VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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

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1. **Tackling Cholera Outbreak Amidst COVID-19 Pandemic in Nigeria: Challenges and Recommendations.**

Sow A, Haruna U, Amos O, Olajide E, Amene T, Odususi O, et al.

ABSTRACT

Background: Since the first confirmed case of the Novel Coronavirus Disease 2019 (COVID-19) in Nigeria, the pandemic has become a major public health challenge, affecting different sectors of the country. While Nigeria is battling to control the spread of COVID-19, the eruption of new cholera cases has put additional pressure on the strained healthcare system. Evidence: We showed how the overwhelming focus on COVID-19 has jeopardized key cholera containment measures such as disease surveillance, risk communication, and case management. Policy Options and Recommendations: We recommend provision and universal access to safe water and sanitation as key cholera preventive and control measures. However, these are resources that developing countries including Nigeria find rather challenging to provide. We also proposed the implementation of well-coordinated multi-sectoral interventions that involve strengthening disease surveillance including access to safe drinking water, vaccines, and treatment, especially in vulnerable communities. Conclusion: This policy brief provides evidence for policymakers, which if acted upon, will foster sustainable solutions to the lingering cholera outbreaks in Nigeria.

START COMMENTARY

In this policy brief, Sow *et al.* describe challenges in controlling cholera amidst the COVID-19 outbreak. This paper is important as it describes some potential negative consequences of COVID-19 prevention and control strategies, which may have diverted resources away from other outbreaks and health system needs. Nigeria has annual seasonal (i.e., rainy season) cholera outbreaks in areas of poor hygiene and sanitation. As a result, a 5-year National Strategic Plan of Action for Cholera Control was developed with the goal of preventing 67% cases of cholera by 2023. As part of this effort, oral cholera vaccines (OCV) have been administered in hotspots across the country. Despite these efforts, Nigeria experienced a large cholera outbreak in April 2021, with a reported 109,189 cases from April to December 2021. Sow *et al.* describe several challenges affecting the ability to control the cholera outbreak, including an overburdened healthcare system and shortage of healthcare workers, the disruption of vaccination programs, and insufficient and poor access to WASH services. The health system issues and shortages are related to COVID-19 as the pandemic disrupted humanitarian response programs and diverted health workers to COVID-19 testing, prevention, and treatment efforts in a country with a deficit of health workers (i.e., 4 doctors per 10,000 patients; 16.1 midwives and nurses per 10,000 patients). Sow *et al.* present several policy options and recommendations to mitigate the spread of cholera, including: 1) outbreak control and prevention through a multi-sectoral approach, 2) rapid case identification and management by distributing rapid diagnostic kits, 3) improved water, hygiene, and sanitation, 4) and health promotion and advocacy on the local, state, and national level.

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2. [Critical success factors for high routine immunization performance: A case study of Nepal.](#)

Hester K, Sakas Z, Ellis A, Bose A, Darwar R, Gautam J, et al.

ABSTRACT

INTRODUCTION: The essential components of a vaccine delivery system are well-documented, but robust evidence on how and why the related processes and implementation strategies drive catalytic improvements in vaccination coverage are not well established. To address this gap, we identified critical success factors that may have led to substantial improvements in routine childhood immunization coverage in Nepal from 2000 through 2019.

METHODS: We identified Nepal as an exemplar in the delivery of early childhood immunization through analysis of DTP1 and DTP3 coverage data. Through interviews and focus group discussions at the national, regional, district, health post, and community level, we investigated factors that contributed to high and sustained vaccine coverage. We conducted a thematic analysis through application of implementation science frameworks to determine critical success factors. We triangulated these findings with quantitative analyses using publicly available data.

RESULTS: The following success factors emerged: 1) Codification of health as a human right, - along with other vaccine-specific legislation - ensured the stability of vaccination programming; 2) National and multi-national partnerships supported information sharing, division of labor, and mutual capacity building; 3) Pro-vaccine messaging through various mediums, which was tailored to local needs, generated public awareness; 4) Female Community Health Volunteers educated community members as trusted and compassionate neighbors; and 5) Cultural values fostered collective responsibility and community ownership of vaccine coverage.

CONCLUSION: This case study of Nepal suggests that the success of its national immunization program relied on the engagement and understanding of the beneficiaries. The immunization program was supported by consistent and reliable commitment, collaboration, awareness, and collective responsibility between the government, community, and partners. These networks are strengthened through a collective dedication to vaccination programming and a universal belief in health as a human right.

