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List of Articles

1 Universal healthcare coverage and health service delivery before and during the COVID-19 pandemic: A difference-in-difference study of childhood immunization coverage from 195 countries.

{Abstract & START Commentary} {Full Article}

- A quasi-experimental difference-in-difference study assessing if progress to universal health coverage affects the impact of COVID-19 on childhood immunization.

2 Cost effectiveness of rotavirus vaccine in Mozambique

{Abstract & START Commentary} {Full Article}

- A cost-effectiveness analysis of rotavirus vaccine introduction in Mozambique.

3 Interventions delivered in secondary or tertiary medical care settings to improve routine vaccination uptake in children and young people: a scoping review.

{Abstract & START Commentary} {Full Article}

- A scoping review assessing interventions aimed at improving vaccine uptake in children.

4 Epidemiological impact and cost-effectiveness analysis of COVID-19 vaccination in Kenya.

{Abstract & START Commentary} {Full Article}

- A study assessing the impact and cost-effectiveness of various COVID-19 vaccination strategies.

5 Progress Toward the Elimination of Mother-to-Child Transmission of Hepatitis B Virus - Worldwide, 2016-2021.

{Abstract & START Commentary} {Full Article}

- An overview of recent progress towards eliminating mother-to-child transmission of Hepatitis B.

6 Missed opportunities for vaccination (MOV) in children up to 5 years old in 19 Médecins Sans Frontières-supported health facilities: a cross-sectional survey in six low-resource countries.

{Abstract & START Commentary} {Full Article}

- A study assessing the prevalence of missed opportunities for vaccination.

7 Exploring public perceptions of vaccine-derived poliovirus and a novel oral polio vaccine in the Democratic Republic of the Congo, Kenya, and Nigeria.

{Abstract & START Commentary} {Full Article}

- A qualitative study assessing views on introducing a novel oral polio vaccine.

8 Small mobile conditional cash transfers (mCCTs) of different amounts, schedules and design to improve routine childhood immunization coverage and timeliness of children aged 0-23 months in Pakistan: An open label multi-arm randomized controlled trial.

{Abstract & START Commentary} {Full Article}

- A randomized controlled trial assessing various amounts, delivery methods, and schedules of small mobile conditional cash transfers to increase immunization coverage.

9 Critical success factors for routine immunization performance: A case study of Zambia 2000 to 2018.

{Abstract & START Commentary} {Full Article}

- A qualitative study summarizing stakeholders' views on factors contributing to successful immunization performance.

10 Contribution of child health interventions under-five mortality decline in Ghana: a modeling study using lives saved and missed opportunity tools

{Abstract & START Commentary} {Full Article}

- A modelling study assessing the impact of varying child health immunizations and the potential future impacts.

Appendix

Details of Articles

1. Universal healthcare coverage and health service delivery before and during the COVID-19 pandemic: A difference-in-difference study of childhood immunization coverage from 195 countries.

Kim S, Headley T, Tozan Y.

PLoS Med. 2022 Aug 18;19(8):e1004060.
PubMed ID: 35972985

ABSTRACT

BACKGROUND: Several studies have indicated that universal health coverage (UHC) improves health service utilization and outcomes in countries. These studies, however, have primarily assessed UHC's peacetime impact, limiting our understanding of UHC's potential protective effects during public health crises such as the Coronavirus Disease 2019 (COVID-19) pandemic. We empirically explored whether countries' progress toward UHC is associated with differential COVID-19 impacts on childhood immunization coverage.

METHODS AND FINDINGS: Using a quasi-experimental difference-in-difference (DiD) methodology, we quantified the relationship between UHC and childhood immunization coverage before and during the COVID-19 pandemic. The analysis considered 195 World Health Organization (WHO) member states and their ability to provision 12 out of 14 childhood vaccines between 2010 and 2020 as an outcome. We used the 2019 UHC Service Coverage Index (UHC SCI) to divide countries into a "high UHC index" group (UHC SCI 80) and the rest. All analyses included potential confounders including the calendar year, countries' income group per the World Bank classification, countries' geographical region as defined by WHO, and countries' preparedness for an epidemic/pandemic as represented by the Global Health Security Index 2019. For robustness, we replicated the analysis using a lower cutoff value of 50 for the UHC index. A total of 20,230 country-year observations were included in the study. The DiD estimators indicated that countries with a high UHC index (UHC SCI 80, n = 35) had a 2.70% smaller reduction in childhood immunization coverage during the pandemic year of 2020 as compared to the countries with UHC index less than 80 (DiD coefficient 2.70; 95% CI: 0.75, 4.65; p-value = 0.007). This relationship, however, became statistically nonsignificant at the lower cutoff value of UHC SCI <50 (n = 60). The study's primary limitation was scarce data availability, which restricted our ability to account for confounders and to test our hypothesis for other relevant outcomes.

CONCLUSIONS: We observed that countries with greater progress toward UHC were associated with significantly smaller declines in childhood immunization coverage during the pandemic. This

identified association may potentially provide support for the importance of UHC in building health system resilience. Our findings strongly suggest that policymakers should continue to advocate for achieving UHC in coming years.

WEB: 10.1371/journal.pmed.1004060
IMPACT FACTOR: 10.5
CITED HALF-LIFE: 8.4

START COMMENTARY

In this quasi-experimental study, Kim *et al.* assess the association between progress to universal health coverage (UHC) and differential COVID-19 impacts on childhood immunization coverage. This is the first study to quantify the association between UHC and childhood immunization during a health crisis. Nearly all prior studies which examine the role of UHC on health system performance do so in peacetime, rather than during a public health crisis (e.g., a pandemic). The COVID-19 pandemic provides an opportunity to understand countries' preparedness and resilience. National immunization data and trends, including absolute numbers and percentages of each type of vaccine by? country, were obtained from the WHO/UNICEF Joint Estimates of National Immunization Coverage. The primary outcome was childhood immunization coverage for 12 routine childhood vaccines, including overall vaccine coverage and specific vaccine coverage. Data for UHC was derived from UHC SCI index from the Institute for Health Metrics and Evaluation (IHME). The index ranges from 0 to 100, with 100 indicating the most effective service coverage. The index is an aggregate of 23 indicators across five health services including promotion, prevention, treatment, rehabilitation, and palliation. In addition to the five health services, the UHC reports indicators for five age groups (newborn; children under 5; children and adolescents between 5-19; adults 20-64; and older adults aged 65 and over). Kim *et al.* divided countries into two groups: the treatment group was defined as UHC SCI greater than or equal to 80, and control was less than 80. A strength of this study is that an alternative assumption was included to check for robustness; countries were assigned to the treatment group if UHC less than 50 and control if greater than or equal to 50. *Table 1* describes each of the categories of the UHC index and the countries that fall within those categories.

