

VACCINE DELIVERY RESEARCH DIGEST

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS,
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REPORT TO THE BILL & MELINDA GATES FOUNDATION

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Details of Articles

1. [Vaccine Delay and Its Association With Undervaccination in Children in Sub-Saharan Africa.](#)

Janusz C, Frye M, Mutua M, Wagner A, Banerjee M, Boulton M.

Am J Prev Med. 2020 Nov 15.

PubMed ID: 33189500

ABSTRACT

INTRODUCTION: Improving the timeliness and completion of vaccination is the key to reducing under-5 childhood mortality. This study examines the prevalence of delayed vaccination for doses administered at birth and age 6 weeks, 10 weeks, 14 weeks, and 9 months and its association with undervaccination among infants in Sub-Saharan Africa.

METHODS: Pooling data across 33 Sub-Saharan Africa countries, vaccination timing and series completion were assessed for children aged 12-35 months who were included in the immunization module of the Demographic and Health Surveys conducted between 2010 and 2019. Survey design-adjusted logistic regression modeled the likelihood of not fully completing the basic immunization schedule associated with dose-specific delays in vaccination. Data were obtained and analyzed in May 2020.

RESULTS: Among children with complete date records (n=70,006), the proportion of children vaccinated with delays by ≥ 1 month was high: 25.9% for Bacille Calmette-Guerin (at birth); 49.1% for the third dose of pentavalent combination vaccine (at 14 weeks); and 63.9% for the first dose of measles vaccines (at 9 months). Late vaccination was more common for children born to mothers with lower levels of educational attainment ($p < 0.001$) and wealth ($p < 0.001$). Controlling for place, time, and sociodemographics, vaccination delays at any dose were significantly associated with not completing the immunization schedule by 12 months (Bacille Calmette-Guerin: AOR=1.93, [95% CI=1.83, 2.02]; pentavalent 3: AOR=1.50 [95% CI=1.35, 1.64]; measles: AOR=3.76 [95% CI=3.37, 4.15]).

CONCLUSIONS: Timely initiation of vaccination could contribute to higher rates of complete immunization schedules, improving the reach and impact of vaccination programs on child health outcomes in Sub-Saharan Africa.

SUPPLEMENT INFORMATION: This article is part of a supplement entitled Global Vaccination Equity, which is sponsored by the Global Institute for Vaccine Equity at the University of Michigan School of Public Health.

WEB: [10.1016/j.amepre.2020.10.003](https://doi.org/10.1016/j.amepre.2020.10.003)

IMPACT FACTOR: 4.420

CITED HALF-LIFE: 8.6

START COMMENTARY

Using Demographic Health Survey (DHS) from 33 sub-Saharan African (SSA) countries, Janusz *et al.* explore delayed vaccination prevalence by vaccination encounters, and study the association between vaccination delays and the completion of the basic immunization schedule. This article is impactful as it is the first to assess the association between delayed vaccination and failure to complete the basic immunization series by 12 months outside of high-income countries. Studying this association in SSA is critical as progress in eliminating vaccine-preventable diseases and deaths has been limited in low- and middle-income countries (LMICs). Despite the importance of timely vaccinations, many countries only collect aggregate measures of vaccine coverage, and do not report age- or visit-disaggregated adherence to vaccines. This article aims to fill this gap in research by studying delayed vaccination across levels of child characteristics (i.e. age, sex, birth order, birth setting, maternal education, maternal age, household wealth quintile, and place of residence). Janusz *et al.* found that <1% of children received no vaccination by 12 months, and another 20% did not complete the schedule. Country-specific estimates of under-vaccination can be found in *Appendix Table 1*. Among children that were vaccinated, late administration ≥ 4 weeks was common across vaccinations. Authors found that delayed vaccination was highest among children with a higher birth order (7+) and those that were born in non-institutional settings without a skilled attendant. Authors also found that delayed administration of any dose was significantly associated with increased odds of not completing the immunization scheduled by 12 months. A few limitations to note are that authors may have overestimated the prevalence of delays (as some countries have schedules that recommend a 4-week interval between doses, which was defined as a delay herein) and that the study may have limited generalizability as authors only included children with complete vaccination schedules, excluding those that had died or likely had lower access and adherence to vaccination. Despite these limitations, Janusz *et al.* underscore the importance of targeting on-time delivery of vaccinations to achieve higher vaccine coverage and improve population health.