START COMMENTARY

In this qualitative study, Hester *et al.* describe factors related to immunization success in Nepal. This study makes an important contribution as success factors related to how and why vaccine coverage improves are not well established and Nepal can serve as an exemplar for other countries seeking to improve vaccine coverage. Prior to data collection, Hester *et al.* developed a conceptual model of the drivers of vaccine coverage (*Figure 1*). Nepal was selected, along with Zambia and Senegal (results reported elsewhere), as an exemplar based on success in improving the first and third dose of diphtheria-tetanus-pertussis containing vaccine (DTP). From 2000 to 2019, Nepal increased DTP3 coverage from 74% to 93% (*Figure 2).* Three provinces were selected for inclusion in the study in an effort to capture diverse geographies (mountains, hills, or terai), performance (high, middle, and low performers of DTP), and an urban area (i.e., Kathmandu). Three districts were selected in each province. Qualitative data were collected between August to November 2019 and included key informant interviews and focus group discussions. *Table 1* presents a summary of the data collection, including the organizations that were represented in the data collection.

Key informant interviews (n=89) were conducted at national and sub-national levels and focus group discussions were conducted with mothers (n=9), fathers (n=6), grandmothers (n=6), and female community health volunteers (n=9). *Figure 5* presents key drivers related to Nepal's immunization success. A key strength of this work is that Hester *et al.* present functional definitions of each of the mechanisms of success, including commitment, collaboration, awareness, and collective responsibility (*Table 3*). In terms of commitment, Nepal codified health as a human right in the constitution in 2007, increased government health spending, legislated and budgeted to ensure long-term access to vaccines. Successful examples of collaborations include partnerships between the Ministry of Health and Population and external partners such as the WHO, UNICEF, Gavi, Rotary International, and the Global Polio Eradication Initiative. In terms of awareness, participants reported pro-vaccine messaging tailored to local needs increased public awareness about new vaccines, immunization days, and routine immunization. Participants also reported that consistent community engagement, including community-led groups and social movements led to strong demand for vaccines, and that female community health volunteers played an important role as trusted community members who could address misinformation and caregiver concerns. In terms of collective responsibility, participants noted that cultural norms of collective responsibility increased engagement, ownership, and subsequent success of the vaccine program. Overall, lessons learned from Nepal's successful immunization program may be applicable to other similar settings.

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3. [Economic Evaluations of HPV Vaccination in Targeted Regions of Low- and Middle-Income Countries: A Systematic Review of Modelling Studies.](#)

Frianto D, Setiawan D, Diantini A, Suwantika A.

ABSTRACT

BACKGROUND: In countries with limited resources, a targeted HPV vaccination strategy by focusing in selected regions is preferable to be implemented than a nationwide vaccination strategy.

OBJECTIVE: This study aimed to review articles on economic evaluations of HPV vaccination in countries over the world that applied targeted vaccination strategies.

METHODS: Approximately 1769 articles were obtained from two databases (1242 and 527 articles from PubMed and ProQuest, respectively). The inclusion criteria in this systematic review were studies about full economic evaluations of HPV vaccination in targeted area or sub-national level and written in English. Full-text screening was applied to evaluate the eligibility. Final articles obtained were referred to the Consolidated Health Economic Evaluation Reporting Standard (CHEERS) checklist. Finally, we included only 4 articles that met all inclusion and exclusion criteria.

RESULTS: Included studies in this review focused in different targeted regions, such as Punjab State in India, Vientiane in Lao PDR, Southern Vietnam in Vietnam, and Brazilian Amazon in Brazil. From 24 criteria in the CHEERS checklist, all included studies could meet 21 criteria (87.5%). All included studies in this review applied modeling approaches, which can estimate the number of cases and treatment costs averted. Applying various settings, the results of this study showed that HPV vaccination could potentially reduce the number of cervical cancer cases by 20-72%. Taking cervical cancer screening into account, this study showed that targeted HPV vaccination was cost-effective or even cost-saving.

CONCLUSION: Implementation of HPV vaccination in sub-national level as the initial step before nationwide vaccination is more favorable to be implemented in countries with limited budget.

START COMMENTARY

In this systematic review, Frianto *et al.* review modelling studies assessing human papillomavirus (HPV) vaccination strategies in targeted geographies, rather than nationally. This review makes an important contribution as it summarizes the evidence and costs on implementation on a sub-national level, which may be a useful approach to increasing HPV coverage. It may be more feasible and less costly to implement such an approach. Two databases (PubMed and ProQuest) were search. Key words included: "economic evaluation" OR "cost minimization" OR "cost-effectiveness" OR "cost utility" OR "cost benefit" AND "human papillomavirus" OR "HPV" AND "vaccine" OR "vaccination" OR "immunization". A total of 1,769 articles were identified. After excluding duplicated, non-English articles, and those that were not economic evaluation, 38 full-text articles were evaluated. Of these, 34 were not evaluating HPV vaccination in targeted areas, one was not available as a full text, and one was an incomplete evaluation.

