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1. Key lessons learned from the immunization supply chain of Malawi, an African country using EVM2.0.

Sethy G, Nenani Chisema M, Sharma L, Folorunso O, Haile D, Reda Berri Z, et al.

Vaccine X. 2022 Nov 22;12:100239.
PubMed ID: 36407821

ABSTRACT

OBJECTIVES: A country's immunization system's effectiveness depends on its supply chain's efficacy. To assess the challenges of maintaining an efficient vaccine supply chain, Malawi conducted its assessment using The EVM2.0 tool (Effective Vaccine Management).

METHODS: It is a cross-sectional study in which all EVM requirements were assessed between September and October 2021. Data were collected from eighty-two randomly selected sites using the site selection tool of the EVM. Data were entered into the EVM assessment tool 2.0 version 1.12 for analysis. This tool generates performance indicators and criteria scores for assessed sites, compared with a WHO minimum score of 80%.

RESULTS: Overall criteria scores across all levels of the immunization supply chain showed a statistically significant mean difference of 5.92 (t = 2.58, P = 0.02). Comparative overall mean criteria scores across different levels of the immunization supply chain showed no statistically significant difference for primary (p = 0.76), sub-national (p = 0.69), and lowest distribution stores (p = 0.12). However, a substantial gap was found in the overall mean scores of the health facility's service point (SP) (t = 4.12, P = 0.001). The overall category scores across all immunization supply chain levels did not show a statistically significant difference. However, among individual category scores, Infrastructure (76 %), Equipment (67 %), Policies and procedures (62 %), Financial (47 %), and Resources (64 %) were found to be below the WHO minimum score.

CONCLUSION: Though the 2021 Malawi EVM assessment findings are promising, they still identified the gaps to be improved to ensure the vaccine availability in the right amount, at the right time, and at the right cost.

WEB: 10.1016/j.jvacx.2022.100239
IMPACT FACTOR: 0.64
CITED HALF-LIFE: 2.2

START COMMENTARY

In this cross-sectional study, Sethy *et al.* quantitatively measures effectiveness of the supply chain, which is critical for a successful immunization system. This study was conducted using the Effective Vaccine Management, an approach launched by the WHO/UNICEF in 2010 to benchmark country supply chains against global standards. This study specifically used the EVM2.0, which is an improved and updated mobile EVM with 13 criteria. In total, 82 sites were randomly selected.

Table 3 and *Figure 1* show the comparative criteria scores across different levels of the supply chain in 2020. The highest score was in the temperature management criteria and the lowest was in the immunization supply chain performance monitoring. Sethy *et al.* used a t-test to assess the difference between the criteria score and the WHO minimum score (score of 80), which found statistically significant differences, indicating that improvement is required across the following criterium: vaccine arrivals, storage and transport capacity, facility infrastructure/equipment, maintenance and repair, stock management, distribution of vaccines and dry goods, annual work planning, supportive supervision, and immunization supply chain performance monitoring. *Table 4* and *Figure 2* present the comparative category scores on different levels of the immunization supply chain (e.g., infrastructure; equipment; human resources). The highest overall score was in human resources (score of 91) and the lowest was in financial resources (score of 47). Infrastructure, equipment, policies/procedures, financial resources, and resources overall were below the WHO minimum score. Overall, this study demonstrates that Malawi has made substantial progress but needs to improve certain components of the supply chain to meet international standards.

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2. Improving routine childhood immunisation outcomes in low-income and middle-income countries: an evidence gap map.

Engelbert M, Jain M, Bagai A, Parsekar S.

BMJ Open. 2022 Nov 16;12(11):e058258.
PubMed ID: 36356993

ABSTRACT

OBJECTIVE: To support evidence-informed decision-making, we created an evidence gap map to characterise the evidence base on the effectiveness of interventions in improving routine childhood immunisation outcomes in low-income and middle-income countries (LMICs).

METHODS: We developed an intervention-outcome matrix with 38 interventions and 43 outcomes. We searched academic databases and grey literature sources for relevant impact evaluations (IEs) and systematic reviews (SRs). Search results were screened on title/abstract. Those included on title/abstract were retrieved for full review. Studies meeting the eligibility criteria were included and data were extracted for each included study. All screening and data extraction was done by two independent reviewers. We analysed these data to identify trends in the geographic distribution of evidence, the concentration of evidence across intervention and outcome categories, and attention to vulnerable populations in the literature.

RESULTS: We identified 309 studies, comprising 226 completed IEs, 58 completed SRs, 24 ongoing IEs and 1 ongoing SR. Evidence from IEs is heavily concentrated in a handful of countries in sub-Saharan Africa and South Asia. Among interventions, the most frequently evaluated are those related to education and material incentives for caregivers or health workers. There are gaps in the study of non-material incentives and outreach to vulnerable populations. Among outcomes, those related to vaccine coverage and health are well covered. However, evidence on intermediate outcomes related to health system capacity or barriers faced by caregivers is much more limited.