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2. [The economic burden of measles in children under five in Bangladesh.](#)

de Broucker G, Ahmed S, Hasan M, Mehdi G, Martin Del Campo J, Ali M, et al.

BMC Health Serv Res. 2020 Nov 17;20(1):1026.

PubMed ID: 33172442

ABSTRACT

BACKGROUND: This study estimated the economic cost of treating measles in children under-5 in Bangladesh from the caregiver, government, and societal perspectives.

METHOD: We conducted an incidence-based study using an ingredient-based approach. We surveyed the administrative staff and the healthcare professionals at the facilities, recording their estimates supported by administrative data from the healthcare perspective. We conducted 100 face-to-face caregiver interviews at discharge and phone interviews 7 to 14 days post-discharge to capture all expenses, including time costs related to measles. All costs are in 2018 USD (\$).

RESULTS: From a societal perspective, a hospitalized and ambulatory case of measles cost \$159 and \$18, respectively. On average, the government spent \$22 per hospitalized case of measles. At the same time, caregivers incurred \$131 and \$182 in economic costs, including \$48 and \$83 in out-of-pocket expenses in public and private not-for-profit facilities, respectively. Seventy-eight percent of the poorest caregivers faced catastrophic health expenditures compared to 21% of the richest. In 2018, 2263 cases of measles were confirmed, totaling \$348,073 in economic costs to Bangladeshi society, with \$121,842 in out-of-pocket payments for households.

CONCLUSION: The resurgence of measles outbreaks is a substantial cost for society, requiring significant short-term public expenditures, putting households into a precarious financial situation. Improving vaccination coverage in areas where it is deficient (Sylhet division in our study) would likely alleviate most of this burden.

WEB: [10.1186/s12913-020-05880-5](https://doi.org/10.1186/s12913-020-05880-5)

IMPACT FACTOR: 1.987

CITED HALF-LIFE: 5.6

START COMMENTARY

In this incidence-based study, De Broucker *et al.* used an ingredient-based approach to evaluate costs and explore the economic burden of measles in Bangladesh. From August 2017 to May 2018, the team collected costs and quantity of items associated with an episode of measles in a low vaccination coverage division (Sylhet, 61.1%) and a high vaccination coverage division (Rajshahi, 83.6%). Surveys with healthcare staff identified utilization and facility costs (i.e., capital, overhead, labor, medical supplies, medications, hospitalization, and treatment), which were then triangulated with administrative records and data from private pharmacies. Interviews with caregivers captured the time spent in inpatient and outpatient healthcare settings due to the measles episode, out-of-pocket costs (e.g., medical and non-medical), and indirect costs due to productivity losses. Overall, the study included 95 measles cases, with the majority of episodes hospitalized (95.8%) for five days

or more (71%), with no significant difference in length of stay between public and private facilities. De Broucker *et al.* found that of societal costs, indirect costs accounted for the largest share (55%) at both public and private facilities. Direct medical costs contributed to 27% and 29%, respectively, although the government bore half of the direct medical cost in public facilities (Figure 3). Catastrophic health expenditures (i.e., out-of-pocket payments over 10% of income, 10% or 25% of monthly expenditures, or 40% of monthly expenditures without food) impacted 78% of the poorest caregivers compared to 21% of the richest caregivers. This is one of few studies to explore costs of a disease with a longstanding presence in national Expanded Program on Immunization. With several recent outbreaks and high associated household costs (\$121,842 in 2018) and society costs (\$348,073 in 2018), the authors argue continued improvement of vaccination coverage is warranted, particularly by consolidating routine immunization to bridge the gap between high and low performing divisions.