In total, four articles were included that assessed the Punjab state of Idia, Vientiane in Lao PDR, Southern Vietnam, and the Brazilian Amazon. Modelling approaches included a Markov model for Brazil, dynamic models for Vietnam and Lao PDR, and a decision tree and Markov model for India. All studies used the bivalent vaccine. Nearly all studies targeted young girls (age 12 for the study in Brazil, age 10-11 for India and Lao PDR, girls 9 years old and older in Vietnam). The study in Vietnam also targeted boys. Detailed study characteristics including the study perspective, methods, type of study, discount rate, and assumptions around screening and vaccination are presented in *Table 1.* Study outcomes are presented in *Table 2.* Overall, studies showed that vaccination could reduce 30-72% of cervical cancer cases. Key findings included that vaccine prices ranged from $4.6-$23.5 per dose. The price threshold for cost-effectiveness was not reported. Program costs were estimated to be $5.6-$13.4 per dose. Detailed cost outcomes and cost-effectiveness values are summarized in *Table 3.* The study in India determined that the incremental cost per quality adjusted life year (QALY) gained is about $1.12 USD. The study in Lao PDR found results ranging between $1,471 USD to $7,272 USD depending on the screening and vaccination strategy. In Vietnam, cost-effectiveness values ranged from $16.4 USD to $3,181 USD depending on the vaccine scenario and outcome. Lastly, in Brazil, when compared to screening only, 3 lifetime screenings and vaccination resulted in $1,141 USD per QALY compared to $1,763 USD per QALY for 10 lifetime screenings and vaccination. Overall, this study demonstrates cost-effective and cost-saving results for targeted HPV vaccination in LMICs.

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4. [Occurrence of yellow fever outbreaks in a partially vaccinated population: An analysis of the effective reproduction number.](#)

Ferreira F, Bastos Camacho L, Villela D.

ABSTRACT

BACKGROUND: Yellow fever is endemic in Africa and the Americas, occurring in urban or sylvatic environments. The infection presents varying symptoms, with high case-fatality among severe cases. In 2016, Brazil had sylvatic yellow fever outbreaks with more than 11 thousand cases, predominantly affecting the country's Southeast region. The state of Minas Gerais accounted for 30% of cases, even after the vaccine had been included in the immunization calendar for at least 30 years.

METHODOLOGY AND PRINCIPAL FINDINGS: We applied parameters described in the literature from yellow fever disease into a compartmental model of vector-borne diseases, using namely generation time intervals, vital host and vector parameters, and force of infection, using macroregions as the spatial unit and epidemiological weeks as the time interval. The model permits obtaining the reproduction number, which we analyzed from reported cases of yellow fever from 2016 to 2018 in residents of the state of Minas Gerais, Brazil. Minas Gerais recorded two outbreak periods, starting in EW 51/2016 and EW 51/2017. Of all the reported cases (3,304), 57% were men 30 to 59 years of age. Approximately 27% of cases (905) were confirmed, and 22% (202) of these individuals died. The estimated effective reproduction number varied from 2.7 (95% CI: 2.0-3.6) to 7.2 (95% CI: 4.4-10.9], found in the Oeste and Nordeste regions, respectively. Vaccination coverage in children under one year of age showed heterogeneity among the municipalities comprising the macroregions.

CONCLUSION: The outbreaks in multiple parts of the state and the estimated Re values raise concern since the state population was partially vaccinated. Heterogeneity in vaccination coverage may have been associated with the occurrence of outbreaks in the first period, while the subsequent intense vaccination campaign may have determined lower Re values in the second period.

WEB: 10.1371/journal.pntd.0010741

START COMMENTARY

In this mathematical modelling study, Ferreira *et al.* aim to understand the occurrence and intensity of yellow fever by estimating the effective reproductive number (R_e) in the Minas Gerais state in Brazil. This study is important as it provides critical insights into the occurrence of yellow fever which can inform future vaccination efforts in Minas Gerais. Authors focus on understanding the spatial variation of R_e for yellow fever epidemic recorded from 2016 to 2018 in the state. Model inputs included the number of yellow fever cases and vaccination coverage from the Ministry of Health and population from the Brazilian Institute of Geography and Statistics. Other model parameters included the growth rate of reported cases, the extrinsic incubation period, mosquito survival time, and environmental factors (i.e., temperature which was assumed to be 25°C. Parameters including definitions and ranges of values are presented in *Table 1.*