Overall, 38,139 country-year observations were assessed (1,658 observations were post-COVID). Prior to COVID, countries with UHC greater than or equal to 80 had average childhood immunization rates of 92.6% compared to 86.6 among countries with UHC less than 80. Detailed summary statistics are presented in *Table 2* and difference-in-difference results are shown in *Table 3.* Key findings indicated that there was an overall fall in global childhood immunization rates (2.72% lower post COVID compared to 2010-2019). Countries with high UHC (greater than or equal to 80) had a 2.70 percent smaller reduction in overall childhood immunization coverage (95% Confidence

Interval [CI]: -3.5, -1.95, p-value <0.001). It can be concluded that these countries barely experienced any decline in immunization coverage compared to countries with lower UHC in which immunization rates significantly declined due to COVID-19 (effect size=-3.11, 95% CI: -3.18, 2.36). Of note, there were no statically significant effect sizes for specific vaccines, only for all vaccines. However, this may have been due to limitations in sample size for specific vaccines. In robustness checks when a cutoff of 50 was used, there was no significant differential impact of COVID-19. Kim *et al.* hypothesized that this may indicate countries need a certain level of UHC to protect against adverse consequences associated with crises. Overall, this study provides evidence on the importance of progress towards UHC in strengthening health system resilience to public health crises.

Return to List of Articles

2. Cost effectiveness of rotavirus vaccine in Mozambique

Lourenço Guimarães E, Chissaque A, Pecenka C, Clark A, Vaz B, et al.

Vaccine. 2022 Aug 26;40(36):5338-5346

PubMed ID: 35933279

ABSTRACT

INTRODUCTION: Rotavirus is one of the most common cause of severe gastroenteritis in children, with the largest mortality burden in low- and middle-income countries. To prevent rotavirus gastroenteritis, Mozambique introduced ROTARIX® vaccine in 2015, however, its cost-effectiveness has never been established in the country. In 2018, additional vaccines became available globally. This study estimates the cost-effectiveness of the recently introduced ROTARIX in Mozambique and compares the cost-effectiveness of ROTARIX®, ROTAVAC®, and ROTASIIL® to inform future use.

METHODS: We used a decision-support model to calculate the potential cost-effectiveness of vaccination with ROTARIX compared to no vaccination over a five-year period (2016-2020) and to compare the cost-effectiveness of ROTARIX, ROTAVAC, and ROTASIIL to no vaccination and to each other over a ten-year period (2021-2030). The primary outcome was the incremental cost per disability-adjusted life-year (DALY) averted from a government perspective. We assessed uncertainty through sensitivity analyses.

RESULTS: From 2016 to 2020, we estimate the vaccine program with ROTARIX cost US$12.3 million, prevented 4,628 deaths, and averted US$3.1 million in healthcare costs. The cost per DALY averted was US$70. From 2021 to 2030, we estimate all three vaccines could prevent 9,000 deaths and avert US$7.8 million in healthcare costs. With Global Alliance for Vaccines and Immunization (Gavi) support, ROTARIX would have the lowest vaccine program cost (US$31 million) and 98 % probability of being cost-effective at a willingness-to-pay threshold of 0.5x GDP per capita. Without Gavi support, ROTASIIL would have the lowest vaccine program cost (US$75.8 million) and 30 % probability of being cost-effective at the same threshold.

CONCLUSION: ROTARIX vaccination had a substantial public health impact in Mozambique between 2016 and 2020. ROTARIX is currently estimated to be the most cost-effective product, but the choice of vaccine should be re-evaluated as more evidence emerges on the price, incremental delivery cost, wastage, and impact associated with each of the different rotavirus vaccines.

WEB: 10.1016/j.vaccine.2022.07.044

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

Lourenço Guimarães *et al.* examined the cost-effectiveness of rotavirus vaccine in Mozambique. This study is timely given that Mozambique introduced a monovalent rotavirus vaccine (ROTARIX) through the Expanded Program on Immunization (EPI). Since the implementation, there are indications that gastroenteritis hospital admissions have decreased; however, cost-effectiveness analyses on ROTARIX or any other rotavirus vaccines (pentavalent ROTASIIL or monovalent ROTAVAC) have not been conducted. Lourenço Guimarães *et al.* project the impact of ROTARIX compared to no vaccination from 2016 to 2020 and the impact of ROTARIX, ROTAVAC, and ROTASIIL compared to no vaccination and to each other from 2021 to 2030. The authors utilized a cost-effectiveness threshold of 0.5 times the Gross Domestic Product (GDP) of Mozambique along with other outputs, since there is no consensus on country-specific willingness-to-pay thresholds. Rotavirus gastroenteritis cases were estimated from three sources (the IHME Global Burden of Disease; WHO; CDC; and the Maternal and Child Health Epidemiology Estimation Group). Detailed input parameters are shown in *Table 1.* Costs of vaccines per dose (with and without Gavi support), wastage rates, international handling, international delivery, and packaging were included as part of the costs (described in *Table 2*).

