

# VACCINE DELIVERY RESEARCH DIGEST

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## 1. [COVID-19 related immunization disruptions in Rajasthan, India: A retrospective observational study.](#)

Jain R, Chopra A, Falzan C, Patel M, Dupas P.

*Vaccine*. 2021 Jul 03.

### ABSTRACT

**INTRODUCTION:** Governments around the world suspended immunization outreach to control COVID-19 spread. Many have since resumed services with an emphasis on catch-up vaccinations. This paper evaluated immunization disruptions during India's March-May 2020 lockdown and the extent to which subsequent catch-up efforts reversed them in Rajasthan, India.

**METHODS:** In this retrospective observational study, we conducted phone surveys to collect immunization details for 2,144 children that turned one year old between January and October 2020. We used logistic regressions to compare differences in immunization timeliness and completed first-year immunization status among children that were due immunizations just before (unexposed), during (heavily exposed), and after (post-exposure) the lockdown.

**RESULTS:** Relative to unexposed children, heavily exposed children were significantly less likely to be immunized at or before 9 months (OR 0.550; 95% CI 0.367-0.824;  $p = 0.004$ ), but more likely to be immunized at 10-12 months (OR 1.761; 95% CI 1.196-2.591;  $p = 0.004$ ). They were also less likely to have completed their key first-year immunizations (OR 0.624; 95% CI 0.478-0.816;  $p = 0.001$ ) by the time of survey. In contrast, post-exposure children showed no difference in timeliness or completed first-year immunizations relative to unexposed children, despite their younger age. First-year immunization coverage among heavily exposed children decreased by 6.9 pp to 10.4 pp (9.7% to 14.0%). Declines in immunization coverage were larger among children in households that were poorer, less educated, lower caste, and residing in COVID red zones, although subgroup comparisons were not statistically significant.

**CONCLUSION:** Disruptions to immunization services resulted in children missing immunization during the lockdown, but catch-up efforts after it was eased ensured many children were reached at later ages. Nevertheless, catch-up was incomplete and children due their immunizations during the lockdown remained less likely to be fully immunized 4-5 months after it lifted, even as younger cohorts due immunizations in June or later returned to pre-lockdown schedules.

**WEB:** [10.1016/j.vaccine.2021.06.022](https://doi.org/10.1016/j.vaccine.2021.06.022)

**IMPACT FACTOR:** 3.143

**CITED HALF-LIFE:** 7.3

## START COMMENTARY

In this retrospective observational study, Jain *et al.* conducted phone interviews with 2,144 guardians' of one-year old children to assess child immunization disruptions during India's first COVID-19 lockdown in March-May 2020 and the success of subsequent catch-up efforts in Rajasthan, India. This article fills an important gap in the literature of understanding immunization coverage decreases during pandemics in low- and middle-income countries (LMIC). Decreases have been previously observed during prior epidemics/pandemics (e.g., Ebola and SARS) due to supply- and demand-side factors such as provider shortages, suspended services, and individuals' fear of contracting the virus. Although the World Health Organization (WHO) issued guidelines that countries should continue routine immunization, there have been several studies, largely in high income countries (HIC), which have documented large decreases in immunization coverage. Jain *et al.* surveyed from low income households participating in a statewide government health insurance program. The phone survey was conducted with a household adult between August and October 2020 and included questions on immunization histories based on immunization cards (when available), immunization disruptions, contacts with the healthcare system, and demographics. Children were divided into three exposure groups by age during the lockdown: 1) unexposed, those who turned 12 months before March 2020, 2) partially exposed, those who turned 12 months in March to May 2020, and 3) heavily exposed, those who turned 12 months during June to August. These categories were determined based on when the Measles 1 vaccine is due at 9 months of age. The authors conducted logistic regressions to assess immunization outcomes on child exposure groups.

Overall, 82% of children had seen a healthcare worker during the lockdown and 31% reported a COVID-related disruption. When asked about disruptions, the most common reported cause was fear of contracting COVID-19 (20%) followed by canceled immunization (15%). Heavily exposure children experienced a statistically significant shift in the timing of their Measles 1 vaccine and were significantly less likely to have completed their first year immunizations at the time of the survey. The latter indicates that catch-up efforts did not make up for lockdown immunization declines. One key strength of this study is that the authors conducted sub-group analysis and identified factors such as education, caste, and lower socioeconomic status to be associated with lower probability of completing first-year immunizations (although not statistically significantly so). Some limitations of note include generalizability; the study population was from an insurance program aimed at low income households. Although only 67% of the households were reached by phone, which is a limitation, the authors assessed characteristics such as mother's age, access to health facilities, village

characteristics, and exposure to COVID red zones and found that the surveyed households were similar to those not surveyed. Lastly, the study relied on immunization cards and caregiver's recall for immunization information. Despite these limitations, this study sheds light on immunization efforts in Rajasthan and shows that there is a need for catch-up efforts to address demand-side factors, such as the fear of contracting COVID-19.

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## 2. [Adjustable Algorithmic Tool for Assessing the Effectiveness of Maternal Respiratory Syncytial Virus \(RSV\) Vaccination on Infant Mortality in Developing Countries.](#)

Cevigney R, Leary C, Gonik B.

*Infect Dis Obstet Gynecol.* 2021 Jun 15;2021:5536633.