From 2016 to 2018, a total of 3,304 yellow fever cases were reported in Minas Gerais and 202 cases died, resulting in a case fatality of 22%. Summaries of cases by sex, age, vaccine status, and region are presented in *Table 2.* Two outbreaks were reported during the period (peaks shown in *Figure 1*). The outbreaks affected specific areas (Centro, Centro-Sul, Leste do Sul, Sudeste, and Sul). *Figure 3* presents maps of vaccination coverage among children under one year of age whereas *Figure 4* presents vaccine coverage among the full population. Overall, 6% of municipalities had coverage lower than 60% for children under one year of age, and 55% of municipalities had vaccine coverage lower than 60% for the full population. *Table 3* presents the effective reproductive numbers and strength of infection by region and week during the outbreaks. The effective reproductive number was higher in the first wave than the second wave and demonstrated spatial variation with a high of Re = 7.2 (95% CI: 4.4–10.9) for the Nordeste region and a low of 2.8 in the Oeste region (95% CI: 2.1-3.6). This study describes observed cases and deaths in areas with partially vaccinated populations and can inform targeted vaccination prevention efforts to specific areas (e.g., Nordeste) and populations (e.g., people over one year of age).

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5. [Does a pay-for-performance health service model improve overall and rural-urban inequity in vaccination rates? A difference-in-differences analysis from the Gambia.](#)

Sowe A, Namatovu F, Cham B, Gustafsson P.

ABSTRACT

OBJECTIVE: To assess whether the implementation of a results-based financing (RBF) project in The Gambia resulted in (1) improved national vaccination coverage (2) higher coverage in intervention than non-intervention areas, and (3) improvement in rural-urban coverage inequality.

METHODS: The study used a difference-in-differences design, based on repeated cross-sectional data from The Gambian Demographic and Health Surveys 2013 (N..=..1650) and 2020 (N..=..1456). Full vaccination (receipt of one BCG, 3 OPV, 3 DTP, and 1 measles-containing vaccine doses) and rural-urban vaccination inequality were our outcome variables. The intervention, RBF, was implemented in 5 of the 7 health regions. Covariates controlled for included child's sex, child's birth order number, socioeconomic status, ethnicity, distance from health facility, maternal education, mother's age group, mother's marital status, and mother's work status. Poisson regression with robust variance was used to estimate whether coverage changed, and difference-in-differences and difference-in-differences-in-differences were used to 'assess differences in vaccination coverage change and change in inequalities, respectively.

RESULTS: Total crude full vaccination coverage in The Gambia was 76% in 2013 and 84.6% in 2020. Overall vaccination significantly increased by 16% (95% CI: 9% to 24%) in 2020 compared to 2013, but with a smaller increase in intervention relative to non-intervention areas [PRR 0.88 (CI: 0.78-0.99)]. Rural-urban inequality in vaccination coverage decreased more - by 13% [0.87 (0.78-0.98)] - in RBF than non-RBF regions.

CONCLUSION: Vaccination coverage improved over the study period though we have no evidence to ascribe the coverage gains to the RBF intervention. However, our study suggests that the RBF project has contributed to reducing rural-urban inequalities in the regions it was implemented.

START COMMENTARY

In this difference-in-difference study using repeat cross-sectional data, Sowe *et al.* assess the impact of results-based financing (RBF) on vaccination coverage and equity. This study is important as pay for performance initiatives are being implemented widely to improve maternal and child health service delivery, uptake, and equity. This study provides evidence on the impact of such programming. Data was obtained from Demographic Health Surveys (DHS) in 2013 and 2019/2020. Five regions implemented RBF and three regions did not. Outcome variables included full vaccination defined as children 12-23 months who received one dose of Bacillus Calmette Guerin vaccine, three doses of the oral polio vaccine, one dose of a measles-containing vaccine, and three doses of a diphtheria, pertussis, and tetanus-containing vaccine. Covariates included child's birth order, household socioeconomic status, and distance to a health facility.

Table 1 presents the weighted distribution of participants across covariates in RBF and non-RBF intervention areas for the 2013 and 2020 DHS. *Table 2* presents the weighted full vaccination coverage in The Gambia from 2013 to 2020 (the pre- and post-intervention coverage). Vaccine coverage was 76% in 2013 and 84.6% in 2020. Overall, coverage increased when adjusting for covariates by an estimated 16% (95 CI: 9%-24%) (*Table 2*). When assessing the difference in the change in coverage between intervention (those which implemented RBF) and control regions, the prevalence rate ratio was 0.88 (CI: 0.78-0.99) in adjusted analyses, indicating that there was less improvement in vaccine coverage in intervention regions compared to control regions. However, one positive finding was that the difference in rural-urban coverage was reduced by 13% (PPR: 0.87%, CI: 0.78-0.98), indicating that vaccine inequality decreased more in the intervention regions. Overall, the study concludes that RBF may not improve overall vaccine coverage challenges but may improve some rural-urban differences in vaccine coverage.