CONCLUSIONS: There is valuable evidence available to decision-makers for use in identifying and deploying effective strategies to increase routine immunisation in LMICs. However, additional research is needed to address gaps in the evidence base.

WEB: 10.1136/bmjopen-2021-058258
IMPACT FACTOR: 2.496
CITED HALF-LIFE: 3.5

START COMMENTARY

In this review, *Engelbert et al.* synthesized published data from academic databases and grey literature supporting routine childhood immunization outcomes in low-income and middle-income countries (LMICs). Authors developed a theory of change to conceptualize the contributing factors of completed vaccinations among children (*Figure 1)*. This theory of change includes categories of programs targeted toward improving immunization coverage of children at the following levels: caregiver/community subgroup, provider, health system, and non-health infrastructure and policy. These categories of interventions are connected to specific outcomes of including behavioral, social, and practical factors, delivery of vaccination services, vaccination coverage, and health outcomes (*Figure 2*). Interventions included in this review span 85 countries, and include 309 studies, with the most robust body of evidence found in sub-Saharan Africa (95 impact evaluations) and South Asia (75 impact evaluations).

The purpose of this review was not to determine coverage of immunization activities, but instead, to present the areas of evidence for these activities, map the interventions and outcomes by geography, and assess the quality of evidence. Authors found the most common interventions represented in the literature to be material incentives for caregivers, health system strategic planning, pay-for-performance schemes, and health worker training and education (*Figure 5)*. The most common outcome used to assess interventions was overwhelmingly vaccination coverage, with 210 impact evaluations and 52 systematic reviews examining vaccination coverage (*Figure 6*). Though far less common, health outcomes were also measured (38 impact evaluations and 14 systematic reviews). Additionally, the inclusion of attention to equity was assessed for included studies (*Figure 10)*. Authors identified four categories of vulnerable populations: socioeconomic status (SES), hard to reach populations, sex of child, and maternal education; SES was the most measured (35 impact evaluations). This paper provides a broad overview of interventions for improving childhood immunization coverage and show that data is distributed unequally across geographies, and highlighted gaps in evidence for some coverage areas. Additionally, evidence provide justification for more research on equity in immunization and intermediate outcomes.

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3. Spatial distribution of rotavirus immunization coverage in Ethiopia: a geospatial analysis using the Bayesian approach.

Atalell K, Liyew A, Alene K.

BMC Infect Dis. 2022 Nov 11;22(1):830.

PubMed ID: 36352357

ABSTRACT

INTRODUCTION: Rotavirus causes substantial morbidity and mortality every year, particularly among under-five children. Despite Rotavirus immunization preventing severe diarrheal disease in children, the vaccination coverage remains inadequate in many African countries including Ethiopia. Measuring rotavirus immunization coverage in a lower geographic area can provide information for designing and implementing a targeted immunization campaign. This study aimed to investigate the spatial distributions of rotavirus immunization coverage in Ethiopia.

METHODS: Rotavirus immunization coverage data were obtained from the recent Ethiopian Demographic and Health Survey (EDHS 2019). Covariate data were assembled from different publicly available sources. A Bayesian geostatistics model was used to estimate the national rotavirus immunization coverage at a pixel level and to identify factors associated with the spatial clustering of immunization coverages.

RESULT: The national rotavirus immunization coverage in Ethiopia was 52.3% (95% CI: 50.3, 54.3). The immunization coverage varied substantially at the sub-national level with spatial clustering of low immunization coverage observed in the Eastern, Southeastern, and Northeastern parts of Ethiopia. The spatial clustering of the rotavirus immunization coverage was positively associated with altitude of the area [mean regression coefficient (β): 0.38; 95% credible interval (95% CrI): 0.18, 0.58] and negatively associated with travel time to the nearest cities in minutes [mean regression coefficient (β): - 0.45; 95% credible interval (95% CrI): (- 0.73, - 0.18)] and distance to the nearest health facilities [mean regression coefficient (β): - 0.71908; 95% credible interval (95% CrI): (- 1.07, - 0.37)].

CONCLUSIONS: This study found that the rotavirus immunization coverage varied substantially at sub-national and local levels in Ethiopia. The spatial clustering of rotavirus immunization coverage was associated with geographic and healthcare access factors such as altitude, distance to health facilities, and travel time to the nearest cities. The immunization program should be strengthened in Ethiopia, especially in the Eastern, Southeastern, and Northeastern parts of the Country. Outreach immunization services should be also implemented in areas with low coverage.

WEB: 10.1186/s12879-022-07825-1
IMPACT FACTOR: 2.688
CITED HALF-LIFE: 5.0

START COMMENTARY

Atalell *et al.* investigate the spatial distribution and drivers of rotavirus coverage in Ethiopia. This study makes an important contribution as an understanding of immunization coverage on a subnational level can inform targeted efforts to increase rotavirus coverage. Data from this study was obtained from several existing sources; the mini-Ethiopian demographic and health survey (MEDHS-2019) provided rotavirus immunization coverage at a pixel level. The central statistical agency of Ethiopia provided administrative boundary shape files and the WorldClim website provided climate variables including mean annual precipitation and temperature. Population data was obtained from WorldPop whereas travel time to health facilities was obtained from the Malaria Atlas Program. The outcome variable was full rotavirus immunization.