### ABSTRACT

Acute lower respiratory infection (ALRI) due to RSV is a common cause of global infant mortality, with most cases occurring in developing countries. Using data aggregated from priority countries as designated by the United States Agency for International Development's (USAID) Maternal Child Health and Nutrition (MCHN) program, we created an adjustable algorithmic tool for visualizing the effectiveness of candidate maternal RSV vaccination on infant mortality. Country-specific estimates for disease burden and case fatality rates were computed based on established data. Country-specific RSV-ALRI incidence rates for infants 0-5 months were scaled based on the reported incidence rates for children 0-59 months. Using in-hospital mortality rates and predetermined "inflation factor," we estimated the mortality of infants aged 0-5 months. Given implementation of a candidate maternal vaccination program, estimated reduction in infant RSV-ALRI incidence and mortality rates were calculated. User input is used to determine the coverage of the program and the efficacy of the vaccine. Using the generated algorithm, the overall reduction in infant mortality varied considerably depending on vaccine efficacy and distribution. Given a potential efficacy of 70% and a maternal distribution rate of 50% in every USAID MCHN priority country, annual RSV-ALRI-related infant mortality is estimated to be reduced by 14,862 cases. The absolute country-specific reduction is dependent on the number of live births; countries with the highest birth rates had the greatest impact on annual mortality reduction. The adjustable algorithm provides a standardized analytical tool in the evaluation of candidate maternal RSV vaccines. Ultimately, it can be used to guide public health initiatives, research funding, and policy implementation concerning the effectiveness of potential maternal RSV vaccination on reducing infant mortality.

**WEB:** [10.1155/2021/5536633](https://doi.org/10.1155/2021/5536633)

**IMPACT FACTOR:** N/A

**CITED HALF-LIFE:** N/A

### START COMMENTARY

Cevigney *et al.* developed an adjustable algorithmic tool for assessing the effectiveness of implementing maternal respiratory syncytial virus (RSV) vaccination on infant mortality in LMICs. This article makes an important contribution as it describes a tool that can be used to quantify the benefits of maternal RSV vaccination which can guide public health initiatives, funding, and implementation when an RSV vaccine is approved. The tool combines country-specific estimates for RSV disease

burden (incidence among infants aged 0-5 months and incidence among infants aged 0-59) and case fatality for 0-5 month old infants across countries and regions. The user can select a USAID MCHN priority country, distribution (defined as the percentage of expectant mothers to receive the vaccine), and maternal vaccine effectiveness in preventing RSV in infants aged 0-5 months. Further, the user can decide if they want incidence and mortality rates to be calculated using high or low published estimates, and if they want to view country-specific or region-specific estimates. *Figure 2* shows the control panel for the interactive detail where each of these parameters are listed.

Cevigney *et al.* report example findings for Pakistan with the following parameters: 50% of pregnant women covered and 70% vaccine effectiveness. In this scenario, 195,000 cases of RSV and 1,100 RSV-associated deaths could be avoided in Pakistan. If this scenario were to be expanded to all USAID MCHN priority countries, 2 million cases and 15,000 infant deaths could be prevented each year. This study is subject to some limitations. Firstly, the tool estimates national and region-specific estimates of incidence and mortality based on published data on population, incidence, hospitalization rates and in-hospital mortality rates and mathematical assumptions which introduces uncertainty into the estimates. Secondly, the tool only includes vaccination success as binary (i.e., that the vaccine prevents RSV and does not reduce virulence and severity of disease). This may underestimate the benefit of RSV maternal vaccines as they may have indirect protective effects. Overall, this tool provides a standardized approach for assessing the impact of RSV vaccines which can be used to inform future vaccine initiatives, funding, and implementation efforts.

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### 3. [Child health and the implementation of Community and District-management Empowerment for Scale-up \(CODES\) in Uganda: a randomised controlled trial.](#)

Waiswa P, Mpanga F, Bagenda D, Kananura R, O'Connell T, Henriksson D, et al.

*BMJ Glob Health.* 2021 Jun 24;6(6).

#### ABSTRACT

**INTRODUCTION:** Uganda's district-level administrative units buttress the public healthcare system. In many districts, however, local capacity is incommensurate with that required to plan and implement quality health interventions. This study investigates how a district management strategy informed by local data and community dialogue influences health services.

**METHODS:** A 3-year randomised controlled trial (RCT) comprised of 16 Ugandan districts tested a management approach, Community and District-management Empowerment for Scale-up (CODES). Eight districts were randomly selected for each of the intervention and comparison areas. The approach relies on a customised set of data-driven diagnostic tools to identify and resolve health system bottlenecks. Using a difference-in-differences approach, the authors performed an intention-to-treat analysis of protective, preventive and curative practices for malaria, pneumonia and diarrhoea among children aged 5 and younger.

**RESULTS:** Intervention districts reported significant net increases in the treatment of malaria (+23%), pneumonia (+19%) and diarrhoea (+13%) and improved stool disposal (+10%). Coverage rates for immunisation and vitamin A consumption saw similar improvements. By engaging communities and district managers in a common quest to solve local bottlenecks, CODES fostered demand for health services. However, limited fiscal space-constrained district managers' ability to implement solutions identified through CODES.

**CONCLUSION:** Data-driven district management interventions can positively impact child health outcomes, with clinically significant improvements in the treatment of malaria, pneumonia and diarrhoea as well as stool disposal. The findings recommend the model's suitability for health systems strengthening in Uganda and other decentralised contexts.

**TRIAL REGISTRATION NUMBER:** ISRCTN15705788.

**WEB:** [10.1136/bmjgh-2021-006084](https://doi.org/10.1136/bmjgh-2021-006084)

**IMPACT FACTOR:** 4.280

**CITED HALF-LIFE:** 1.9

## START COMMENTARY

Waiswa *et al.* describe the impact of a multi-year initiative called Community and District-management Empowerment for Scale-up (CODES) developed to enhance the government's ability to prevent diarrhea, pneumonia, and malaria. The program was developed to identify and address health system bottlenecks with a primary focus on challenges faced by the district's management. This randomized clinical trial is important as it tests the impact of a district-level management intervention on population level health outcomes. The intervention included three pillars. Pillar 1 was focused on collating, analyzing, and applying survey and program data to track indicators and identify bottlenecks. Additionally, UNICEF provided each district a 'bottleneck fund' of 10,000 USD each year to facilitate implementation of local solutions for bottlenecks. Pillar 2 consisted of regular review of district work plans, which included quality improvement efforts and inter-district learning. Pillar 3 was aimed at increasing demand for services through community engagement activities. 16 high-mortality districts were matched districts based on child indicators and randomly assigned to intervention or comparison arm. Based on the child survival indicators, districts were shown to be heterogeneous, indicating stratified randomized was required. Outcomes included protective, preventative, and curative indicators. Protective indicators included exclusive breastfeeding for 6 months and adherence to the schedule for Vitamin A supplementation. Preventative indicators included full immunization based on standard age-specific vaccination within the first year of life, diphtheria-pertussis-tetanus (DTP) 3, use of long-lasting insecticide treated nets, improved sanitation, and handwashing with soap. Curative indicators included appropriate case management for malaria, diarrhea, and pneumonia symptoms.