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6. Creation of a Global Vaccine Risk Index.

Nuzhath T, Hotez P, Damania A, Liu P, Colwell B.

ABSTRACT

The World Health Organization has identified vaccine hesitancy as one of its top ten global health threats for 2019. Efforts are underway to define the factors responsible for reductions in vaccine confidence. However, as global measles cases accelerated beginning in 2018, it became evident that additional factors were promoting measles re-emergence, including war, political and socio-economic collapse, shifting poverty, and vulnerability to weather events and climate change. Accordingly, we propose a Global Vaccine Risk Index (VRI) to consider these variables as a more comprehensive means to identify vulnerable nations where we might expect measles and other vaccine-preventable diseases to emerge or re-emerge. In Sub-Saharan African and Middle Eastern nations, conflict and political instability predominated as the basis for high vaccine risk scores, whereas in Southeast Asian countries, the major reasons included climate variability, current levels of measles vaccination coverage, and economic and educational disparities. In Europe, low vaccine confidence and refugee movements predominated, while in the Americas, economic disparities and vaccine confidence were important. The VRI may serve as a useful indicator and predictor for international agencies committed to childhood immunizations and might find relevance for accelerating future COVID19 vaccination programs.

WEB: 10.1371/journal.pone.0272784
IMPACT FACTOR: 2.740

START COMMENTARY

In this study, Nuzhath *et al.* propose a Global Vaccine Risk Index (VRI) to help identify nations where measles and other vaccine-preventable disease may emerge. This study is important as it proposed a standardized indicator which can help an understanding of variability in factors related to vaccination coverage which can inform future policies and programs. Data included in the index includes the vaccine confidence index, Notre Dame Global Adaptation Initiative index, climate risk index, human development index, measles incidence rate, measles vaccine coverage, percent of the population internally displaced by a disaster, peace index, urban population percent, refugee population by country of origin, and percent of the population internally displaced due to conflict and violence. Sources are provided in *Table 1. Figure 1* presents the spearman correlations between variables involved in the derivation of VRI.

Figure 3 presents a visual heat map of countries within different categories of the VRI. Nearly all of the high-risk countries are in sub-Saharan Africa. High risk countries include Montenegro, Bosnia and Herzegovina, Ukraine, Russia, France, Ukraine, Haiti, Peru, Mexico, Bolivia, Papua New Guinea, the Philippines, Laos, Cambodia, the Central African Republic, Chad, Mali, Equatorial Guinea, DR Congo, Madagascar, Angola, Cote d'Ivoire, and Gabon. *Figure 4* presents the factors (vaccinations, vaccine confidence, conflict, climate, and education and poverty) and their distributions for each of the WHO regions to understand which components contribute to high VRIs. For example, in the Americas, climate change is the major contributor. *Table 3* compares VRI rankings with a ranked list of the top 20 countries with measles incidence. Although 25% of the countries appear on both lists (Madagascar, Ukraine, Central African Republic, Yemen, and the Democratic Republic of Congo), the lists differ. Nuzhath *et al.* conclude that this is due to the VRI comprising of a broader set of factors beyond measles incidence, which may be important to consider to prevent future outbreaks.

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7. [Zero- or missed-dose children in Nigeria: Contributing factors and interventions to overcome immunization service delivery challenges.](#)

Mahachi K, Kessels J, Boateng K, Jean Baptiste A, Mitula P, Ekeman E, et al.

ABSTRACT

'Zero-dose' refers to a person who does not receive a single dose of any vaccine in the routine national immunization schedule, while 'missed dose' refers to a person who does not complete the schedule. These peopleremain vulnerable to vaccine-preventable diseases, and are often already disadvantaged due to poverty, conflict, and lack of access to basic health services. Globally, more 22.7 million children are estimated to be zero- or missed-dose, of which an estimated 3.1 million (14%) reside in Nigeria.We conducted a scoping review tosynthesize recent literature on risk factors and interventions for zero- and missed-dosechildren in Nigeria. Our search identified 127 papers, including research into risk factors only (n=66); interventions only (n=34); both risk factors and interventions (n=18); and publications that made recommendations only (n=9). The most frequently reported factors influencing childhood vaccine uptake were maternal factors (n=77), particularly maternal education (n=22) and access to ante- and perinatal care (n=19); heterogeneity between different types of communities - including location, region, wealth, religion, population composition, and other challenges (n=50); access to vaccination, i.e., proximity of facilities with vaccines and vaccinators (n=37); and awareness about immunization - including safety, efficacy, importance, and schedules (n=18).Literature assessing implementation of interventions was more scattered, and heavily skewed towards vaccination campaigns and polio eradication efforts. Major evidence gaps exist in how to deliver effective and sustainable routine childhood immunization. Overall, further work is needed to operationalise the learnings from these studies, e.g. through applying findings to Nigeria's next review of vaccination plans, and using this summary as a basis for further investigation and specific recommendations on effective interventions.