Key findings indicate that the national full immunization coverage was an estimated 52.3% (95% confidence Interval [CI]: 50.3-54.3) although there were substantial variations at regional levels. *Table 1* presents the rotavirus dose 1 and dose 2 coverage by region. High covered was observed in the following regions: Central, Northern and Northwestern. Low coverage was shown in several regions (Southern, Southeastern, and Eastern), presented in *Figure 1. Figure 2* shows the predicted map of immunization coverage using the Bayesian geospatial model. Altitude, population density, and distance to health facilities were statically significant spatial drivers of immunization factors. Altitude was positively associated with immunization coverage (β [mean regression coefficient]: 0.38, 95% CI: 0.18-0.58); travel time to the nearest city and distance to health facilities were both negatively associated (β= - 0.45, 95% Credible Interval: -0.73, -0.18, and β= - 0.719, 95% Credible Interval -1.07, -0.37, respectively). Overall, this study provides critical insight on the areas and factors which should be targeted in future rotavirus immunization implementation.

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4. Feasibility of novel adult tuberculosis vaccination in South Africa: a cost-effectiveness and budget impact analysis.

Jayawardana S, Weerasuriya C, Pelzer P, Seeley J, Harris R, Tameris M, et al.

NPJ Vaccines. 2022 Nov 16;7(1):138.

PubMed ID: 36344523

ABSTRACT

Early trials of novel vaccines against tuberculosis (TB) in adults have suggested substantial protection against TB. However, little is known about the feasibility and affordability of rolling out such vaccines in practice. We conducted expert interviews to identify plausible vaccination implementation strategies for the novel M72/AS01E vaccine candidate. The strategies were defined in terms of target population, coverage, vaccination schedule and delivery mode. We modelled these strategies to estimate long-term resource requirements and health benefits arising from vaccination over 2025-2050. We presented these to experts who excluded strategies that were deemed infeasible, and estimated cost-effectiveness and budget impact for each remaining strategy. The four strategies modelled combined target populations: either everyone aged 18-50, or all adults living with HIV, with delivery strategies: either a mass campaign followed by routine vaccination of 18-year olds, or two mass campaigns 10 years apart. Delivering two mass campaigns to all 18-50-year olds was found to be the most cost-effective strategy conferring the greatest net health benefit of 1.2 million DALYs averted having a probability of being cost-effective of 65-70%. This strategy required 38 million vaccine courses to be delivered at a cost of USD 507 million, reducing TB-related costs by USD 184 million while increasing ART costs by USD 79 million. A suitably designed adult TB vaccination programme built around novel TB vaccines is likely to be cost-effective and affordable given the resource and budget constraints in South Africa.

WEB: 10.1038/s41541-022-00554-1

IMPACT FACTOR: 5.699

CITED HALF-LIFE: 2.0

START COMMENTARY

In this modelling analysis, *Jayawardana et al.* assess the feasibility and affordability of potential implementation strategies of a novel tuberculosis (TB) vaccine. The current vaccine, bacille Calmette-Guérin (BCG), is a key part of neonatal vaccinations in areas where TB is common, however, efficacy wanes in adulthood, resulting in adults bearing most of global TB burden. In phase II trials, a vaccine candidate, M72/AS01$_E$, demonstrated 50% efficacy in preventing pulmonary tuberculosis disease in *Mycobacterium tuberculosis*-infected 18–50 year olds and is now being assessed in phase III trial as an adjunct to neonatal BCG.

This study utilized interviews with experts to identify vaccine implementation strategies in South Africa, ensuring feasibility and preferences of country decision makers are reflected in modelling scenarios. Two strategies were included in the vaccine scenarios assessed: 1) one mass vaccination campaign with annual vaccination of those aged 18, or 2) two mass campaigns in 2025 and 2035. Both strategies were assessed among two target populations: all aged 18 – 50, or all adults living with HIV (PLHIV). The four resulting vaccine scenarios were modelled to estimate costs and health benefits from 2025 to 2050.

The four vaccine implementation scenarios were evaluated for epidemiologic impact (e.g., TB prevalence, TB mortality, vaccines delivered, TB treatment initiation) and costs (e.g., ART costs, total costs), as compared to baseline (*Figure 1*). Mass vaccination among those aged 18 – 50 (2025 and 2030) was most cost-effective, followed by the scenario of two vaccination campaigns among PLHIV (2025 and 2030). The two strategies involving annual routine vaccination had a 0% probability of being the most cost-effective option based on the health care opportunity cost threshold. Overall, this analysis provides important insight on implementation of novel TB vaccines in South Africa.

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5. Routine Vaccination Coverage - Worldwide, 2021.

Rachlin A, Danovaro-Holliday M, Murphy P, Sodha S, Wallace A.