Key findings for the analysis comparing ROTARIX to no vaccination from 2016 to 2020 estimated that 963,701 rotavirus gastroenteritis cases were averted, resulting in a 42% reduction in both severe cases and deaths. Compared to no vaccination, ROTARIX was associated with an incremental cost effectiveness ratio (ICER) of US$ 70 per DALY averted (95% Uncertainty Interval [UI]: 36-159) from a government perspective, which was considered cost-effective. However, without Gavi support, ROTARIX was no longer cost-effective due to the higher vaccine cost. *Figure 1* presents the scenario analysis results compared to no vaccination. In analyses from 2021 to 2030, of ROTARIX, ROTAVAC and ROTASIIL, results varied depending on if Gavi supported programs. With Gavi support ROTARIX was the least costly (US$31 million) compared to ROTASIIL and ROTAVAC, which were both about $40 million. This could be explained by the additional doses required for the latter. Without Gavi support, ROTASIIL was the cheapest, compared to ROTARIX and ROTAVAC. Similar trends were shown in the cost-effectiveness analyses. This may be explained by ROTASIIL's lower vaccine price. Overall, this study shows that cost-effectiveness differs based on the source of financing (Gavi vs. self-financed).

Return to List of Articles

3. Interventions delivered in secondary or tertiary medical care settings to improve routine vaccination uptake in children and young people: a scoping review.

Blagden S, Newell K, Ghazarians N, Sulaiman S, Tunn L, Odumala M, et al.

BMJ Open. 2022 Aug 04;12(8):e061749.

PubMed ID: 35918116

ABSTRACT

OBJECTIVE: To identify and analyse the interventions delivered opportunistically in secondary or tertiary medical settings, focused on improving routine vaccination uptake in children and young people.

DESIGN: Scoping review.

SEARCH STRATEGY: We searched CINAHL, Web of Science, Medline, Embase and Cochrane Database of Systematic Reviews for studies in English published between 1989 and 2021 detailing interventions delivered in secondary or tertiary care that aimed to improve childhood vaccination coverage. Title, abstract and full-text screening were performed by two independent reviewers.

RESULTS: After deduplication, the search returned 3456 titles. Following screening and discussion between reviewers, 53 studies were included in the review. Most papers were single-centre studies from high-income countries and varied considerably in terms of their study design, population, target vaccination, clinical setting and intervention delivered. To present and analyse the study findings, and to depict the complexity of vaccination interventions in hospital settings, findings were presented and described as a sequential pathway to opportunistic vaccination in secondary and tertiary care comprising the following stages: (1) identify patients eligible for vaccination; (2) take consent and offer immunisations; (3) order/prescribe vaccine; (4) dispense vaccine; (5) administer vaccine; (6) communicate with primary care; and (7) ongoing benefits of vaccination.

CONCLUSIONS: Most published studies report improved vaccination coverage associated with opportunistic vaccination interventions in secondary and tertiary care. Children attending hospital appear to have lower baseline vaccination coverage and are likely to benefit from vaccination interventions in these settings. Checking immunisation status is challenging, however, and electronic immunisation registers are required to enable this to be done quickly and accurately in hospital settings. Further research is required in this area, particularly multicentre studies and cost-effectiveness analysis of interventions.

WEB: 10.1136/bmjopen-2022-061749

IMPACT FACTOR: 2.496

CITED HALF-LIFE: 3.5

START COMMENTARY

In this scoping review, Blagden *et al.* identify and analyze interventions delivered opportunistically in secondary or tertiary health settings to improve vaccination among children and young people (CYP). This review is important since it is recommended that immunizations should be reviewed at every healthcare opportunity including out-of-patient visits, hospitalizations, and points of contact to increase immunization coverage. This is particularly relevant in the context of declining immunization coverage during the COVID-19 outbreak. The eligibility criteria for articles was: 1) delivered in secondary or tertiary care settings; 2) published between January 1, 1989 and October 11, 2021; and 3) assessing opportunistic interventions, i.e. immunization was not the primary reason for seeking care. *Figure 1* presents the flow diagram including identification of studies, title screening, abstract screening, full-text screening, and inclusion.

A total of 53 studies were included in the review. *Table 1* provides a detailed description of the included studies. Briefly, most studies were from high-income countries, with most from the United States (n=26) and Australia (n=10). The majority of studies took place in pediatric inpatient wards (n=16) followed by antenatal/neonatal settings (n=14). Most interventions involved offering a pre-discharge vaccination at the healthcare setting (n=45) followed by patient/family education (n=20). Others included extra staff/funding for interventions (n=18), staff training/education (n=17), multidisciplinary approaches for leadership and delivery (n=12), automatic vaccine ordering (n=8), ongoing feedback to staff (n=6), and collaboration with other organizations (n=4). Beyond summarizing characteristics of studies, Blagden *et al.* describe the complex pathway of opportunistic vaccination, supported by literature. This includes seven steps: 1) identifying eligible patients; 2) obtaining consent and offering vaccination; 3) ordering/prescribing vaccinations; 4) dispensing vaccination; 5) administering vaccination; 6) communicating with primary care; 7) ongoing benefits of vaccination. *Table 2* summarizes the ranges of administration of vaccination among eligible patients. Uptake varied across studies. However, all studies assessing uptake found an improvement in coverage post-intervention. Overall, this study demonstrates the importance and potential of opportunistic vaccination in secondary and tertiary care settings.

Return to List of Articles

4. Epidemiological impact and cost-effectiveness analysis of COVID-19 vaccination in Kenya.

Orangi S, Ojal J, Brand S, Orlendo C, Kairu A, Aziza R, et al.

BMJ Glob Health. 2022 Aug 05;7(8).

PubMed ID: 35914832

ABSTRACT

BACKGROUND: A few studies have assessed the epidemiological impact and the cost-effectiveness of COVID-19 vaccines in settings where most of the population had been exposed to SARS-CoV-2 infection.