WEB: [10.1016/j.vaccine.2022.07.058](https://doi.org/10.1016/j.vaccine.2022.07.058)
IMPACT FACTOR: 3.143

START COMMENTARY

In this scoping review, Mahachi *et al.* summarize recent literature on risk factors and interventions for zero- and missed-dose children in Nigeria. This study is important as there are an estimated 3.1 million zero- and missed dose children in the country, an estimated 14% of the global total and this is the first scoping review to comprehensively summarize all identified risk factors and interventions, which can result in a greater understanding of issues and recommendations for the country and others. Three databases were searched: PubMed/MEDLINE and Embase. Key words included: "zero-dose" OR "immunization coverage" OR "under-immunization" OR "under-vaccinated" OR "equitable uptake of vaccines" AND "children" OR "child". Inclusion criteria included studies that were published between April 2011-2021; peer-reviewed; focusing on Nigeria; explicitly covering risk factors and interventions for 0–5-year-old children; and written in English.

Of 19,015 articles identified, 127 were deemed eligible. *Figure 1* presents the study flow diagram. *Appendix 1* presents detailed information on each study including the author, title, year, study type, study location, and the outcomes (primary vaccine; risk factors; interventions; recommendations). Polio (n=26) was studied most often, followed by measles (n=15). Other vaccines were included in five or fewer articles. Most studies (n=86) were focused on regional areas rather than the whole country (n=33) or a multi-country study (n=5). Mahachi *et al.* present risk factors for three categories: individual; community; and health system. Detailed factors within each category are summarized in *Table 1.* Individual factors positively associated with vaccination include maternal literature, health facility birth, older age, maternal discretion to make decisions without a husband's permission and others. Community factors associated negatively with vaccination status include geographic factors (i.e., northern communities less likely to be vaccinated), rurality, conflict, and others. On a health system level, distance to health facilities, lack of vaccines, absence of vaccinators at health centers, and others were negatively associated. *Figure 2* presents a graphic showing the frequency of risk factors identified in the review. When assessing interventions to improve immunization coverage, several interventions across four categories (community engagement, sensitization, and mobilization; sustaining vaccination coverage; targeting zero- or missed-dose children; and vaccination campaigns). *Table 2* summarizes each of the categories and corresponding interventions. The most frequent types of interventions were focused on community engagement, including training community volunteers and engaging hard-to-reach communities. Overall, the authors conclude that the literature on risk factors and interventions is extensive. This evidence should be used to inform recommendations to reduce the number of missed- and zero-dose children in the country.

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8. [Estimating the impact of health systems factors on antimicrobial resistance in priority pathogens.](#)

Awasthi R, Rakholia V, Agrawal S, Dhingra L, Nagori A, Kaur H, et al.

ABSTRACT

OBJECTIVES: Antimicrobial resistance (AMR) is the next big pandemic that threatens humanity. The One Health approach to AMR requires quantification of interactions between health, demographic, socioeconomic, environmental, and geopolitical factors to design interventions. This study is focused on learning health system factors on global AMR.

METHODS: This study analysed longitudinal data (2004-2017) of AMR having 6 33 820 isolates from 70 middle and high-income countries. We integrated AMR data with the Global Burden of Disease (GBD), Governance (WGI), and Finance data sets to find AMR's unbiased and actionable determinants. We chose a Bayesian decision network (BDN) approach within the causal modelling framework to quantify determinants of AMR. Further, we integrated Bayesian networks' global knowledge discovery approach with discriminative machine learning to predict individual-level antibiotic susceptibility in patients.

RESULTS: From MAR (multiple antibiotic resistance) scores, we found a non-uniform spread pattern of AMR. Components-level analysis revealed that governance, finance, and disease burden variables strongly correlate with AMR. From the Bayesian network analysis, we found that access to immunization, obstetric care, and government effectiveness are strong, actionable factors in reducing AMR, confirmed by what-if analysis. Finally, our discriminative machine learning models achieved an individual-level AUROC (Area under receiver operating characteristic curve) of 0.94 (SE=0.01) and 0.89 (SE=0.002) to predict Staphylococcus aureus resistance to ceftaroline and oxacillin, respectively.