MMWR Morb Mortal Wkly Rep. 2022 Nov 07;71(44):1396-1400.
PubMed ID: 36327156

ABSTRACT

In 2020, the World Health Assembly endorsed the Immunization Agenda 2030, an ambitious global immunization strategy to reduce morbidity and mortality from vaccine-preventable diseases (1). This report updates a 2020 report (2) with global, regional,* and national vaccination coverage estimates and trends through 2021. Global estimates of coverage with 3 doses of diphtheria-tetanus-pertussis-containing vaccine (DTPcv3) decreased from an average of 86% during 2015-2019 to 83% in 2020 and 81% in 2021. Worldwide in 2021, 25.0 million infants (19% of the target population) were not vaccinated with DTPcv3, 2.1 million more than in 2020 and 5.9 million more than in 2019. In 2021, the number of infants who did not receive any DTPcv dose by age 12 months (18.2 million) was 37% higher than in 2019 (13.3 million). Coverage with the first dose of measles-containing vaccine (MCV1) decreased from an average of 85% during 2015-2019 to 84% in 2020 and 81% in 2021. These are the lowest coverage levels for DTPcv3 and MCV1 since 2008. Global coverage estimates were also lower in 2021 than in 2020 and 2019 for bacillus Calmette-Guérin vaccine (BCG) as well as for the completed series of Haemophilus influenzae type b vaccine (Hib), hepatitis B vaccine (HepB), polio vaccine (Pol), and rubella-containing vaccine (RCV). The COVID-19 pandemic has resulted in disruptions to routine immunization services worldwide. Full recovery to immunization programs will require context-specific strategies to address immunization gaps by catching up missed children, prioritizing essential health services, and strengthening immunization programs to prevent outbreaks (3).

WEB: 10.15585/mmwr.mm7144a2
IMPACT FACTOR: 13.606
CITED HALF-LIFE: 4.4

START COMMENTARY

In this report, *Rachlin et al.* provide updated global, region, and national vaccination coverage estimates to support the World Health Assembly supported Immunization Agenda 2030. Coverage estimates for 194 World Health Organization Member States are provided across 13 different vaccinations. Coverage was estimated through a range of methods, including administrative (number of vaccine doses administered divided by the target population), surveys (interviews with representative sample of households), and in some cases, extrapolation using previously reported

data (representing just 6% of the global birth cohort). *Table 1* presents 2021 vaccination coverage for each vaccine (BCG, DTP, HepB, Hib3, HPV, MCV, PCV, Pol, RCV, Rota) by WHO region. Vaccines with the lowest coverage, as determined by the inclusion of a vaccine in a country's vaccine schedule, were HPV (based on last dose given among females) and Rota (number of doses to complete the series varies), which were included in 60% and 61% of country vaccine schedules, respectively.

Figure 1 and *Table 2* present estimates of zero-dose children and the estimated coverage with first and third dose of DTP from 2015, 2019, 2020, and 2021. Number of zero-dose children was highest in the WHO African region across all years. Additionally, number of zero-dose children increased across all regions (apart from the Eastern Mediterranean region), with the lowest number of zero-dose children in 2019 (apart from the Region of the Americas). Global coverage decreased for the following recommended childhood vaccines from 2019 to 2021: BCG, from 88% to 84%; Hib (completed series), from 73% to 71%; RCV, from 69% to 66%; 3-dose HepB series, from 85% to 80%; HepB birth dose, from 44% to 42%; and the third Pol dose, from 86% to 80%. Additionally, coverage of the first dose of HPV vaccine declined from 20% in 2019 to 15% in 2021.This disruption to routine immunization services worldwide coincide with the COVID-19 pandemic, which led to increased burden on health systems and COVID-19 vaccine delivery. These gaps are particularly felt for the most vulnerable populations, and this updated data highlights the need for increased efforts to address immunization gaps and perform catch-up services.

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6. A Tale of 2 Countries: Implementation of the Cold Chain Equipment Optimization Platform in Guinea and Kenya.

Stammer E, Teklemariam L, Barry A, Millimono R, Chweya A, Danfakha N, et al.

Glob Health Sci Pract. 2022 Nov 02;10(5).

PubMed ID: 36316144

ABSTRACT

In 2016, the Gavi Cold Chain Equipment Optimization Platform (CCEOP) was approved and launched in recognition of the fact that functional cold chain equipment (CCE) is essential to strengthening vaccine supply chains and ultimately achieving Gavi's immunization equity and coverage goals. Through CCEOP, Gavi committed to investing US$250 million between 2016 and 2021 to commission CCE in more than 63,000 facilities to upgrade and expand their CCE footprint while stimulating the market to provide affordable, technologically advanced, and accessible equipment. We present case studies from Guinea and Kenya, both of which received CCEOP support, that highlight 2 ways for countries to prioritize investments and implement activities through a large funding and support mechanism. The studies explore the different ways that each country implemented CCEOP and consider how aspects of leadership and technical capacity influence country priorities and results. They also uncover key lessons on sustainability of a large immunization supply chain effort. The experiences of Guinea and Kenya can help other countries embarking on similarly large health system interventions, especially related to supply chain strengthening and immunization programs. In particular, these experiences offer important lessons in leadership, processes and systems, country ownership, technical capacity, and sustainability.