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3. [Global assessment of national mandatory vaccination policies and consequences of non-compliance.](#)

Gravagna K, Becker A, Valeris-Chacin R, Mohammed I, Tambe S, Awan F, et al.

Vaccine. 2020 Nov 10;38(49):7865-7873.

PubMed ID: 33164808

ABSTRACT

BACKGROUND: Declining vaccination coverage and increasing hesitancy is a worldwide concern. Many countries have implemented mandatory vaccination policies to promote vaccination. However, mandatory vaccination policies differ significantly by country. Beyond case studies, no comprehensive study has compared these policies or the penalties for non-compliance on a global scale.

METHODS: We conducted extensive keyword, policy, and literature searches to identify mandatory national vaccination policies globally and develop a comprehensive database. A mandatory national vaccination policy was defined as a policy from a national authority that requires individuals to receive at least one vaccination based on age or to access a service. Two reviewers independently evaluated evidence for a mandate and whether non-compliance penalties were incorporated. We categorized penalties into four types, based on the nature of the penalty. These penalties impact an individual's financial, parental rights, educational (i.e., child's school entry and access), and liberty status. We rated the severity within each category.

RESULTS: Of 193 countries investigated, 54% (n = 105) had evidence of a nationwide mandate as of December 2018. The frequency, types, and severity of penalties varied widely across all regions. We found that 59% (n = 62) of countries with national mandates defined at least one penalty for non-compliance with a vaccine mandate. Among those, educational penalties (i.e., limiting a child's entry or ongoing access to school) were the most common (69%; n = 43), with most countries with educational penalties refusing school enrollment until vaccination requirements are met (81%; n = 35).

CONCLUSION: We undertook a comprehensive assessment of national mandatory vaccination policies and identified a diversity of penalties in place to promote compliance. Our results highlight the need to critically evaluate the implementation of non-compliance penalties in order to determine their effectiveness and to define best practices for sustaining high vaccination uptake worldwide.

WEB: [10.1016/j.vaccine.2020.09.063](https://doi.org/10.1016/j.vaccine.2020.09.063)

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

Gravagna *et al.* comprehensively identified and described mandatory national vaccination policies, penalties, and the severity of policies and penalties. This article has global relevance, as vaccine hesitancy and refusal were considered one of the highest global health threats by the World Health Organization (WHO) in 2019. Further, it has particular relevance for the ongoing COVID-19 pandemic, which will likely include challenges related to vaccine hesitancy and refusal. Mandatory vaccination policies are implemented to mandate that individuals or specific groups must be vaccinated to protect individuals and communities. However, these policies vary widely, and a comprehensive global review of policies and comparison of penalties has not been conducted. This article fills this critical gap in research. Gravagna *et al.* report that over 100 countries have national mandatory vaccination policies. They report that most countries report only one type of penalty and that severe penalties (i.e. lost of child custody) are rare. Most countries have educational penalties in place in the form of not allowing students to enroll or enforcing absences for school. The authors provide a detailed database of policies and penalties by country in the *Supplementary Materials*. One limitation of this study is that only national policies are evaluated, whereas in the US, and elsewhere, mandates are implemented on a state-, province-, or local-level. Such variations were not captured in this review. Further, this analysis was conducted cross-sectionally, which may not have captured policies that change over time across countries and geographies.

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4. [Patterns in Wealth-related Inequalities in 86 Low- and Middle-Income Countries: Global Evidence on the Emergence of Vaccine Hesitancy.](#)

Cata-Preta B, Wehrmeister F, Santos T, Barros A, Victora C.

Am J Prev Med. 2020 Nov 02.

PubMed ID: 33131990

ABSTRACT

INTRODUCTION: Coverage of health interventions usually shows social gradients with higher levels among wealthy than among poor individuals. Owing to the upsurge of vaccine hesitancy in high-income countries, the authors hypothesized that the social gradient may be changing over time also in the low- and middle-income countries and set out to test this hypothesis.