CONCLUSION: Causal machine learning revealed that immunisation strategies and quality of governance are vital, actionable interventions to reduce AMR.

WEB: [10.1016/j.jgar.2022.04.021](#)
IMPACT FACTOR: 4.349

START COMMENTARY

In this longitudinal study from 2004 to 2017, Awasthi *et al.* analysis antimicrobial resistance (AMR) in critical pathogens and associated factors. This study is important as it considers the connection between AMR and numerous factors (e.g., socioeconomic factors, governance) which provide a deeper understanding of susceptibility and future risk of AMR among pathogens. *Figure 1* shows a machine learning model developed to conceptualize the relationships between factors and disease. Data on AMR was extracted from 633,820 isolates included in the AMR surveillance competition database. The age and temporal distribution of data is presented in *Table 1.* Data on governance and finance were obtained from the World Bank whereas covariates (i.e., socioeconomic, access to health, climate) were obtained from the Global Burden of Disease data.

Awasthi *et al.* calculated multiple antibiotic resistance scores and found that each pathogen had a markedly different pattern of resistance spread in specific geographies. For example, *K. pneumoniae* had a high spread with a multiple antibiotic resistance score of 0.64 in Serbia and a low of 0.09 in Japan. In component-level Bayesian network analysis, there were strong associations between global burden of disease covariates, governance, finance, and AMR (shown in *Figure 3*). Detailed inferences are presented in *Table 3* for each pathogen. Each pathogen's AMR probability is assessed in the context of specific factors (i.e., high hospital beds versus low hospital beds). For example, *K. pneumonia* cefepime resistance was 19.87% higher in countries where the level of unsafe sanitation was high. Additionally, a counterfactual analysis was conducted to quantify the reduction in ceftriaxone resistance if countries with limited access to immunization and obstetric care (see *Figure 4*). One notable finding is that middle-income countries could reduce ceftriaxone resistance in *Acinetobacter baumannii* by nearly 90% if they improve access to these health services. Lastly, Awasthi *et al.* predict susceptibility for each pathogen and antibiotic type (*Figure 5* presents prediction models for *Staphylococcus aureus*). Overall, this study demonstrates the large and growing threat of AMR and factors which could be addressed to reduce susceptibility to AMR, such as increasing access to immunization and obstetric care.

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9. [Hepatitis B Vaccination Impact and the Unmet Need for Antiviral Treatment in Blantyre, Malawi.](#)

Stockdale A, Meiring J, Shawa I, Thindwa D, Silungwe N, Mbewe M, et al.

ABSTRACT

BACKGROUND: Hepatitis B is the leading cause of cirrhosis and liver cancer in sub-Saharan Africa. To reduce mortality, antiviral treatment programs are needed. We estimated prevalence, vaccine impact, and need for antiviral treatment in Blantyre, Malawi.

METHODS: We conducted a household study in 2016-2018. We selected individuals from a census using random sampling and estimated age-sex-standardized hepatitis B surface antigen (HBsAg) seroprevalence. Impact of infant hepatitis B vaccination was estimated by binomial log-linear regression comparing individuals born before and after vaccine implementation. In HBsAg-positive adults, eligibility for antiviral therapy was assessed.

RESULTS: Of 97386 censused individuals, 6073 (median age 18 years; 56.7% female) were sampled. HBsAg seroprevalence was 5.1% (95% confidence interval [CI], 4.3%-6.1%) among adults and 0.3% (95% CI, .1%-.6%) among children born after vaccine introduction. Estimated vaccine impact was 95.8% (95% CI, 70.3%-99.4%). Of HBsAg-positive adults, 26% were HIV-positive. Among HIV-negative individuals, 3%, 6%, and 9% were eligible for hepatitis B treatment by WHO, European, and American hepatology association criteria, respectively.

CONCLUSIONS: Infant HBV vaccination has been highly effective in reducing HBsAg prevalence in urban Malawi. Up to 9% of HBsAg-positive HIV-negative adults are eligible, but have an unmet need, for antiviral therapy.

WEB: [10.1093/infdis/jiab562](#)
IMPACT FACTOR: 5.226

START COMMENTARY

In this household study, Stockdale *et al.* estimate age-sex-standardized hepatitis B surface antigen (HBsAg) seroprevalence among individuals in Ndirande, Blantyre, Malawi using single-stage random probability sampling. Sampling was stratified by age to include younger children. Blood samples were collected and tested for HBsAg using an immunoassay. Households where individuals ≥16 years who tested HBsAg positive were asked to participate in an evaluative study for liver disease. *Figure 1* presents a flow chart of census and recruitment to the study.