WEB: 10.9745/GHSP-D-22-00066

IMPACT FACTOR: 3.409

CITED HALF-LIFE: 4.7

START COMMENTARY

In this case study, Stammer *et al.* explores how two countries (Kenya and Guinea) implemented the Gavi Cold Chain Equipment Optimization Platform (CCEOP). The authors explore how technical capacities and leadership influenced implementation and outcomes. This paper is important as it describes experiences of Ministries of Health implementing a large funding and support mechanism to strengthen vaccine supply chains and increase immunization coverage and equity. Other countries can benefit from their experiences and lessons learned. CCEOP was launched in 2016 and included two key approaches: 1) A global-level market-shaping approach to improve the availability of cold chain equipment (CCE); 2) a country-level approach to upgrade and expand CCE. In 2017, Kenya and Guinea received funding to expand and extend their immunization supply chains

through replacements/upgrades of old or inadequate CCE. The table, titled ‘Cold Chain Equipment Optimization Platform Activities in Guinea and Kenya” describes key features and activities for each country. Data for this case study was obtained from a mixed-methods evaluation of CCEOP conducted by the JSI Research and Training Institute.

Stammer *et al.* report planning, implementation, and management of large health system intervention findings for each country. In Guinea, there was strong country leadership from the program management team which contributed to a successful first deployment of CCE in the country; however, this leadership was not as active for the second deployment. In terms of human resource capacity, there were some positive findings (i.e., training on preventative maintenance of equipment), there were some concerns about effectiveness of the training, lack of access to resources for maintenance requests, and differing training/skill level needs of staff. In terms of sustainability, CCEOP contributed to improvements in equipment selection and installation and management. This, along with preventative maintenance, may contribute to long term sustainability. In Kenya, there were strong indicators of leadership and country ownership, which contributed to successful implementation, including by the National Vaccines and Immunization Program, a subnational network of expanded program on immunization (EPI) logisticians and cold chain staff, and the program management term. One concern related to sustainability was the cost of service bundles for CCE. National-level respondents also noted a lack of clarity on what is or is not covered by equipment warranties. These frustrations may have contributed to Kenya’s decision to remove in-country private service bundle providers after the first deployment and replace them with a robust maintenance system. Stammer *et al.* summarize findings and provide a set of recommendations. For example, they state there is a need to set priorities, coordinate with partners, and apply a systems approach (i.e., consideration of complementary activities).

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7. Strengthening vaccination delivery system resilience in the context of protracted humanitarian crisis: a realist-informed systematic review.

Ismail S, Lam S, Bell S, Fouad F, Blanchet K, Borghi J.

BMC Health Serv Res. 2022 Oct 25;22(1):1277.

PubMed ID: 36274130

ABSTRACT

BACKGROUND: Childhood vaccination is among the most effective public health interventions available for the prevention of communicable disease, but coverage in many humanitarian settings is sub-optimal. This systematic review critically evaluated peer-review and grey literature evidence on the effectiveness of system-level interventions for improving vaccination coverage in protracted crises, focusing on how they work, and for whom, to better inform preparedness and response for future crises.

METHODS: Realist-informed systematic review of peer-reviewed and grey literature. Keyword-structured searches were performed in MEDLINE, EMBASE and Global Health, CINAHL, the Cochrane Collaboration and WHOLIS, and grey literature searches performed through the websites of UNICEF, the Global Polio Eradication Initiative (GPEI) and Technical Network for Strengthening Immunization Services. Results were independently double-screened for inclusion on title and abstract, and full text. Data were extracted using a pre-developed template, capturing information on the operating contexts in which interventions were implemented, intervention mechanisms, and vaccination-related outcomes. Study quality was assessed using the MMAT tool. Findings were narratively synthesised.

RESULTS: 50 studies were included, most describing interventions applied in conflict or near-post conflict settings in sub-Saharan Africa, and complex humanitarian emergencies. Vaccination campaigns were the most commonly addressed adaptive mechanism (n = 17). Almost all campaigns operated using multi-modal approaches combining service delivery through multiple pathways (fixed and roving), health worker recruitment and training and community engagement to address both vaccination supply and demand. Creation of collaterals through service integration showed generally positive evidence of impact on routine vaccination uptake by bringing services closer to target populations and leveraging trust that had already been built with communities. Robust community engagement emerged as a key unifying mechanism for outcome improvement across almost all of the intervention classes, in building awareness and trust among crisis-affected populations. Some potentially transformative mechanisms for strengthening resilience in vaccination delivery were identified, but evidence for these remains limited.

CONCLUSION: A number of interventions to support adaptations to routine immunisation delivery in the face of protracted crisis are identifiable, as are key unifying mechanisms (multi-level community engagement) apparently irrespective of context, but evidence remains piecemeal. Adapting these approaches for local system resilience-building remains a key challenge.