The intervention had a statistically significant impact on vitamin A use among children 6-11, although this was not shown among older children. There no impacts on exclusive breastfeeding. In terms of prevention coverage indicators, there were positive impacts on DTP3 and full immunization, but these results were not statistically significant. Coverage levels and effective bed net use were not different by arm. Positive findings include that the percentage of households with drinking water from safe sources increased significantly by 7.4% (95% CI: 1.6-16.5) and the percentage of households with safe stool disposal increased significantly with a rise of 10.4% (95% CI 4.9-15.9). In terms of coverage indicators, there was a statistically significant impact on recommended treatment for malaria (23.3%, 95% CI 9.1 to 37.5), pneumonia (9.2%, 95% CI 7.9 to 30.6), and diarrhea (13.2%, 95% CI 5.6 to 20.7). However, the intervention did not have an impact on the two week prevalence of the three diseases. One strength of this study that the authors included the intervention dose delivered in *Online Supplemental Table 2*, which is critical to understanding the intervention but is often excluded from studies. Overall, this article demonstrates that the CODES approach was moderately successful and should be considered as a tool to scale up child-health interventions.

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#### 4. [Delivery channels and socioeconomic inequalities in coverage of reproductive, maternal, newborn, and child health interventions: analysis of 36 cross-sectional surveys in low-income and middle-income countries.](#)

Leventhal D, Crochemore-Silva I, VIDALETTI L, Armenta-Paulino N, Barros A, Victora C.  
*Lancet Glob Health.* 2021 May 29.

### ABSTRACT

**BACKGROUND:** Global reports have described inequalities in coverage of reproductive, maternal, newborn, and child health (RMNCH) interventions, but little is known about how socioeconomic inequality in intervention coverage varies across multiple low-income and middle-income countries (LMICs). We aimed to assess the association between wealth-related inequalities in coverage of RMNCH interventions.

**METHODS:** In this cross-sectional study, we identified publicly available Demographic Health Surveys and Multiple Indicator Cluster Surveys from LMICs containing information on household characteristics, reproductive health, women's and children's health, nutrition, and mortality. We identified the most recent survey from the period 2010-19 for 36 countries that contained data for our preselected set of 18 RMNCH interventions. 21 countries also had information on two common malaria interventions. We classified interventions into four groups according to their predominant delivery channels: health facility based, community based, environmental, and culturally driven (including breastfeeding practices). Within each country, we derived wealth quintiles from information on household asset indices. We studied two summary measures of within-country wealth-related inequality: absolute inequalities (akin to coverage differences among children from wealthy and poor households) using the slope index of inequality (SII), and relative inequalities (akin to the ratio of coverage levels for wealthy and poor children) using the concentration index (CIX). Pro-poor inequalities are present when intervention coverage decreased with increasing household wealth, and pro-rich inequalities are present when intervention coverage increased as household wealth increased.

**FINDINGS:** Across the 36 LMICs included in our analyses, coverage of most interventions had pro-rich patterns in most countries, except for two breastfeeding indicators that mostly had higher coverage among poor women, children and households than wealthy women, children, and households. Environmental interventions were the most unequal, particularly use of clean fuels, which had median levels of SII of 48.8 (8.6-85.7) and CIX of 67.0 (45.0-85.8). Interventions primarily delivered in health facilities—namely institutional childbirth (median SII 46.7 [23.1-63.3] and CIX 11.4 [4.5-23.4]) and antenatal care (median SII 26.7 [17.0-47.2] and CIX 10.0 [4.2-17.1])—also usually had pro-rich patterns. By comparison, primarily community-based interventions, including those against malaria, were more equitably distributed—eg, oral rehydration therapy (median SII 9.4 [2.9-19.0] and

CIX 3 4 [1 3-25 0]) and polio immunisation (SII 12 1 [2 3-25 0] and CIX 3 1 [0 5-7 1]). Differences across the four types of delivery channels in terms of both inequality indices were significant (SII  $p=0.0052$ ; CIX  $p=0.0048$ ).

**INTERPRETATION:** Interventions that are often delivered at community level are usually more equitably distributed than those primarily delivered in fixed facilities or those that require changes in the home environment. Policy makers need to learn from community delivery channels to promote more equitable access to all RMNCH interventions.

**FUNDING:** Bill & Melinda Gates Foundation and Wellcome Trust.

**TRANSLATIONS:** For the French, Portuguese and Spanish translations of the abstract see Supplementary Materials section.