In total, 6,073 individuals participated in the serological study and ~2.6% (n=160) participants tested positive for HBsAg. When standardizing for age and sex, the prevalence of HBsAg was 3.1% (95% CI: 2.6-3.7%). The prevalence stratified be age and sex is shown in *Figure 3.* The highest prevalence was among men aged 30-39 years. Vaccination status was obtained from 56.2% of children ≤10 and 67.8% of children under ≤5. Among these, nearly all children were vaccinated (97.4% for ≤10-year-olds and 98.1% for ≤5-year-olds), although this is likely an overestimate of the true vaccination coverage given it was only obtained from about half of the sample. Prevalence of HBsAg by birth date and vaccination status is presented in *Table 1.* HBsAg-positive individuals aged ≥16 years were more likely to be paid/self-employed, be married, separated, or divorced, and be male. HBC infection odds were higher in males and those who were divorced/separated. Of the 150 participants who were over 16 years of age and HBsAg, 114 were located and 94 agreed to participate in the treatment trial. *Table 3* shows the characteristics of participants including HIV status, CD4 count, medical history, and alcohol use. Overall, this study makes an important contribution as it quantifies the prevalence of HBsAg, which was notably low (less than 0.5% among children born after HBV vaccine implementation) and provides evidence of vaccine impact (i.e., demonstrated through high vaccine coverage levels).

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10. [Prospects of malaria vaccination in Nigeria: Anticipated challenges and lessons from previous vaccination campaigns](#)

Effiong FB, Makata VC, Elebesunu EE, Bassey EE, Salachi KI, Sagide MR, et al.

ABSTRACT

Malaria is a severe public health issue in Nigeria, with higher morbidity and mortality rates than any other country. An estimated 100 million malaria cases and over 300,000 deaths are recorded yearly in Nigeria. Vaccination is an effective strategy in combating and eliminating infectious diseases such as malaria, thus, the deployment of a prospective malaria vaccine in Nigeria offers hope to the country's health sector. However, vaccination programmes face challenges, particularly in communities that are difficult to reach geographically or culturally, and these obstacles can only be overcome through continued international, national, and individual commitment. There is a need for expanded and continuous public health information, education, and communication particularly on contemporary health issues such as malaria and vaccination hesitancy. This will enable easier implementation and compliance to strategies for the sustainable control and eventual elimination of malaria. This article highlights some of the lessons learned from previous vaccination programs in Nigeria and how the insight gotten can be pivotal in ensuring the success of a prospective malaria vaccination programme in Nigeria.

WEB: [10.1016/j.amsu.2022.104385](https://doi.org/10.1016/j.amsu.2022.104385)
IMPACT FACTOR: N/A

START COMMENTARY

In this article, Effiong *et al.* describe lessons learned from prior vaccination campaigns that can be applied to increase success of a future malaria vaccination program in Nigeria. This paper is important as it describes the dire need for a malaria vaccine in Nigeria and potential strategies for rolling out the program successfully. Nigeria has the highest malaria burden globally with nearly 100 million cases annually. Effiong *et al.* summarize vaccine candidates in *Table 1* including RTS,S vaccine, which is furthest along the development pipeline in Phase 4. Vaccines are categorized based on the stage of the parasite's life cycle they target. Despite promising candidates and results of malaria vaccines, there are anticipated challenges to rolling out the vaccine. Firstly, Effiong *et al.* describe a need to address misinformation and hesitancy. Prior vaccination campaigns have been harmed by fears of adverse effects (e.g., rumors about microchipping). To prevent misinformation and vaccine hesitancy, authors recommend collaboration between vaccine staff and rural community leaders. The second anticipated challenge is a need to address vaccine storage and transportation. For the RTS,S vaccine, cold chain systems will be required, which may be difficult given infrastructural challenges in Nigeria which have negatively impacted other vaccination supply chains (e.g., polio). Lastly, Effiong *et al.* highlight a need to include large population subgroups in clinical trials to better capture a real-world scenario for the malaria vaccine. Prior studies have had limited sample sizes, resulting in poor representation of demographic populations, which may contribute to vaccine hesitancy. Overall, the authors provide context-specific examples and lessons to apply to future malaria vaccine programs.

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Appendix

The literature search for the October 2021 Vaccine Delivery Research Digest was conducted on October 4, 2022. We searched English language articles indexed by the US National Library of Medicine and published between August 15, 2022 and September 14, 2022. The search resulted in 676 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]) ("2022/8/15"[PDAT] : "2022/09/14"[PDAT]))