METHODS: We conducted a cost-effectiveness analysis of COVID-19 vaccine in Kenya from a societal perspective over a 1.5-year time frame. An age-structured transmission model assumed at least 80% of the population to have prior natural immunity when an immune escape variant was introduced. We examine the effect of slow (18 months) or rapid (6 months) vaccine roll-out with vaccine coverage of 30%, 50% or 70% of the adult (>18 years) population prioritising roll-out in those over 50-years (80% uptake in all scenarios). Cost data were obtained from primary analyses. We assumed vaccine procurement at US$7 per dose and vaccine delivery costs of US$3.90-US$6.11 per dose. The cost-effectiveness threshold was US$919.11.

FINDINGS: Slow roll-out at 30% coverage largely targets those over 50 years and resulted in 54% fewer deaths (8132 (7914-8373)) than no vaccination and was cost saving (incremental cost-effectiveness ratio, ICER=US$-1343 ($US$-1345 to US$-1341) per disability-adjusted life-year, DALY averted). Increasing coverage to 50% and 70%, further reduced deaths by 12% (810 (757-872) and 5% (282 (251-317) but was not cost-effective, using Kenya's cost-effectiveness threshold (US$919.11). $Rapid roll-out with 30$-1607 (US$-1609 to US-1604) per DALY averted) compared with slow roll-out at the same coverage level, but 50% and 70% coverage scenarios were not cost-effective.

INTERPRETATION: With prior exposure partially protecting much of the Kenyan population, vaccination of young adults may no longer be cost-effective.

WEB: 10.1136/bmjgh-2022-009430

IMPACT FACTOR: 4.280

CITED HALF-LIFE: 1.9

START COMMENTARY

Orangi *et al.* assessed the impact and cost-effectiveness of COVID-19 vaccination from a societal perspective. This study is important as it provides data to inform future COVID-19 vaccination efforts in Africa, an area which has had limited research and is of critical importance to contain COVID-19 in Kenya, on the continent, and beyond. Four scenarios are included for an 18-month period beginning in September 2021 when coverage is assumed to be 0%. Scenarios are presented in *Table 1* and include 1) no vaccination; 2) 30% adult vaccination coverage; 3) 50% adult vaccination coverage; 4) 70% vaccination adult coverage. A dynamic transmission model was extended as part of this study. The model assumptions on age and setting-specific contact rates, frequency of COVID-19 variants, vaccine protection time, and prior primary infections are presented in *Table 2.*

Figure 1 presents model-based results of the impact of the vaccine scenarios on hospital occupancy, intensive care unit (ICU) occupancy, and deaths. *Table 3* presents health outcomes (averted infections and deaths), economic outcomes (total costs, total disability adjusted life-years [DALYs], incremental cost-effectiveness ratios (ICERs) for all scenarios (no vaccine, 30%, 50%, 70%) and for two vaccine strategies (non-rapid, administered over 1.5 years vs. rapid, administered within 6 months). Key findings indicate that the strategy focused on vaccinating older adults (80% of people over 50) who are at high risk may optimize reductions in infections and deaths, in spite of low population coverage (30%). A rapid roll out averts more infections and deaths than a non-rapid roll out. In a non-rapid roll out with 30% coverage, the ICER is estimated to be US$ -1343 per DALY averted (US$ -1345 to US$ 1341), indicating cost-savings. Vaccine coverage of 50% or 70% was not cost effective (ICER= US$3291 and US$22,623 respectively). Similar trends are shown for the rapid vaccination strategy scenarios. The most cost-effective option among all scenarios and vaccination strategies was a 30% coverage, rapid deployment with cost savings of US$ -1607 (US$ -1609 to US$ -1604). In sensitivity analyses, the vaccine prices had a large effect on the ICER. Overall, Orangi *et al.* conclude that a targeted rapid strategy which prioritizes older people may result in the greatest health impacts at the lowest cost.

Return to List of Articles

5. Progress Toward the Elimination of Mother-to-Child Transmission of Hepatitis B Virus - Worldwide, 2016-2021.

Khetsuriani N, Lesi O, Desai S, Armstrong P, Tohme R.

MMWR Morb Mortal Wkly Rep. 2022 Aug 01;71(30):958-963.

PubMed ID: 35900928

ABSTRACT

Mother-to-child transmission (MTCT) of hepatitis B virus (HBV) often results in chronic HBV infection, the leading cause of cirrhosis and liver cancer (1). If not vaccinated, nine in 10 children infected at birth will become chronically infected. Globally, an estimated 6.4 million (range= 4.4-10.8 million) children aged 5 years are living with chronic HBV infection (2). In 2016, the World Health Assembly endorsed the goal to eliminate viral hepatitis as a public health threat by 2030, including the elimination of MTCT of HBV (3). Elimination of MTCT of HBV can be validated by demonstrating 0.1% prevalence of HBV surface antigen (HBsAg) among children aged 5 years, as well as 90% coverage with hepatitis B birth dose (HepB-BD) and 3 doses of hepatitis B vaccine (HepB3) (4,5). This report describes global progress toward elimination of MTCT of HBV during 2016-2021. By December 2020, 190 (98%) of 194 World Health Organization (WHO) member states* had introduced universal infant vaccination with hepatitis B vaccine (HepB), and 110 (57%) countries provided HepB-BD to all newborns. During 2016-2020, global HepB3 coverage remained between 82% and 85%, whereas HepB-BD coverage increased from 37% to 43%. In 2020, among the 99 countries reporting both HepB3 and HepB-BD coverage, 41 (41%) achieved 90% coverage with both. By December 2021, serosurveys documented 0.1% HBsAg prevalence among children in 11 countries. Accelerating HepB-BD introduction, increasing HepB3 coverage, and monitoring programmatic and impact indicators are essential for elimination of MTCT of HBV.