WEB: 10.1186/s12913-022-08653-4
IMPACT FACTOR: 1.987
CITED HALF-LIFE: 5.6

START COMMENTARY

In this systematic review, *Ismali et al.* evaluated peer-reviewed and grey literature on the effectiveness of system-level interventions to increase the resilience of vaccination delivery systems and maintain vaccination coverage in humanitarian crises. This paper sought to evaluate vaccine delivery systems in the context of both routine childhood vaccinations and vaccines against vaccine-preventable diseases (VPDs). Within geographies of active conflict, near-post conflict, and complex humanitarian emergencies, effective delivery of routine health services and vaccinations are majorly impeded. The need for strengthening service delivery in these contexts is underlined by recent data that suggests the average length of humanitarian crises worldwide is increasing to least 9 years.

Authors developed a conceptual framework for this review, breaking components into Health System Context (i.e., governance, financing, workforce, products, services, information and intelligence, service users), Mechanisms (i.e., absorption, adaptation, transformation), and outcomes (i.e., primary, secondary) (Figure 1). This framework was used to evaluate the primary outcome of population-level vaccination coverage, and secondarily in vaccination delivery outcomes and system resilience indicators. Interventions were grouped into eight classes: campaigns (n = 17, 34%), multi-dimensional (n = 8, 16%), health financing (n = 7, 14%), service integration (n = 6, 12%), community engagement and mobilization (n = 4, 8%), health information and surveillance (n = 3, 6%), governance and coordination (n = 3, 6%), and health workforce (n = 3, 4%). In these broad intervention categories, adaptive resilience capacities, including vaccination campaigns through supplementary immunization activities (SIAs) were well-supported. Strategies around governance (e.g., engagement with civil military in contexts of insecurity) and workforce interventions (e.g., flexible contracting) are novel, and have the potential to make a large impact, both in for immediate outreach and longer-term systems strengthening through increasing trained workforce and bolstering infrastructure. Some themes were common across papers were strengthening trust among communities, increasing the range of access points, and a stable flow of funding. Especially in contexts with lack of trust in government, engagement with the community through religious leaders and community volunteers is critical. Though many of these papers were informed by polio eradication efforts, which have slightly different strategies than other VPDs, the main finding is clear:

there is no one answer to strengthening vaccine delivery in humanitarian settings, it necessary to include multiple strategies in tandem.

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8. Assessment of the inclusion of vaccination as an intervention to reduce antimicrobial resistance in AMR national action plans: a global review.

van Heuvel L, Caini S, Dückers M, Paget J.

Global Health. 2022 Oct 19;18(1):85.

PubMed ID: 36253789

ABSTRACT

BACKGROUND: Vaccination can reduce antibiotic use by decreasing bacterial and viral infections and vaccines are highlighted in the WHO Global Action Plan on Antimicrobial Resistance (AMR) as an infection prevention measure to reduce AMR. Our study aimed to analyze whether WHO Member States have developed AMR national action plans that are aligned with the Global Action Plan regarding objectives on vaccination.

METHODS: We reviewed 77 out of 90 AMR national action plans available in the WHO library that were written after publication of the Global Action Plan in 2015. Each plan was analyzed using content analysis, with a focus on vaccination and key components as defined by WHO (I. Strategic plan (e.g. goals and objectives), II. Operational plan, III. Monitoring and Evaluation plan).

RESULTS: Vaccination was included in 67 of 77 AMR plans (87%) across all WHO Regions (Africa: n = 13/13, the Eastern Mediterranean: n = 15/16, Europe: n = 10/14, the Americas: n = 8/8, South-East Asia: n = 8/11, and the Western Pacific: n = 13/15). Pneumococcal and influenza vaccination were most frequently highlighted (n = 12 and n = 11). We found indications that vaccination objectives are more often included in AMR plans from higher income countries, while lower income countries more often include specific vaccines. The key WHO components of national action plans were frequently not covered (I. 47% included, II. 57%, III. 40%). In total, 33 countries (43%) included indicators (e.g. strategic objectives) to capture the role of vaccines against AMR.

CONCLUSIONS: While vaccination to reduce AMR is seen as an important global public health issue by WHO, there appears to be a gap in its adoption in national AMR plans. Country income levels seem to influence the progress, implementation and focus of national action plans, guided by a lack of funding and prioritization in developing countries. To better align the global response to AMR, our review suggests there is a need to update national action plans to include objectives on vaccination with more focus on specific vaccines that impact antibiotic use.

WEB: 10.1186/s12992-022-00878-6

IMPACT FACTOR: 10.427

CITED HALF-LIFE: 3.3

START COMMENTARY

In this review, *Heuvel et al.* analyzed Antimicrobial Resistance (AMR) national action plans among WHO Member States to assess alignment with the WHO Global Action Plan on AMR, which includes vaccinations a key component. In 2015, WHO was among the first to include vaccination as an appropriate strategy in reducing AMR burden globally, and in 2020, WHO published a framework "Leveraging Vaccines to Reduce Antibiotic Use and Prevent AMR" which encouraged increased update of Influenza, Pneumococcal vaccines, Typhoid vaccines, and *Haemophilus Influenzae* type B (Hib) vaccines. This study focusing on the inclusion of PVC, TCV, Hib vaccines, influenza vaccines, rotavirus, and measles vaccines, screening 77/90 AMR national action plans.