**WEB:** [10.1016/S2214-109X\(21\)00204-7](https://doi.org/10.1016/S2214-109X(21)00204-7)

**IMPACT FACTOR:** 21.597

**CITED HALF-LIFE:** 3.1

## START COMMENTARY

In this cross-sectional study, Leventhal *et al.* utilize Demographic Health Surveys (DHS), Multiple Indicator Cluster Surveys (MICS), and the International Center for Equity in Health (ICEH) Countdown database to describe associations between wealth-related inequalities in coverage of reproductive, maternal, newborn, and child health (RMNCH) interventions. This article is impactful as it comprehensively describes within-country inequalities of coverage for 20 RMNCH interventions in 36 countries. Further, it considers four types of RMNCH delivery channels: environmental, health-facility based, community-based, and culturally-driven interventions. Environmental interventions include clean cooking fuels, improved sanitation and piped water. Health facility based interventions include four or more antenatal care visits, institutional childbirth, postnatal visits for mothers, and birth registration. Community-based interventions included demand met for modern contraceptives, DPT3 immunization, postnatal visit, vitamin A supplement, care seeking for any disease, oral rehydration treatment for diarrhea, antimalarial treatment for fever, minimum dietary diversity, and household insecticide bed net or household spraying. Cultural treatment included exclusive breastfeeding when the infant is 0-5 months and continued breastfeeding when the infant is 12-15 months.

Environmental interventions were determined to be the most unequal with both absolute and relative socioeconomic inequalities. Health facility based interventions were also shown to be pro-rich, whereas community-based interventions were more equitably distributed. Culturally driven interventions (exclusive and continued breastfeeding) were shown to have pro-poor inequality. *Table 1* shows detailed results from the variance-weighted least squares regression with the summary indices

of inequality as outcomes, according to RMNCH delivery channel. The authors found similar patterns among low-income countries and middle-income countries, but relative inequalities were slightly smaller in middle-income countries (*Figure 3*). There are a few limitations to note; firstly, only countries with data for the key indicators of interest were included in this study (36 of over 100 countries in the ICEH/Countdown database). Secondly, the study used the most recent survey data available from 2010-2019, which may result in some countries having outdated data which does not reflect the current state of RMNCH coverage. In conclusion, this study demonstrates the success of community-based interventions in terms of equity, which can be used as a guide for future efforts to reduce inequalities in environmental and health-based interventions.

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## 5. [The impact of the COVID-19 pandemic on rabies reemergence in Latin America: The case of Arequipa, Peru.](#)

Raynor B, D az E, Shinnick J, Zegarra E, Monroy Y, Mena C, et al.

*PLoS Negl Trop Dis.* 2021 Jun 14;15(5):e0009414.

### ABSTRACT

In Latin America, there has been tremendous progress towards eliminating canine rabies. Major components of rabies elimination programs leading to these successes have been constant and regular surveillance for rabid dogs and uninterrupted yearly mass dog vaccination campaigns. Unfortunately, vital measures to control COVID-19 have had the negative trade-off of jeopardizing these rabies elimination and prevention activities. We aimed to assess the effect of interrupting canine rabies surveillance and mass dog vaccination campaigns on rabies trends. We built a deterministic compartment model of dog rabies dynamics to create a conceptual framework for how different disruptions may affect rabies virus transmission. We parameterized the model for conditions found in Arequipa, Peru, a city with active rabies virus transmission. We examined our results over a range of plausible values for  $R_0$  (1.36-2.0). Also, we prospectively evaluated surveillance data during the pandemic to detect temporal changes. Our model suggests that a decrease in canine vaccination coverage as well as decreased surveillance could lead to a sharp rise in canine rabies within months. These results were consistent over all plausible values of  $R_0$ . Surveillance data from late 2020 and early 2021 confirms that in Arequipa, Peru, rabies cases are on an increasing trajectory. The rising rabies trends in Arequipa, if indicative to the region as whole, suggest that the achievements made in Latin America towards the elimination of dog-mediated human rabies may be in jeopardy.

**WEB:** [10.1371/journal.pntd.0009414](https://doi.org/10.1371/journal.pntd.0009414)

**IMPACT FACTOR:** 3.885

**CITED HALF-LIFE:** 4.8

### START COMMENTARY

In this modelling study, Raynor *et al.* develop a deterministic compartment model of dog rabies to assess how COVID-19 disruptions may affect rabies virus transmission in Arequipa, Peru. This study is important as it highlights the issues of canine rabies reemergence associated with delaying, diminishing, or suspending rabies control due to COVID-19 in a region which is near eliminating canine rabies. The authors utilized data from two sources: a longitudinal survey conducted from 2015-2019 which collected data on dog demographics and vaccination campaign participation, and from epidemic data on samples submitted to the Ministry of Health. Data included the dates of first clinical signs, death, sample submission, positive sample confirmation, and focus control activities. The model included four canine populations states: vaccinated, susceptible, exposed, and infectious. Parameters

were estimated based on the longitudinal survey and Ministry of Health data, and are described in detailed in the *Supplementary Information Text A*. The model also included simulations for a range of  $R_0$  values and included a 1-year and 5-year simulation.

Overall, there were 214 reports of rabid dogs from March 2015-March 2020. *Figure 1* demonstrates the cyclic nature of immunity and transmission due to yearly vaccination campaigns. Authors note that there is a quick decay of population immunity due to high canine population turnover. *Figure 2* shows different simulations of disruption scenarios for the 1-year simulation. In a scenario assuming dog vaccination campaigns are cancelled, cases would grow exponentially. Decreased surveillance would likely result in increased rabid dog survival from 2.5 to 3.7 days. During COVID-19 restrictions, vaccinations campaign coverage was reduced leading to a mere 12.3% in Arequipa. Surveillance was also severely reduced measured by the number of samples received by the Ministry of Health (i.e., an average of 2.7 samples per month compared to 35.7 before COVID-19). The model predicts that there has been a substantial increase in rabies cases in the last few months, which has been shown in preliminary surveillance data for recent months. There are a few limitations to note in the study including the uncertainty with the model. The model was parameterized using data known to have issues with underreporting. However, Raynor *et al.* tried to account for this issue by making some assumptions about reporting (i.e., that 10% of canine rabies cases are detected). In conclusion, this article describes the detrimental impacts of COVID-19 on rabies prevention and control efforts, which may reverse some of the achievements made in Latin America towards elimination.