WEB: 10.15585/mmwr.mm7130a2
IMPACT FACTOR: 13.606
CITED HALF-LIFE: 4.4

START COMMENTARY

Khetsuriani *et al.* summarize the global progress toward eliminating mother-to-child transmission of hepatitis B from 2016 to 2021. This article is important as can provide guidance on interventions and countries to focus on for improvement. Currently, global guidelines recommend a birth dose of HepB vaccine, followed by 2-3 doses. *Table 1* summarizes vaccination policies and coverage globally. Universal infant HepB vaccines have been introduced in nearly all countries (96% of 194 countries in 2016; 98% in 2020). Birth dose rates are lower, although improving (52% in 2016; 57% in 2020). There are geographic inequities related to birth doses. For example, in Africa, 72%

(34 of 47) of countries do not provide a birth dose. Although global coverage did not change drastically from 2016-2020 (between 82-85%), timely coverage with birth dose (defined as within 24 hours) increased from 37% to 43%. Other interventions to prevent mother-to-child transmission include antenatal screening and antiviral treatment for mothers and post-exposure prophylaxis for exposed infants. Impact and programmatic targets for validation of elimination of mother-to-child transmission vary across countries, as is demonstrated in *Table 2.* Overall, Khetsuriani *et al.* conclude that substantial progress has been made since 41 countries report > 90% coverage with a birth dose vaccine and three doses of HepB vaccine, leading to decreases in prevalence among children. However, this trend has not held for the African region. As such, there is a need for additional efforts to introduce birth doses and HepB vaccines into high prevalence countries. Further, authors state that there may be an opportunity to integrate HPV into ongoing interventions to prevent HIV and syphilis mother-to-child transmission.

Return to List of Articles

6. Missed opportunities for vaccination (MOV) in children up to 5 years old in 19 Médecins Sans Frontières-supported health facilities: a cross-sectional survey in six low-resource countries.

Borras-Bermejo B, Panunzi I, Bachy C, Gil-Cuesta J.

BMJ Open. 2022 Aug 17;12(7):e059900.
PubMed ID: 35882455

ABSTRACT

OBJECTIVE: To describe missed opportunities for vaccination (MOV) among children visiting Médecins Sans Frontières-supported facilities, their related factors, and to identify reasons for non-vaccination.

DESIGN: Cross-sectional surveys conducted between 2011 and 2015.

SETTING AND PARTICIPANTS: Children up to 59 months of age visiting 19 MSF-supported facilities (15 primary healthcare centres and four hospitals) in Afghanistan, Democratic Republic of the Congo, Mauritania, Niger, Pakistan and South Sudan. Only children whose caregivers presented their vaccination card were included.

OUTCOME MEASURES: We describe MOV prevalence and reasons for no vaccination. We also assess the association of MOV with age, type of facility and reason for visit.

RESULTS: Among 5055 children's caregivers interviewed, 2738 presented a vaccination card of whom 62.8% were eligible for vaccination, and of those, 64.6% had an MOV. Presence of MOV was more likely in children visiting a hospital or a health facility for a reason other than vaccination. MOV occurrence was significantly higher among children aged 12-23 months (84.4%) and 24-59 months (88.3%) compared with children below 12 months (56.2%, p0.001). Main reasons reported by caregivers for MOV were lack of vaccines (40.3%), reason unknown (31.2%) and not being informed (17.6%).

CONCLUSIONS: Avoiding MOV should remain a priority in low-resource settings, in line with the new 'Immunization Agenda 2030'. Children beyond their second year of life are particularly vulnerable for MOV. We strongly recommend assessment of eligibility for vaccination as routine healthcare practice regardless of the reason for the visit by screening vaccination card. Strengthening implementation of 'Second year of life' visits and catch-up activities are proposed strategies to reduce MOV.

WEB: 10.1136/bmjopen-2021-059900
IMPACT FACTOR: 2.496
CITED HALF-LIFE: 3.5

START COMMENTARY

In this cross-sectional study, Borras-Bermejo *et al.* describe missed opportunities for vaccination (MOVs) for among children aged five years and younger seeking care at Médecins Sans Frontières-supported facilities, including related factors and reasons for not being vaccinated. This study is of critical importance because when a child encounters the health system, it provides a critical opportunity to administer life-saving vaccines to those who are not-vaccinated (zero-dose children) or under vaccinated. As such, efforts to understand and address missed opportunities (defined as when a child remains unvaccinated or partially vaccinated at the end of a healthcare encounter) are urgently needed. Countries included in this study are Afghanistan, the Democratic Republic of Congo, Mauritania, Niger, Pakistan, and South Sudan. In total, 19 healthcare facilities were included – four hospitals and 15 primary healthcare centers. Data was collected using a cross-sectional exist survey of caregivers at the clinics. One strength of this analysis is that caregivers were required to show a vaccination card, which limits bias caused by caregivers reporting vaccines. MOVs were determined based on the immunization schedule (shown in *Figure 2*). Of note, once children/caregivers were identified as MOVs, they were then sent back to the clinic's vaccination unit to receive the missing vaccine.

In total, caregivers of 5,055 children were included in the study and interviewed. However, only 53.5% (n=2706) had the vaccination card present at the time of the survey and are included in this analysis. The vast majority were from Niger (n=1888) followed by South Sudan (n=447). Most children (63.7%) were eligible for vaccination. Among these, most (62.9%) experienced an MOV. There were high rates of MOV – even among those who came in specifically for vaccination (33.7% of children who came in for vaccination had an MOV). When asked why MOVs occurred, reasons included lack of vaccines (40.1% of caregivers), unknown reason (32%), not being informed (17.3%), limited staff (3.3%), and long waiting times (1.7%). In adjusted analyses, Borras-Bermejo *et al.* found that being older (12-59 months compared to 0-11 months), a having non-vaccination reason for attending the health facility, and going to a primary care clinic rather than a hospital were significantly associated with higher risk of MOV (Adjusted Odds Ratio: 3.74 [95% CI: 2.84-5.07], 3.52 [95% CI 2.70-4.58], 2.75 [95% CI: 2.02-3.73], respectively). Overall, this study indicates that numbers of MOVs are alarmingly high. Authors recommend integrating systematic screening for vaccines into all services – regardless of the reason for a healthcare encounter.

Return to List of Articles

7. Exploring public perceptions of vaccine-derived poliovirus and a novel oral polio vaccine in the Democratic Republic of the Congo, Kenya, and Nigeria.