Countries of all income levels were included (LIC: n = 9, LMIC: n = 24, UMIC: n = 20, and HIC: n = 24), as were countries from every WHO region. Overall, 87% of national action plans included mention of vaccination as a strategy, and seventeen countries included information on the effect of specific vaccines on AMR (*Figure 2*). All LIC countries included vaccination in their national plan, but only one (Afghanistan) mentioned of specific vaccines. *Table 5* summarizes the components of vaccine interventions included in national action plans published after 2016 (n = 70). Overall, 33/70 national action plans include a strategic plan, 40/70 include an operational plan, and 28/70 include a monitoring and evaluation (M&E) plan component. Included components vary widely by WHO region, with a strategic plan included for 69% of countries in the EMR and AFR regions to 13% in WPR; an operational plan included for 88% of EMR countries to 18% of SEAR countries; and an included M&E plan for 81% in EMR to 7% in EUR. Only 5% of all WHO Member States included all three implementation components in their national action plans. This review demonstrates that while vaccination is often included in the discourse of AMR mitigation strategies, integrating vaccination in national strategic objectives and action plans is a continued gap.

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9. Exploring the subnational inequality and heterogeneity of the impact of routine measles immunisation in Africa.

Echeverria-Londono S, Hartner A, Li X, Roth J, Portnoy A, Sbarra A, et al.

Vaccine. 2022 Nov 07;40(47):6806-6817.

PubMed ID: 36244882

ABSTRACT

Despite vaccination being one of the most effective public health interventions, there are persisting inequalities and inequities in immunisation. Understanding the differences in subnational vaccine impact can help improve delivery mechanisms and policy. We analyse subnational vaccination coverage of measles first-dose (MCV1) and estimate patterns of inequalities in impact, represented as deaths averted, across 45 countries in Africa. We also evaluate how much this impact would improve under more equitable vaccination coverage scenarios. Using coverage data for MCV1 from 2000-2019, we estimate the number of deaths averted at the first administrative level. We use the ratio of deaths averted per vaccination from two mathematical models to extrapolate the impact at a subnational level. Next, we calculate inequality for each country, measuring the spread of deaths averted across its regions, accounting for differences in population. Finally, using three more equitable vaccination coverage scenarios, we evaluate how much impact of MCV1 immunisation could improve by (1) assuming all regions in a country have at least national coverage, (2) assuming all regions have the observed maximum coverage; and (3) assuming all regions have at least 80% coverage. Our results show that progress in coverage and reducing inequality has slowed in the last decade in many African countries. Under the three scenarios, a significant number of additional deaths in children could be prevented each year; for example, under the observed maximum coverage scenario, global MCV1 coverage would improve from 76% to 90%, resulting in a further 363(95%CrI:299-482) deaths averted per 100,000 live births. This paper illustrates that estimates of the impact of MCV1 immunisation at a national level can mask subnational heterogeneity. We further show that a considerable number of deaths could be prevented by maximising equitable access in countries with high inequality when increasing the global coverage of MCV1 vaccination.

WEB: 10.1016/j.vaccine.2022.09.049

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

Echeverria-Londono et al. analyze subnational coverage of the measles first dose (MCV1) to estimate patterns of inequality across 45 countries in Africa. They also model potential improvements if coverage were more equitable. This study is important as it provides detailed

information on coverage beyond national estimates, which may mask heterogeneity and inequities. Such inequities are critical to address in immunization policy and implementation efforts. Outcome data (measles-containing vaccine, first dose) were obtained from the Institute for Health Metrics and Evaluation (IHME) on the first administrative area level (e.g., region). Population data was extracted from WorldPop. Impacts of immunization activities were obtained from the Vaccine Impact Modelling consortium, a group which applies mathematical models to understand various immunizations scenarios on deaths, DALYs, and cases. The authors used the index of inequality, which measures the differences between each region's vaccine impact, and the impact of the country. To understand potential improvements, Echeverria-Londono *et al.* calculate the impact of vaccination for three scenarios: 1) at least national scenario, defined as all regions having at least the national coverage estimate; 2) regional max scenario, defined as the highest coverage within a specific year was obtained in all regions; 3) Global Vaccine Action Plan scenario which depends on total health improvement expected at a national level if all regions achieved 80%.