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## 6. [Mobile nudges and financial incentives to improve coverage of timely neonatal vaccination in rural areas \(GEVaP trial\): A 3-armed cluster randomized controlled trial in Northern Ghana.](#)

Levine G, Salifu A, Mohammed I, Fink G.  
*PLoS One*. 2021 May 28;16(5):e0247485.

### ABSTRACT

**BACKGROUND:** Despite progress in vaccination coverage, timeliness of childhood vaccination remains a challenge in many settings. We aimed to assess if mobile phone-based reminders and incentives to health workers and caregivers could increase timely neonatal vaccination in a rural, low-resource setting.

**METHODS:** We conducted an open-label cluster randomized controlled 1:1:1 trial with three arms in 15 communities in Northern Ghana. Communities were randomized to 1) a voice call reminder intervention; 2) a community health volunteer (CHV) intervention with incentivized rewards; 3) control. In the voice call reminder arm, a study staff member made voice calls to mothers shortly after birth to encourage vaccination and provide personalized information about available vaccination services. In the incentive arm, CHVs promoted infant vaccination and informed women with recent births about available vaccination opportunities. Both CHVs and women were provided small monetary incentives for on-time early infant vaccination in this arm, delivered using mobile phone-based banking applications. No study activities were conducted in control communities. A population-based survey compared vaccination coverage across arms in the pre-intervention and intervention periods. The primary endpoint was completion of at least one dose of Polio vaccine within 14 days of life and BCG vaccination within 28 days of life.

**RESULTS:** Six-hundred ninety births were identified; 106, 88, and 88 from pre-intervention and 150, 135, and 123 in the intervention period, in the control, voice call reminder and CHV incentive arms, respectively. In adjusted intent-to-treat analysis, voice call reminders were associated with 10.5 percentage point (95% CI: 4.0, 17.1) higher coverage of on-time vaccination, while mobile phone-based incentives were associated with 49.5 percentage point (95% CI: 26.4, 72.5) higher coverage.

**CONCLUSION:** Community-based interventions using mobile phone technologies can improve timely early vaccination coverage. A CHV approach with incentives to community workers and caregivers was a more effective strategy than voice call reminders. The impact of vaccination “nudges” via voice calls may be constrained in settings where network coverage and phone ownership are limited.

**TRIAL REGISTRATION:** This trial was registered at ClinicalTrials.gov; NCT03797950.



**WEB:** [10.1371/journal.pone.0247485](https://doi.org/10.1371/journal.pone.0247485)

**IMPACT FACTOR:** 2.740

**CITED HALF-LIFE:** 5.6

## START COMMENTARY

In this randomized controlled trial, Levine *et al.* describe the impact of mobile, phone-based reminders and financial incentives to increase timely neonatal vaccination. The study was conducted in rural Karaga District in the Northern Region, where socioeconomic and health status are generally worse than the rest of Ghana. In this region, about 41% of children received all age-appropriate vaccinations by age 2 years. 15 communities within the district were randomized to three arms: 1) voice call reminder intervention; 2) a community health volunteer (CHV) intervention with incentivized rewards (1 Ghana cedi reward for verified on time vaccination with first dose of Polio and with BCG); 3) standard of care. The primary outcome was on-time completion of both early vaccinations, which included receiving at least one dose of Polio vaccine within the first 14 days of life and BCG vaccine within 28 days. Secondary outcomes included on-time receipt of each vaccine, and receipt of each vaccine and both vaccines at any age.

Levine *et al.* include 690 infants that survived at least one day of life after birth in the analysis. *Table 1* describes the study population characteristics by time period and study arm. Key findings included that 97% or more in each arm received some vaccination in the pre- and intervention periods, and 95% in each arm had a vaccination card or health booklet available during the interview. When assessing program impact with an intent-to-treat analysis, it was shown that the proportion of infants in the call reminder group who were vaccinated on time with the first dose of Polio and BCG was higher than in the control arm (10.5 percentage points different, 95% CI: 4.0, 17.1) whereas the proportion of infants vaccinated on time in the CHV and incentives arm during the intervention period was 49.5% percentage points higher (95% CI: 26.4, 72.5) after adjusting for baseline differences in vaccination coverage and other covariates. Relatedly, timely Polio vaccination was 48.8 percentage points (95% CI: 24.5, 73.1) higher in the CHV group compared to the control arm. However, timely BCG vaccination was not statistically significantly different between the intervention and control arms. Overall, this study finds that outreach aimed at encouraging vaccination can improve vaccination coverage, particularly when outreach is combined with incentives.

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## 7. [Barriers and activities to implementing or expanding influenza vaccination programs in low- and middle-income countries: A global survey.](#)

Kraigsley A, Moore K, Bolster A, Peters M, Richardson D, Arpey M, et al.  
*Vaccine*. 2021 Jun 07;39(25):3419-3427.

### ABSTRACT

**INTRODUCTION:** Despite considerable global burden of influenza, few low- and middle-income countries (LMICs) have national influenza vaccination programs. This report provides a systematic assessment of barriers to and activities that support initiating or expanding influenza vaccination programs from the perspective of in-country public health officials.

**METHODS:** Public health officials in LMICs were sent a web-based survey to provide information on barriers and activities to initiating, expanding, or maintaining national influenza vaccination programs. The survey primarily included Likert-scale questions asking respondents to rank barriers and activities in five categories.

**RESULTS:** Of 109 eligible countries, 62% participated. Barriers to influenza vaccination programs included lack of data on cost-effectiveness of influenza vaccination programs (87%) and on influenza disease burden (84%), competing health priorities (80%), lack of public perceived risk from influenza (79%), need for better risk communication tools (77%), lack of financial support for influenza vaccine programs (75%), a requirement to use only WHO-prequalified vaccines (62%), and young children require two vaccine doses (60%). Activities for advancing influenza vaccination programs included educating healthcare workers (97%) and decision-makers (91%) on the benefits of influenza vaccination, better estimates of influenza disease burden (91%) and cost of influenza vaccination programs (89%), simplifying vaccine introduction by focusing on selected high-risk groups (82%), developing tools to prioritize target populations (80%), improving availability of influenza diagnostic testing (79%), and developing collaborations with neighboring countries for vaccine procurement (74%) and regulatory approval (73%). Responses varied by country region and income status.