METHODS: In January 2020, surveys conducted from 2010 to 2018 in 86 low- and middle-income countries were analyzed to assess full immunization coverage in children aged 12-23 months. The authors calculated full immunization coverage point estimates and 95% CIs for each country and wealth quintile. To explore wealth-related inequalities, the authors estimated the slope index of inequality and calculated the Pearson correlation coefficient between these values and per capita gross domestic product. Time trends were analyzed in 10 countries with recent evidence of hesitancy.

RESULTS: Pro-poor patterns were defined as significant slope index of inequality values with higher coverage among poor children, and pro-rich patterns were defined as the reverse pattern. A total of 11 countries showed pro-poor patterns in the most recent survey, accounting for 20% of upper middle- and 7% of low-income countries. The correlation between the slope index of inequality and log per capita gross domestic product was -0.38 ($p < 0.001$). Among the 10 countries with recent evidence of hesitancy, 5 showed full immunization coverage declines over time in the wealthiest quintiles, and 4 switched from pro-rich to pro-poor patterns throughout the years.

CONCLUSIONS: Lower full immunization coverage was found among the wealthy than among the poor in the 10 countries, especially in the upper middle-income group, consistent with the emergence of vaccine hesitancy.

SUPPLEMENT INFORMATION: This article is part of a supplement entitled Global Vaccination Equity, which is sponsored by the Global Institute for Vaccine Equity at the University of Michigan School of Public Health.

WEB: [10.1016/j.amepre.2020.07.028](https://doi.org/10.1016/j.amepre.2020.07.028)

IMPACT FACTOR: 4.420

CITED HALF-LIFE: 8.6

START COMMENTARY

Cata-Preta *et al.* analyzed cross-sectional health surveys to determine the status and trends of inequalities by wealth on childhood immunization coverage in low- and middle-income countries. Nationally representative Demographic and Health Surveys (DHS) and the Multiple Indicator Cluster Surveys (MICS) conducted from 2010 to 2018 provided data on the full immunization coverage and socioeconomic position across countries. The authors used logistic regression to calculate slope index of inequality (SII), which summarizes wealth-related inequalities by representing the absolute difference in coverage between the fitted values at the extremes of the wealth distribution. The most distinct pro-rich (i.e., wealthy present better coverage than the poor) inequality patterns were in Nigeria with SII=56.4 percentage points (95% CI=51.5, 61.4), whereas the most marked pro-poor (i.e., poor present better coverage than the wealthy) occurred in Tunisia with SII=-41.2 percentage points (95% CI= -51.4, -28.3). The study found that the classical pro-rich inequality pattern appears to be changing, especially in upper middle-income countries. Of the 10 countries included in the time trend analysis with pro-poor patterns, seven presented either a switch in the pattern from pro-rich to pro-poor or faster decline among the rich than observed among the poor. Kyrgyzstan, Gabon, Serbia, and Namibia all had statistically significant changes due to a combination of reduced coverage among the rich with increased coverage among the poor. While vaccine hesitancy was not measured directly, the authors suggest that the observed shift towards pro-poor patterns may be due to vaccine hesitancy among the wealthy families. Therefore, in addition to continued efforts to secure access to vaccination, special attention may be required to prevent vaccine hesitancy from affecting coverage in LMICs moving forward.

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5. [Immunization costs, from evidence to policy: Findings from a nationally representative costing study and policy translation effort in Tanzania.](#)

Vaughan K, Clarke-Deelder E, Tani K, Lyimo D, Mphuru A, Manzi F, et al.

Vaccine. 2020 Nov 10;38(48):7659-7667.

PubMed ID: 33077300

ABSTRACT

INTRODUCTION: Information on the costs of routine immunization programs is needed for budgeting, planning, and domestic resource mobilization. This information is particularly important for countries such as Tanzania that are preparing to transition out of support from Gavi, the Vaccine Alliance. This study aimed to estimate the total and unit costs for of child immunization in Tanzania from July 2016 to June 2017 and make this evidence available to key stakeholders.