Lorenzetti L, Haydarov R, Namey E, Lawton A, Nam H, Ridwan Hasan M, et al.

Vaccine. 2022 Jul 23.

PubMed ID: 35871107

ABSTRACT

BACKGROUND: The Global Polio Eradication Initiative introduced novel oral polio vaccine Type 2 (nOPV2) to address circulating vaccine-derived poliovirus Type 2 (cVDPV2). Although nOPV2 is a more genetically stable vaccine, it may not have the immediate trust of communities and health workers due to its novelty, potential side effects, and introduction under an Emergency Use Listing (EUL). We explored how nOPV2 introduction might be perceived by stakeholders and identified communications barriers related to nOPV2 hesitancy.

METHODS: This work was conducted in the Democratic Republic of the Congo, Kenya, and Nigeria between January and March 2020. We used a rapid qualitative approach to conduct focus group discussions and in-depth interviews with four stakeholder groups: caregivers of children under 5, polio frontline workers, healthcare practitioners, and social/health influencers. Data are presented according to awareness, attitudes/beliefs, and concerns about cVDPV2 and nOPV2.

RESULTS: Stakeholders were largely unaware of cVDPV2. The causes of recent polio outbreaks were characterized as poor sanitation, under-immunization/in-migration, or poor vaccine management procedures. Caregivers were aware of and concerned by repeated vaccination campaigns. All stakeholder groups anticipated initial hesitancy, fear, and suspicion from caregivers due to nOPV2 introduction, with primary concerns linked to vaccine testing, safety, effectiveness, side effects, and support from authorities. Stakeholders thought the term “genetic modification” could be controversial but that introduction under an EUL would be acceptable given the emergency nature of cVDPV2 outbreaks. Stakeholders called for adequate and timely information to counter concerns.

CONCLUSIONS: Despite initial concerns, stakeholders felt nOPV2 would ultimately be accepted by caregivers. However, public health officials have a small window for “getting things right” when introducing nOPV2. Strategic communication interventions addressing key concerns and targeted communications with stakeholder groups, especially frontline workers, could improve community acceptance of nOPV2.

WEB: 10.1016/j.vaccine.2022.05.020
IMPACT FACTOR: 3.143
CITED HALF-LIFE: 7.3

START COMMENTARY

In this qualitative study, Lorenzetti *et al.* explore stakeholder perceptions of novel oral polio vaccine Type 2 (nOPV2) in the Democratic Republic of Congo, Kenya, and Nigeria. They focus on communication barriers which may affect nOPV2 hesitancy. This study is important as nOPV2 may reduce cases of circulating vaccine-derived poliovirus Type 2 (cVDPV2). Stakeholder groups included were caregivers of young children, polio frontline workers, healthcare practitioners, and social influencers. *Table 1* describes the type of stakeholders sampled in each country. Focus group discussions and in-depth interviews were conducted (details shown in *Table 2*). One strength of this study was that participants were asked specifically about genetic modification of the virus in the vaccine, which may be a source of potential hesitancy in the future if and when the vaccine is rolled out.

Key findings included that knowledge of cVDPV2 was low across sites and stakeholder types. Recent polio outbreaks were believed to be caused by poor hygiene and under-immunization due to cross-border travel. Healthcare workers also noted causes such as social resistance among religious/rural people, in-migration, and viral mutation/resistance. *Table 3* describes potential causes of cVDPV2/polio outbreaks along with illustrative quotes. Nearly all participants stated that a new product would cause hesitancy and questioning early on in communities. *Table 4* presents the contextual, nOPV2 specific and logistical questions that were posed by stakeholders regarding the vaccine (e.g., safety, side effects). Despite concerns, stakeholders shared insights into how to communicate about the vaccine to increase acceptability. Ideas included information and training or frontline workers and awareness campaigns and trust with religious and community leaders. In contrast, some participants recommended not sharing information about nOPV2 to prevent limited acceptability. When genetic modification questions were asked, there were mixed levels of awareness and knowledge. Some participants advised against using the term “genetic modification” as it may lead to negative public perceptions, whereas a term such as “improved” may be more acceptable. Overall, the stakeholders presented important and interesting findings related to nOPV2 which should be considered as immunization programs are planned and implemented.

Return to List of Articles

8. Small mobile conditional cash transfers (mCCTs) of different amounts, schedules and design to improve routine childhood immunization coverage and timeliness of children aged 0-23 months in Pakistan: An open label multi-arm randomized controlled trial.

Chandir S, Siddiqi D, Abdullah S, Duflo E, Khan A, Glennerster R.

EClinicalMedicine. 2022 Jul 16;50:101500.

PubMed ID: 35784436

ABSTRACT

BACKGROUND: Cost-effective demand-side interventions are needed to increase childhood immunization. Multiple studies find tying income support programs (USD 50 per year) to immunization raises coverage. Research on maximizing impact from small mobile-based conditional cash transfers (mCCTs) (USD 15 per fully immunized child) delivered in lower-income settings remains sparse.

METHODS: Participants in Karachi, Pakistan, were individually randomized into a seven arm, factorial open label study with five mCCT arms, one reminder (SMS) only arm, and one control arm. The mCCT arms varied by amount (high USD 15 per fully immunized child versus low USD 5 per fully immunized child), schedule (flat versus rising payments over the schedule), design (certain versus lottery payments), and payment method (airtime or mobile money). Children were enrolled at BCG, pentavalent-1 (penta-1) or pentavalent-2 (penta-2) vaccination and followed until at least 18 months of age. A serosurvey in 15% sub-sample validated reported study coverage. The full immunization coverage (FIC) at 12 months (primary outcome) was analyzed using logit regression. ClinicalTrials.gov (NCT03355989), 3ie registry (58f6ee7725fc1), and AEA RCT Registry (AEARCTR-0001953).