**CONCLUSIONS:** Local governments and key international stakeholders can use the results of this survey to improve influenza vaccination programs in LMICs, which is a critical component of global pandemic preparedness for influenza and other pathogens such as coronaviruses. Additionally, strategies to improve global influenza vaccination coverage should be tailored to country income level and geographic location.

**WEB:** [10.1016/j.vaccine.2021.04.043](https://doi.org/10.1016/j.vaccine.2021.04.043)

**IMPACT FACTOR:** 3.143

**CITED HALF-LIFE:** 7.3

## START COMMENTARY

In this cross-sectional study, Kraigsley *et al.* assess the barriers and activities that support influenza vaccination programs using a web-based survey of health officials in LMICs. This article is important as it is the first study that identifies barriers and activities that could help develop, expand, or maintain influenza vaccination programs in LMICs with in-country health officials. These are critical to understand as seasonal influenza accounts for large morbidity and mortality annually, with most cases in LMICs. Despite the high burden, only 37% of lower-middle-income countries and 3% of low-income countries have an influenza vaccination policy, compared to 74% of upper-middle-income countries. In this study, Expanded Program on Immunization (EPI) managers were identified through the WHO Department on Immunization, Vaccines, and Biologicals. The web-based survey was focused on challenges, opportunities, and solutions for developing and maintaining influenza vaccination programs in LMICs.

*Table 3* summarizes the top 4 activities and barriers by category based on frequency distribution. Reported barriers related to establishing or maintaining an influenza vaccination program included a lack of data on influenza morbidity/mortality, competing health priorities, and a lack of domestic financial support. Activities that were deemed critically important or important included educating health workers, showing the value of seasonal influenza vaccination for pandemic preparedness, among others. Other notable barriers include a lack of cost-effectiveness data for influenza vaccination programs, limited number of influenza vaccines registered in country, a lack of commitment from governments for vaccines, and lack of public health risk communication tools. There were significant differences in response distributions by country income status (as shown in *Table 4*) and by WHO region (*Table 5*). When asked an open-ended question about the most critical activity to improve the use of influenza vaccines, common responses included lowering the cost of vaccines or acquiring additional financial support for vaccine programs, determining influenza disease burden or cost-effectiveness and improving risk communication and education. One notable limitation is that only 62% of 109 eligible countries participated. However, authors aimed to assess if responding countries were representative of all 109 eligible countries by evaluating several independent variables such as country income level, presence of a national influenza vaccination program, and presence of social or economic fragility. Kraigsley *et al.* found that only participation in the Partnership for Influenza Vaccine Introduction was significantly different between groups in a multivariate logistic regression analysis and participation in Partnership for Influenza Vaccine Introduction and having a national influenza vaccination program were significantly different in the univariate analysis. Overall, results from this survey can inform strategic priorities for local governments and international organizations aiming to improve influenza vaccination programs in LMICs.

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## 8. [Prevention of hepatitis B mother-to-child transmission in Namibia: A cost-effectiveness analysis.](#)

Tamandjou Tchuem C, Andersson M, Wiysonge C, Mufenda J, Preiser W, Cleary S.  
*Vaccine*. 2021 May 27;39(23):3141-3151.

### ABSTRACT

Despite access to a safe and effective vaccine, mother-to-child transmission (MTCT) of hepatitis B virus (HBV) persists in Africa. This is of concern since perinatally-infected infants are at highest risk of developing hepatocellular carcinoma, a life-threatening consequence of chronic HBV infection. While tools to prevent HBV MTCT are available, the cost implications of these interventions need consideration prior to implementation. A Markov model was developed to determine the costs and health outcomes of (1) universal HBV birth dose (BD) vaccination, (2) universal BD vaccination and targeted hepatitis B immunoglobulin (HBIG), (3) maternal antiviral prophylaxis using sequential HBV viral load testing added to HBV BD vaccination and HBIG, and (4) maternal antiviral prophylaxis using sequential HBeAg testing combined with HBV BD vaccination and HBIG. Health outcomes were assessed as the number of paediatric infections averted and disability-adjusted life years (DALYs) averted. Primary cost data included consumables, human resources, and hospital facilities. HBV epidemiology, transitions probabilities, disability weights, and the risks of HBV MTCT were extracted from the literature. Incremental cost-effectiveness ratios (ICERs) were calculated to compare successive more expensive interventions to the previous less expensive one. One-way sensitivity analyses were conducted to test the robustness of the model's outputs. At the Namibian cost/DALY averted threshold of US\$3 142, the (1) BD vaccination + targeted HBIG, and (2) maternal antiviral prophylaxis with sequential HBeAg testing interventions were cost-effective. These interventions had ICERs equal to US\$1909.03/DALY and US\$2598.90/DALY averted, respectively. In terms of effectiveness, the maternal antiviral prophylaxis with sequential HBeAg testing intervention was the intervention of choice. The analysis showed that elimination of HBV MTCT is achievable using maternal antiviral prophylaxis with active and passive immunization. There is an urgent need for low cost diagnostic tests to identify those women who will most benefit from drug therapy to attain this laudable goal.