Overall, there was substantial regional variation in MCV1 coverage (29-100%). *Figure 2* presents a map and coverage distribution, demonstrating the masking of sub-national trends when using national estimates. *Figure 3* presents both the distribution of the mean of deaths averted per 100,00 per across regions by country and inequality in vaccine impact. There are substantial variations in both within, and across countries. Angola, Nigeria, Chad, Ethiopia, and Somalia demonstrated the highest subnational inequality in deaths averted by MCV1 in 2019. *Figure 5* presents the potential improvements in deaths per 100,000 live births in 2019. Impacts vary depending on the scenario and the country. For example, in Chad, the Global Vaccine Action Plan scenario would increase the MCV1 impact by 1,273 deaths averted per 100,000 live births. *Table 2* presents gains in deaths averted in each country and scenario. Overall, in the "at least national scenario", an additional 97 per 100,000 deaths would be averted. In the "regional max" scenario, an additional 363 deaths per 100,000 would be averted. In the Global Vaccine Action Plan scenario, an additional 255 per 100,000 deaths could be averted. Overall, this study underscores the urgency of addressing subnational inequities in MCV1 coverage.

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10. One Full or Two Fractional Doses of Inactivated Poliovirus Vaccine for Catch-up Vaccination in Older Infants: A Randomized Clinical Trial in Bangladesh.

Aziz A, Verma H, Jeyaseelan V, Yunus M, Nowrin S, Moore D, et al.

J Infect Dis. 2022 Oct 18;226(8):1319-1326.
PubMed ID: 35575051

ABSTRACT

BACKGROUND: The polio eradication endgame called for the removal of trivalent oral poliovirus vaccine (OPV) and introduction of bivalent (types 1 and 3) OPV and inactivated poliovirus vaccine (IPV). However, supply shortages have delayed IPV administration to tens of millions of infants, and immunogenicity data are currently lacking to guide catch-up vaccination policies.

METHODS: We conducted an open-label randomized clinical trial assessing 2 interventions, full or fractional-dose IPV (fIPV, one-fifth of IPV), administered at age 9-13 months with a second dose given 2 months later. Serum was collected at days 0, 60, 67, and 90 to assess seroconversion, priming, and antibody titer. None received IPV or poliovirus type 2-containing vaccines before enrolment.

RESULTS: A single fIPV dose at age 9-13 months yielded 75% (95% confidence interval [CI], 6%-82%) seroconversion against type 2, whereas 2 fIPV doses resulted in 100% seroconversion compared with 94% (95% CI, 89%-97%) after a single full dose (P < .001). Two doses of IPV resulted in 100% seroconversion.

CONCLUSIONS: Our study confirmed increased IPV immunogenicity when administered at an older age, likely due to reduced interference from maternally derived antibodies. Either 1 full dose of IPV or 2 doses of fIPV could be used to vaccinate missed cohorts, 2 fIPV doses being antigen sparing and more immunogenic.

CLINICAL TRIAL REGISTRATION: NCT03890497.

WEB: 10.1093/infdis/jiac205
IMPACT FACTOR: 5.022
CITED HALF-LIFE: 9.8

START COMMENTARY

In this open-label randomized clinical trial, *Aziz et al.* assessed full or fractional-dose inactivated poliovirus vaccine (fIPV), with the first dose given at age 9 -13 months, and the second dose given 2 months later. In the global effort of polio eradication, two main categories of poliovirus vaccines are

utilized: inactivated poliovirus vaccine (IPV) and the oral poliovirus vaccine (OPV). Though OPV has been an effective strategy in reducing polio burden, it has also created vaccine-derived polioviruses (VDPV), which could establish transmission of VDPV in a population. As such, the Global Polio Eradication Initiative (GPEI) strategy includes plans to remove OPV from circulation, and the inclusion of IPV in routine immunization programs. Unfortunately, the supply of IPV has been insufficient until 2019, and as such, the World Health Organization has recommended fractional-dose IPV as a strategy, which requires 60% less antigen than a single full dose. Previous evidence demonstrates that the immunogenicity of 1 full dose IPV is superior to fIPV, but 2 fIPV doses are noninferior to 2 full doses of IPV among young infants. However, evidence of fIPV as compared to IPV in older infants has not been published; this study aims to fill this gap.

In this trial, eligible children in Bangladesh were randomly assigned to receive a first dose of fIPV or full-dose IPV, and a second dose after 2 months. Results of seroconversion rates stratified by poliovirus serotypes 1, 2, & 3 are presented in *Table 2*. For poliovirus type 1 and type 2, the cumulative 2-dose seroconversion was 100% in the fractional-dose group and 100% in the full-dose group. For poliovirus type 3, the cumulative 2-dose response was 73/74 (99%) and 70/70 (100%) for fIPV and IPV, respectively. This study is the first to assess immunogenicity on IPV vaccination for infants naïve to poliovirus type 2 and demonstrated almost universal immunity after the 2-dose schedule (seroconversion and antibody titers of either fIPV and IPV) and that fIPV doses resulted in significantly higher seroconversion rates than a single full dose of IPV.

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Appendix

The literature search for the [MONTH] 2021 Vaccine Delivery Research Digest was conducted on [MONTH-1] [DATE], [YEAR]. We searched English language articles indexed by the US National Library of Medicine and published between [MONTH-2] 15, 2022 and [MONTH-1] 14, 2022. The search resulted in 624 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])) 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]) (“2022/15/07”[PDAT] : “2022/14/08”[PDAT]))