FINDINGS: Between November 6, 2017, and October 10, 2018, a total of 11,197 caregiver-child pairs were enrolled, with 1598-1600 caregiver-child pairs per arm. FIC at 12 months was statistically significantly higher for any mCCT versus SMS (OR:1.18, 95% CI: 1.05-1.33; p=0.005). Within the mCCT arms, FIC was statistically significantly higher for high versus low amount (OR: 1.16, 95% CI: 1.04-1.29; p=0.007), certain versus lottery payment (OR: 1.30, 95% CI: 1.17-1.45; p<0.001) and airtime versus mobile money (OR: 1.17, 95% CI:1.01-1.36; p=0.043). There was no statistically significant difference between a flat and increasing schedule (OR: 1.03, 95% CI: 0.93-1.15; p=0.550). SMS had a marginally statistically significant impact on FIC versus control (OR: 1.16, 95% CI: 1.00-1.35; p=0.046). Findings were similar for up-to-date coverage of penta-3, measles-1 and measles-2 at 18 months.

INTERPRETATION: Small mCCTs (USD 0.8-2.4 per immunization visit) can increase FIC at 12 months and up-to-date coverage at 18 months at USD 23 per additional fully immunized child, in

resource-constrained settings like Pakistan. Design details (certainty, schedule and delivery method of mCCTs) matter as much as the size of payments.

FUNDING: Global Innovation Fund, GiveWell.

WEB: 10.1016/j.eclinm.2022.101500
IMPACT FACTOR: N/A
CITED HALF-LIFE: N/A

START COMMENTARY

This randomized control trial assessed the impact of small mobile conditional cash transfers (mCCTs) on improving routine childhood immunization in Pakistan. This study is important as evidence on the impact of small CCTs is limited. This study provided evidence on varying amounts ($US 15 vs. $US 5), schedules (flat version rising payments over a schedule), design (certainty vs. lottery) and payment methods (airtime vs. mobile money). Participants were randomized into one of seven treatment arms. Study arms included five mCCT arms (as aforementioned), one group which received only a reminder SMS and another which was the control. *Figure 1* shows the factorial study design, including the vaccines which are administered, and the scenarios. The primary outcome was full immunization coverage at 12 months. Full immunization was defined as one dose of BCG, three doses of Penta, PCV, and OPV and one doses of measles vaccines.

A total of 11,197 child-caregiver pairs were included. *Table 1* presents participant characteristics across study arms. Overall, full immunization coverage was 62.3% for participants receiving mCCT compared to 58.4% for the SMS group (aOR: 1.18, 95% CI: 1.05-1.33). Trends differ based on vaccine type. mCCT had a positive impact on the timeliness of penta-3, measles-1, and measles-2 but not penta-3, measles-1, or measles-2. Detailed findings comparing any mCCT, SMS-only, and control are presented in *Table 1.* When comparing all seven groups, the highest statically significant coverage was found in the flat rate, high-payment arm (64.2%) and the sharp rate, high payment arm (63.6%). Treatment effects are visualized in *Figure 3.* Airtime payments were the most effective delivery method. Overall, this study demonstrates that small mCCTs can have a positive impact on health outcomes if designed effectively.

Return to List of Articles

9. Critical success factors for routine immunization performance: A case study of Zambia 2000 to 2018.

Micek K, Hester K, Chanda C, Darwar R, Dounebaine B, Ellis A, et al.

Vaccine X. 2022 Jul 16;11:100166.

PubMed ID: 35707220

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 prove effective at driving coverage is not well-established. To address this gap, we identified critical success factors associated with advancing key policies and programs that may have led to the substantial changes in routine childhood immunization coverage in Zambia between 2000 and 2018.

METHODS: We identified Zambia as an exemplar in the delivery of childhood vaccines through analysis of DTP1 and DTP3 coverage data. Through interviews and focus group discussions at the national and subnational levels, we investigated factors that contributed to high and sustained vaccination 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) the Inter-agency Coordinating Committee was strengthened for long-term engagement which, complemented by the Zambia Immunization Technical Advisory Group, is valued by the government and integrated into national-level decision-making; 2) the Ministry of Health improved the coordination of data collection and review for informed decision-making across all levels; 3) Regional multi-actor committees identified development priorities, strategies, and funding, and iteratively adjusted policies to account for facilitators, barriers, and lessons learned; 4) Vaccine messaging was disseminated through multiple channels, including the media and community leaders, increasing trust in the government by community members; 5) The Zambia Ministry of Health and Churches Health Association of Zambia formalized a long-term organizational relationship to leverage the strengths of faith-based organizations; and 6) Neighborhood Health Committees spearheaded community-driven strategies via community action planning and ultimately strengthened the link between communities and health facilities.

CONCLUSION: Broader health systems strengthening and strong partnerships between various levels of the government, communities, and external organizations were critical factors that accelerated vaccine coverage in Zambia. These partnerships were leveraged to strengthen the overall health system and healthcare governance.

WEB: 10.1016/j.jvacx.2022.100166
IMPACT FACTOR: N/A
CITED HALF-LIFE: N/A

START COMMENTARY

In this qualitative case study, Micet *et al.* identify critical success factors which contributed to Zambia's progress in routine immunization coverage from 2000 to 2018. This study is important as Zambia can serve as an exemplar for other countries seeking to improve their vaccination coverage. A detailed understanding of the factors, processes, and implementation strategies can aide in this effort. Quantitative data were collected from the Ministry of Health to determine routine immunization trends from 2000 to 2019. *Figure 1* presents DTP3 coverage in Zambia by Province from 2000 to 2016. Micet *et al.* also developed a conceptual framework of the drivers of vaccine delivery (*Figure 2*).

Qualitative data collection took place in October 2019 to February 2020 and consisted of key informant interviews at the national (n=22) and subnational level (n=45) and focus group discussions with community-based volunteers (CBVs), mothers, fathers, and grandparents. Participant characteristics are presented in *Table 2.* Immunization coverage trends, along with annotated events (including GAVI support, introduction of vaccines, policies, programs, and disease control) are presented in *Figure 3.* Factors which contributed to Zambia's success include strong partnerships between the government, faith-based organizations, and communities, context-specific policies and interventions, and well-structure communication systems to engage with the public. Other countries may benefit from applying lessons learned to their immunization policies and programming.