**WEB:** [10.1016/j.vaccine.2021.04.041](https://doi.org/10.1016/j.vaccine.2021.04.041)

**IMPACT FACTOR:** 3.143

**CITED HALF-LIFE:** 7.3

### START COMMENTARY

In this cost-effectiveness study, Tamandjou Tchuem *et al.* develop a Markov model to project the costs and health outcomes of four hepatitis B virus (HBV) vaccine interventions. This study is

important as it demonstrates the cost-effectiveness of birth dose (BD) vaccinations with other prevention strategies, which are critical for eliminating HBV mother to child transmission. This study included four interventions; the first intervention included only HBV BD vaccination within 24 hours of delivery, regardless of the mother's HBV status. The second included the universal BD vaccination and targeted hepatitis B immunoglobulin (HBIG) for babies born to women who tested HBsAg positive at the antenatal (ANC) visit. The third intervention included all components of the second intervention and an additional viral load test for HBsAg positive pregnant women. If women had greater than 200,000 IU/ml, they received antiviral prophylaxis with tenofovir from the third trimester. The fourth intervention was closely related to the third. Instead of a viral load test, HBsAg positive pregnant women were tested for HBeAg and given tenofovir if found seropositive. Costs included were collected during a screen-treat-vaccinate intervention study that was conducted alongside this study. Detailed costs are shown in *Table 1* and include categories such as staff costs, patient-specific costs, overheads, and capital costs (e.g., furniture and space). Epidemiological data, HBV diagnostic data, and rates of HBV mother to child transmission were determined based on published literature. Transition probabilities were determined using an established Mozambican Markov model whereas disability weights were taken from the Global Burden of Disease (GBD) study. Details on each model input are shown in *Table 2*. The cost-effectiveness threshold of US\$3,142 per DALY averted was based on prior literature (Ochalek *et al.* 2018). Lastly, authors conducted one-way sensitivity analyses to test the robustness of the model results. Model outcomes include perinatal HBV infections averted and disability-adjusted life years averted (DALYs).

Key findings included that adding HBID to universal vaccination resulted in ICERs of US\$ 4,600.08 per pediatric infection averted and US \$1,909.03 per DALY averted. The intervention with HBeAg testing was cheaper than the intervention with viral load testing. Detailed findings for each intervention are presented in *Table 3*. Overall, all interventions were below the ICER threshold. In sensitivity analyses, ICERs were highly dependent on several model parameters, which varied depending on the intervention of interest. Importantly, some of these parameters made the ICERs higher than the cost-effective threshold. This study included a few limitations to note, namely that only direct medical costs were included, which may bias the findings positively, indicating that the intervention is more cost-effective than it might be when other direct, indirect, and economic costs are taken into account. Further, longer term health outcomes (e.g., chronic HBV complications) were not included. However, this study demonstrates that the current policy (universal HBV vaccine and targeted HBIG) is cost-effective and other preventions (i.e., viral load testing and treatment and HBeAg testing and treatment) could be cost-effective in Namibia.

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## 9. [The effects of polio eradication efforts on health systems: a cross-country analysis using the Develop-Distort Dilemma.](#)

Rodriguez D, Neel A, Mahendradhata Y, Deressa W, Owoaje E, Akinyemi O, et al.

*Health Policy Plan.* 2021 Jun 05;36(5):707-719.

### ABSTRACT

Vertical disease control programmes have enormous potential to benefit or weaken health systems, and it is critical to understand how programmes' design and implementation impact the health systems and communities in which they operate. We use the Develop-Distort Dilemma (DDD) framework to understand how the Global Polio Eradication Initiative (GPEI) distorted or developed local health systems. We include document review and 176 interviews with respondents at the global level and across seven focus countries (Afghanistan, Bangladesh, Democratic Republic of Congo, Ethiopia, India, Indonesia and Nigeria). We use DDD domains, contextual factors and transition planning to analyse interactions between the broader context, local health systems and the GPEI to identify changes. Our analysis confirms earlier research including improved health worker, laboratory and surveillance capacity, monitoring and accountability, and efforts to reach vulnerable populations, whereas distortions include shifting attention from routine health services and distorting local payment and incentives structures. New findings highlight how global-level governance structures evolved and affected national actors; issues of country ownership, including for data systems, where the polio programme is not indigenously financed; how expectations of success have affected implementation at programme and community level; and unresolved tensions around transition planning. The decoupling of polio eradication from routine immunization, in particular, plays an outsize role in these issues as it removed attention from system strengthening. In addition to drawing lessons from the GPEI experience for other efforts, we also reflect on the use of the DDD framework for assessing programmes and their system-level impacts. Future eradication efforts should be approached carefully, and new initiatives of any kind should leverage the existing health system while considering equity, inclusion and transition from the start.

**WEB:** [10.1093/heapol/czab044](https://doi.org/10.1093/heapol/czab044)

**IMPACT FACTOR:** 2.704

**CITED HALF-LIFE:** 7.2

### START COMMENTARY

Rodriguez *et al.* use the Develop-Distort Dilemma (DDD) framework to assess the Global Polio Eradication Initiative (GPEI)'s interactions with health systems across countries (Afghanistan, Bangladesh, Democratic Republic of Congo, Ethiopia, India, Indonesia, and Nigeria). This study is impactful as it summarizes the history of the 30+ year effort to eradicate polio, and the impact on

health systems. Data sources include a cross-case analysis of seven country cases studies, which included key informant interviews (KII). As part of the case studies, health system indicators were captured at various timepoints. Key informants were selected based on areas of expertise and to ensure representativeness of key stakeholders (e.g., governments, implementers). Characteristics of the key informants are summarized in *Table 3*. Interview transcripts were analyzed using deductive analysis based on the six DDD domains (actors, functions, expectations, inclusion, indigeneity, and cost), the WHO health system building blocks, transition planning, and broader contextual factors.