METHODS: We used an ingredients-based approach to collect routine immunization cost data from the facility, district, regional, and national levels. We collected data on the cost of vaccines as well as non-vaccine delivery costs. We estimated total and unit costs from a provider perspective for each level and overall, and examined how costs varied by delivery strategy, geographic area, and facility-level service delivery volume. An evidence-to-policy plan identified key opportunities and stakeholders to target to facilitate the use of results.

RESULTS: The total annual economic cost of the immunization program, inclusive of vaccines, was estimated to be US\$138 million (95% CI: 133, 144), or \$4.32 (\$3.72, \$4.98) per dose. The delivery costs made up \$45 million (38, 52), or \$1.38 (1.06, 1.70) per dose. The costs of facility-based delivery were similar in urban and rural areas, but the costs of outreach delivery were higher in rural areas than in urban areas. The facility-level delivery cost per dose decreased with the facility service delivery volume.

DISCUSSION: We estimated the costs of the routine immunization program in Tanzania, where no immunization costing study had been conducted for five years. These estimates can inform the program's budgeting and planning as Tanzania prepares to transition out of Gavi support. Next steps for evidence-to-policy translation have been identified, including technical support requirements for policy advocacy and planning.

WEB: [10.1016/j.vaccine.2020.10.004](https://doi.org/10.1016/j.vaccine.2020.10.004)

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

Vaughan *et al.* used an ingredients-based approach to estimate economic costs of vaccination programs in Tanzania to inform planning, budgeting, and decision-making. An increased understanding of the need for domestic financing of immunization is important as Tanzania prepares to transition out of Gavi support. Vaughn *et al.* found a large difference in delivery costs between different delivery strategies, with outreach delivery costing \$3.08 (95% CI 1.41, 4.75) per dose and facility-based delivery costing \$1.02 (95% CI 0.72, 1.32). They also found that outreach was most expensive in rural areas with nomadic populations, followed by rural areas without nomadic populations, and lastly, urban areas. This article is impactful as it contributes to the literature on costs of immunizations with varying vaccination strategies. An important strength of this study is that authors used data collection methods (the Expanded Program on Immunization Costing and Financing Tool), allowing these estimates to be compared across countries. Results are well-aligned with similar findings from recent studies in Benin, Ghana, Uganda, and Zambia, providing further

evidence on the economic costs of vaccination in Sub-Saharan Africa.

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6. [Assessment of missed opportunities for vaccination \(MOV\) in Burkina Faso using the World Health Organization's revised MOV strategy: Findings and strategic considerations to improve routine childhood immunization coverage.](#)

Kaboré L, Meda B, Médah I, Shendale S, Nic Lochlainn L, Sanderson C, et al.

Vaccine. 2020 Nov 18;38(48):7603-7611.

PubMed ID: 33077298

ABSTRACT

BACKGROUND: Despite the remarkable achievements of the Expanded Programme on Immunization (EPI) in Burkina Faso, numerous challenges remain, including missed opportunities for vaccination (MOV) which occur when people visit a health facility with at least one vaccine due according to the national immunization schedule, are free of contraindications, and leave without receiving all due vaccine doses. In 2016, we used the revised World Health Organization's (WHO) MOV strategy to assess the extent of and reasons for MOV in Burkina Faso.

METHODS: We purposively selected 27 primary health facilities (PHFs) from the eight health districts with the highest absolute numbers of children who missed the first dose of measles-rubella (MR1) in 2015. We conducted exit interviews with caregivers of children aged 0-23 months, and requested health workers to complete a self-administered knowledge, attitudes and practices (KAP) questionnaire.