Return to List of Articles

10. Contribution of child heatlh interventions to under-five mortality decline in Ghana: a modeling study using lives saved and missed opportunity tools

Kolekang A, Sarfo B, Danso-Appiah A, Dwomoh D, Akweongo P.

PLoS One. 2022 Aug 1;17(8):e0267776.

PubMed ID: 35913919

ABSTRACT

BACKGROUND: Increased coverage of interventions have been advocated to reduce under-five mortality. However, Ghana failed to achieve the Millennium Development Goal on child survival in 2015 despite improved coverage levels of some child health interventions. Therefore, there is the need to determine which interventions contributed the most to mortality reduction and those that can further rapidly reduce mortality to inform the prioritization of the scale-up of interventions.

MATERIALS AND METHODS: Deterministic mathematical modeling was done using Lives Saved and Missed Opportunity Tools. Secondary data was used, and the period of the evaluation was between 2008 and 2014. Some of the interventions assessed were complementary feeding, skilled delivery, and rotavirus vaccine.

RESULTS: A total of 48,084 lives were saved from changes in coverage of interventions and a reduction in the prevalence of stunting and wasting. Reduction in wasting prevalence saved 10,372(21.6%) lives, insecticide-treated net/indoor residual spraying 6,437(13.4%) lives saved, reduction in stunting 4,315(9%) lives saved and artemisinin-based combination therapy (ACTs) 4,325(9.0%) lives saved. If coverage levels of interventions in 2014 were scaled up to 90% in 2015, among neonates, full supportive care for prematurity (5,435 lives saved), full supportive care for neonatal sepsis/pneumonia (3,002 lives saved), and assisted vaginal delivery (2,163 lives saved), would have saved the most lives among neonates, while ACTs (4,925 lives saved), oral rehydration salts (ORS) (2,056 lives saved), and antibiotics for the treatment of pneumonia (1,805 lives saved) would have made the most impact on lives saved among children 1-59 months. Lastly, if all the interventions were at 100% coverage in 2014, the under-five mortality rate would have been 40.1 deaths per 1,000 live births in 2014.

CONCLUSION: The state of the package of interventions will likely not lead to rapid mortality reduction. Coverage and quality of childbirth-related interventions should be increased. Additionally, avenues to further reduce stunting and wasting, including increased breastfeeding and complementary feeding, will be beneficial.

WEB: 10.1371/journal.pone.0267776
IMPACT FACTOR: 10.5
CITED HALF-LIFE: 8.4

START COMMENTARY

In this mathematical modelling study, Kolekang *et al.* examine which child health interventions contributed most to under-five mortality decline in Ghana from 2008 to 2014. This study is important as it can provide evidence to prioritize future programming and polices to reduce child mortality. Such efforts are critical needed in Ghana, which did not meet the Millennium Development Goal targets to reduce child mortality. Several tool were used in this analysis including the Lives Saved Tool (LiST) and the Missed Opportunity Tool (MOT). LiST is able to evaluate multiple interventions simultaneously whereas the MOT estimates which interventions would have the most impact if coverage were increased to 90%. The combination of tools allows for an understanding of present and future impacts of interventions.

Overall, LiST estimated that 48,084 lives were saved in Ghana. Detailed findings are presented in *Table 1.* Several interventions saved high numbers of lives included insecticide-treated net/indoor residual spraying (6,344), artemisinin-based combination therapy within 48 hours (4,322), case management of neonatal sepsis and pneumonia (n=4,271), pneumococcal vaccine (3,931), and caesarian delivery (4,145). Beyond the intervention-based modeling, reductions in wasting saved the most lives (10,372). MOT estimated impacts of scaling up interventions to 90% and found that the interventions which would make the most impact on reducing mortality among 1-59 month old children are: artemisinin-based combination therapy; antibiotics for pneumonia, and prevention of mother-to-child transmission of HIV. Among neonates, care for prematurity, care for sepsis/pneumonia, assisted vaginal delivery, and kangaroo mother care would have the greatest impact if scaled up. Detailed findings are presented in *Table 2.* Kolekang *et al.* also estimate the impact of scaling up intervention coverage levels to 100% (*Table 3*). Overall, this study demonstrates the impacts of implementing various interventions interventions on child mortality in Ghana.

Appendix

The literature search for the September 2022 Vaccine Delivery Research Digest was conducted on August 29, 2022. We searched English language articles indexed by the US National Library of Medicine and published between July 15, 2022 and August 14, 2022. The search resulted in 517 items.

Search Terms

(((((vaccine[tiab] OR vaccines[tiab] OR vaccination[tiab] OR immunization[tiab] OR immunisation[tiab] OR vaccine[mesh] OR immunization[mesh]) AND (logistics[tiab] OR supply[tiab] OR “supply chain”[tiab] OR implementation[tiab] OR expenditures[tiab] OR financing[tiab] OR economics[tiab] OR “Cost effectiveness”[tiab] OR coverage[tiab] OR attitudes[tiab] OR belief[tiab] OR beliefs[tiab] OR refusal[tiab] OR “Procurement”[tiab] OR timeliness[tiab] OR systems[tiab])) OR (“vaccine delivery”[tiab])) NOT (“in vitro”[tiab] OR “immune response”[tiab] OR gene[tiab] OR chemistry[tiab] OR genotox*[tiab] OR sequencing[tiab] OR nanoparticle*[tiab] OR bacteriophage[tiab] OR exome[tiab] OR exogenous[tiab] OR electropor*[tiab] OR “systems biology”[tiab] OR “animal model”[tiab] OR cattle[tiab] OR sheep[tiab] OR goat[tiab] OR rat[tiab] OR pig[tiab] OR mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR rodent[tiab] OR fish[tiab])) AND (English[LA]) (“2022/15/07”[PDAT] : “2022/14/08”[PDAT]))