zero. {Full Article}
31 Influence of women empowerment on childhood (12-23 months) immunization coverage: Recent evidence from 17 sub-Saharan African countries. {Full Article}
32 Cost and operational context for national human papillomavirus (HPV) vaccine delivery in six low- and middle-income countries. {Full Article}
33 Childhood vaccine refusal and what to do about it: a systematic review of the ethical literature. {Full Article}
34 Supporting the Manufacturing of Medical Supplies in Africa: Collaboration Between Africa CDC, Partners, and Member States. {Full Article}

Appendix

The literature search for the December 2023 Vaccine Delivery Research Digest was conducted on November 21, 2023. We searched English language articles indexed by the US National Library of Medicine and published between October 15, 2023 and November 14, 2023. The search resulted in 406 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]) (“2023/15/10”[PDAT] : “2023/14/11”[PDAT]))