RESULTS: A total of 489 caregivers were interviewed, of which 411 were eligible for inclusion in our analysis. Medical consultation (35%) and vaccination (24.5%) were the most frequent reasons for visiting PHFs. Among the 73% of children eligible for vaccination, 76% of vaccination opportunities were missed. Among eligible children, the percentage with MOV was significantly higher in those aged ≥ 12 months and also in those attending for a reason other than vaccination. A total of 248 health workers completed the KAP questionnaire. Of these, 70% ($n = 168/239$) considered their knowledge on immunization to be insufficient or outdated; 83% failed to correctly identify valid contraindications to vaccination.

CONCLUSION: Addressing MOV offers the potential for substantial increases in vaccine coverage and equity, and ultimately reducing the burden of vaccine-preventable diseases (VPDs). This will require the implementation of a series of interventions aimed at improving community knowledge and practices, raising health workers' awareness, and fostering the integration of immunization with other health services.

WEB: [10.1016/j.vaccine.2020.10.021](https://doi.org/10.1016/j.vaccine.2020.10.021)

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

In this cross-sectional study of data from 2016, Kaboré *et al.* assess missed opportunities for vaccination (MOV) to evaluate the prevalence and identify possible causes of MOV among health facility attendees in Burkina Faso. The assessment consisted of caregiver exit interviews (n= 489) and self-administered health worker knowledge, attitudes and practices (KAP) surveys (n=248) among 27 primary health facilities in eight health districts. Nurse assistants and nurses/midwives completed the majority of KAP surveys (96%). Over one-third of those of KAP respondents indicated that they had never received training about vaccines and 40% considered their knowledge about vaccination to be insufficient for their health facility needs. The study found the magnitude of MOV to be substantial, with nearly eight in 10 children experiencing a MOV during a health facility visit. Among the 205 children who were eligible for vaccination but did not receive any of their scheduled vaccine(s), 69% (n=142) of caregivers indicated that non-vaccination was related to health workers either incorrectly considering the child “up-to-date” (n=76) or not checking whether the child was due (n=62). The majority of health workers (70%; n = 168/239) reported having insufficient or outdated knowledge about vaccination and only 50% (n = 116/233) considered that a child’s vaccination status should be systematically assessed at every health visit. Additionally, one-third of health workers (n = 73/220) reported that the main reason for incomplete vaccination among children was due to the caregivers’ negative opinion about vaccination. These findings illustrate gaps in health worker training, as well as potential room for improvement in patient communication and education. The authors also found that the proportion of MOV was highest among children aged 12–23 months and varied between health districts, revealing potential immunization inequities. This study highlights the need for strengthening the vaccine administration platform in Burkina Faso, especially in the second year of life, including identification and mitigation of barriers that may prevent older children from receiving vaccines.

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7. [How much does it cost to measure immunity? A costing analysis of a measles and rubella serosurvey in southern Zambia.](#)

Carcelen A, Hayford K, Moss W, Book C, Thuma P, Mwansa F, et al.

PLoS One. 2020 Oct 22;15(10):e0240734.

PubMed ID: 33057405

ABSTRACT

BACKGROUND: Serosurveys are a valuable surveillance tool because they provide a more direct measure of population immunity to infectious diseases, such as measles and rubella, than vaccination coverage estimates. However, there is concern that serological surveys are costly. We adapted a framework to capture the costs associated with conducting a serosurvey in Zambia.

METHODS: We costed a nested serosurvey in Southern Province, Zambia that collected dried blood spots from household residents in a post-campaign vaccine coverage survey. The financial costs were estimated using an ingredients-based costing approach. Inputs included personnel, transportation, field consumable items, social mobilization, laboratory supplies, and capital items, and were classified by serosurvey function (survey preparation, data collection, biospecimen collection, laboratory testing, and coordination). Inputs were stratified by whether they were applicable to surveys in general or attributable specifically to serosurveys. Finally, we calculated the average cost per cluster and participant.