For the actors domain, one key finding is that GPEI became more inclusive with decision-making beginning in 2012, which allowed for more accountability between partners. Another interesting finding related to actors was that key informants indicated that polio campaigns diverted staff from usual tasks on a sub-national level. For the functions domain, there were positive (development) and negative (distortion) findings. The polio program increased capacity which could be transferred to other health programs, increased accountability, and promoted a data-driven focus. However, there were indications that the polio program was not integrated into existing routine immunization programs. In the expectations domain, there were notable high expectations related to eradication and concerns about contracts not being renewed once eradication goals were met. In terms of inclusion, the program was successful in trying to reach vulnerable populations to meet the goal of eradication, although these efforts did not seem to translate to routine immunization efforts. For the indigeneity domain, there were mixed findings with a greater involvement of local staff and community decision-making in country, but with programs being financed outside of the country. Lastly, Rodriguez *et al.* found issues relating to the transition of polio eradication activities and assets, with a finding that there was a concern among respondents that the achievements would not be maintained without future external support. In conclusion, this article summarizes some key issues related to the GPEI's efforts to eradicate polio (i.e., developing a parallel system outside of routine immunization) which should be considered as future vaccination efforts are developed.

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## 10. [Impact of campaign-style delivery of routine vaccines: a quasi-experimental evaluation using routine health services data in India.](#)

Clarke-Deelder E, Suharlim C, Chatterjee S, Brenzel L, Ray A, Cohen J, et al.

*Health Policy Plan.* 2021 May 21;36(4):454-463.

### ABSTRACT

The world is not on track to achieve the goals for immunization coverage and equity described by the World Health Organization's Global Vaccine Action Plan. Many countries struggle to increase coverage of routine vaccination, and there is little evidence about how to do so effectively. In India in 2016, only 62% of children had received a full course of basic vaccines. In response, in 2017-18 the government implemented Intensified Mission Indradhanush (IMI), a nationwide effort to improve coverage and equity using a campaign-style strategy. Campaign-style approaches to routine vaccine delivery like IMI, sometimes called 'periodic intensification of routine immunization' (PIRI), are widely used, but there is little robust evidence on their effectiveness. We conducted a quasi-experimental evaluation of IMI using routine data on vaccine doses delivered, comparing districts participating and not participating in IMI. Our sample included all districts that could be merged with India's 2016 Demographic and Health Surveys data and had available data for the full study period. We used controlled interrupted time-series analysis to estimate the impact of IMI during the 4-month implementation period and in subsequent months. This method assumes that, if IMI had not occurred, vaccination trends would have changed in the same way in the participating and not participating districts. We found that, during implementation, IMI increased delivery of 13 infant vaccines, with a median effect of 10.6% (95% confidence interval 5.1% to 16.5%). We did not find evidence of a sustained effect during the 8...months after implementation ended. Over the 12...months from the beginning of implementation, we estimated reductions in the number of under-immunized children that were large but not statistically significant, ranging from 3.9% (-6.9% to 13.7%) to 35.7% (-7.5% to 77.4%) for different vaccines. The largest effects were for the first doses of vaccines against diphtheria-tetanus-pertussis and polio: IMI reached approximately one-third of children who would otherwise not have received these vaccines. This suggests that PIRI can be successful in increasing routine immunization coverage, particularly for early infant vaccines, but other approaches may be needed for sustained coverage improvements.

**WEB:** [10.1093/heapol/czab026](https://doi.org/10.1093/heapol/czab026)

**IMPACT FACTOR:** 2.704

**CITED HALF-LIFE:** 7.2



## START COMMENTARY

In this quasi-experimental study, Clarke-Deelder *et al.* describe the impact of the government implemented Intensified Mission Indradhanush (IMI) program, which uses campaign-style approaches to increase coverage of routine vaccination. This study makes an important contribution to the literature as there are few studies evaluating the effectiveness of campaign-based strategies to increase routine vaccination coverage although it is a widely used strategy globally. IMI was implemented in districts with weak immunization coverage, defined as less than 70% estimated DTP3 coverage, or greater than 13,000 children missing DTP3 in the previous year, and by request. 187 districts and urban areas were covered by the program. After surveys and planning, immunizations were held for 7 consecutive days each month. Outcome data on vaccinations for children and pregnant women was obtained from India's Health Management Information System (HMIS) from October 2015 to September 2018. This period includes 2 years before and 1 year after the intervention. Covariate data was obtained from DHS surveys and the World Bank. Clarke-Deelder *et al.* included 441 control districts in this comparative interrupted time series (CITS). As part of CITS, time trends in district-level vaccination volumes, defined by doses delivered) were modelled using generalized linear models with a quasi-Poisson distribution and a log link. In addition to the CITS, Clarke-Deelder *et al.* conducted sensitivity analyses to test the robustness of the results by conducting a single interrupted time-series, a matched analysis using a subset of the data, and conducting an analysis by excluding districts where there was a possibility of spillover effects.

Key findings include that IMI had a positive impact on all infant vaccines in the study, as is demonstrated in *Figure 1*, which shows the trends over time in vaccination volume in the treated and comparison districts. However, there was no statistically significant impact of IMI on vaccine delivery for pregnant women. The impact of IMI did not seem to be sustained over time; effects were no longer significant by mid-2018. In the sensitivity analysis, similar results were observed and are described in detail in the *Supplementary Tables S6-S12*. Overall, this study shows that routine immunization coverage using campaign methods did substantially increase infant vaccines, although not pregnancy vaccines, but did not have a sustained effect over time. Limitations to note include the data source and selection of comparison districts. Routine data from the HMIS provides monthly estimates of immunization volumes but may have issues with accuracy and reliability. Relatedly, many (91) comparison districts were excluded due to issues with data and administrative changes during the study period. Despite these limitations, this study demonstrates the impact of campaign-based strategies and underscores the need to follow up campaigns with routine health services to ensure that the progress is sustained.

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# Appendix

The literature search for the July 2021 Vaccine Delivery Research Digest was conducted on June 28, 2021. We searched English language articles indexed by the US National Library of Medicine and published between May 15, 2021, and June 14, 2021. The search resulted in 477 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]) (“2021/05/15”[PDAT] : “2021/06/14”[PDAT]))