RESULTS: We estimated the total nested serosurvey cost was US \$68,558 to collect dried blood spots from 658 participants in one province in Zambia. A breakdown of the cost by serosurvey phase showed data collection accounted for almost one third of the total serosurvey cost (32%), followed by survey preparation (25%) and biospecimen collection (20%). Analysis by input categories indicated personnel costs were the largest contributing input to overall serosurvey costs (51%), transportation was second (23%), and field consumables were third (9%). By combining the serosurvey with a vaccination coverage survey, there was a savings of \$43,957. We estimated it cost \$4,285 per average cluster and \$104 per average participant sampled.

CONCLUSIONS: Adding serological specimen collection to a planned vaccination coverage survey provided a more direct measurement of population immunity among a wide age group but increased the cost by approximately one-third. Future serosurveys could consider ways to leverage existing surveys conducted for other purposes to minimize costs.

WEB: [10.1371/journal.pone.0240734](https://doi.org/10.1371/journal.pone.0240734)

IMPACT FACTOR: 2.740

CITED HALF-LIFE: 5.6

START COMMENTARY

In this study, Carcelen *et al.* estimate the costs of conducting serosurveys to measure population immunity to measles and rubella. Though serosurveys can provide a direct measure of immunity to infectious disease, they are often considered too costly and time-consuming, even compared to traditional survey methods to measure vaccination coverage to implement widely. This article

provides a better understanding of serosurvey costs, and how they could be minimized to make serosurvey implementation in LMICs feasible. Though the costs of implementing serosurveys among 658 participants in one province of Zambia were high (\$68,558), it is estimated that these costs could be nested in a vaccination survey for an estimated additional \$24,600 (a savings of \$43,957). This would be a way to minimize costs given that personnel and transportation were responsible for 51% and 23% of all costs, respectively. Further, authors state that new technologies (i.e., point-of-care serological tests, multiplex bead-based assays) and alternative study designs (i.e., using existing biorepositories) could further minimize costs. This study is important as it provides critical cost information for decision-making regarding the implementation of serosurveys. Authors conclude this information, along with an understanding of the value of information gained from a serosurvey, are relevant to consider when determining benefit estimates. Limitations of this study include that some of the estimates may have not accounted for the actual full costs (e.g., transportation did not capture actual distances, and equipment was not individually valued). Sensitivity analyses of the input parameters could have improved the estimates in this study.

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8. [Integrating public health programs and research after the malaria vaccine implementation program \(MVIP\): Recommendations for next steps.](#)

van der Graaf R, Macklin R, Rid A, Bhan A, Gefenas E, Greco D, et al.

Vaccine. 2020 Oct 09;38(45):6975-6978.

PubMed ID: 32981780

ABSTRACT

BACKGROUND: In February 2020, international controversy arose about the ethical acceptability of the WHO Malaria Vaccine Implementation Program (MVIP). Whereas some have argued that this program must be seen as research that is not in line with international ethical standards, notably regarding informed consent and local ethical review, some WHO representatives consider the MVIP as a public health implementation program that need not adhere to these standards.

METHODS: We performed a case analysis in light of the 2016 CIOMS International Ethical Guidelines for Health-related Research involving Humans.

FINDINGS: We argue that the MVIP has a substantial research component, and that it is prudent to therefore apply ethical norms for research involving humans, such as the CIOMS guidelines. Accordingly, we agree that the ethical requirements of informed consent and independent ethical

review have not been met. In addition, we are concerned that the study might not meet CIOMS's social value requirement.

RECOMMENDATIONS: We urge WHO to release more details about the process that led to the MVIP program and make the MVIP protocol publicly available. The full protocol should be assessed by the relevant ethics committees, new and already enrolled parents should be informed about the uncertainties under investigation and given a real opportunity to consent or refuse (continued) participation, communities should be engaged, and aspects of MVIP that require alteration in light of ethical review should be altered, if possible. Furthermore, in order to improve good ethical practices, it is necessary to engage in international debate regarding the integration of research and public health programs. Procedurally, vaccine implementation programs that combine both prevention and research should involve the wider international ethics community and ensure participation of the target populations in setting the proper conditions for launching such programs.

WEB: [10.1016/j.vaccine.2020.08.077](https://doi.org/10.1016/j.vaccine.2020.08.077)

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

In this case-analysis commentary, van der Graaf *et al.* question the ethical acceptability of the WHO Malaria Vaccine Implementation Program (MVIP) within the guidelines of the 2016 International Ethical Guidelines for Health-related Research Involving Humans of the Council for International Organizations of Medical Sciences (CIOMS). Authors raise concerns that the MVIP program has not been defined as an implementation program or a research project, a distinction which is important for understanding the relevant ethical guidelines that should be followed. van der Graaf *et al.* also raise some ethical concerns about informed consent (e.g., that this study may pose more than minimal risk to participants and therefore requires consent), independent ethical review (e.g., that it is unclear if the WHO Research Ethics Review Committee reviewed the full protocol), and the social value of the research. Authors argue that given the uncertainties about the vaccine and unknowns regarding the study design, it is difficult to conclude if the program meets the social value requirement of the CIOMS guidelines. Recommendations include for WHO to publicly release the protocol, to apply ethical norms for research involving humans for programs that combine research and implementation, and to have greater and more transparent stakeholder involvement before the program (i.e., local and wider human rights and ethics community members; target populations).

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9. [Influenza economic burden among potential target risk groups for immunization in South Africa, 2013-2015.](#)

Tempia S, Moyes J, Cohen A, Walaza S, McMorro M, Edoaka I, et al.
Vaccine. 2020 Oct 24;38(45):7007-7014.
PubMed ID: 32980198

ABSTRACT

BACKGROUND: Data on influenza economic burden in risk groups for severe influenza are important to guide targeted influenza immunization, especially in resource-limited settings. However, this information is limited in low- and middle-income countries.

METHODS: We estimated the cost (from a health system and societal perspective) and years of life lost (YLL) for influenza-associated illness in South Africa during 2013-2015 among (i) children aged 6-59 months, (ii) individuals aged 5-64 years with HIV, pulmonary tuberculosis (PTB) and selected underlying medical conditions (UMC), separately, (iii) pregnant women and (iv) individuals aged ≥ 65 years, using publicly available data and data collected through laboratory-confirmed influenza surveillance and costing studies. All costs were expressed in 2015 prices using the South Africa all-items Consumer Price Index.

RESULTS: During 2013-2015, the mean annual cost of influenza-associated illness among the selected risk groups accounted for 52.1% (\$140.9/\$270.5 million) of the total influenza-associated illness cost (for the entire population of South Africa), 45.2% (\$52.2/\$115.5 million) of non-medically attended illness costs, 43.3% (\$46.7/\$107.9 million) of medically-attended mild illness costs and 89.3% (\$42.0/\$47.1 million) of medically-attended severe illness costs. The YLL among the selected risk groups accounted for 86.0% (262,069 /304,867 years) of the total YLL due to influenza-associated death.

CONCLUSION: In South Africa, individuals in risk groups for severe influenza accounted for approximately half of the total influenza-associated illness cost but most of the cost of influenza-associated medically attended severe illness and YLL. This study provides the foundation for future studies on the cost-effectiveness of influenza immunization among risk groups.

WEB: [10.1016/j.vaccine.2020.09.033](https://doi.org/10.1016/j.vaccine.2020.09.033)

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

Tempia *et al.* evaluated costs from the healthcare system and societal perspectives, absenteeism, and years of life lost (YLL) due to influenza-associated illness in risk groups in South Africa from 2013 to 2015. The health systems perspective contained direct medical costs related to treatment of

influenza-associated illness incurred by the public health system, whereas the societal perspective additionally incorporated patients and their caregivers' non-medical costs (e.g., transportation, additional food costs, accommodation) and indirect costs of absenteeism (lost productivity due to time lost from work or school). To estimate economic burden, the study included both medically and non-medically attended mild (i.e., not warranting hospitalization) and severe (i.e., warranting hospitalization) influenza-associated illness. Of the total cost of influenza-associated illness among individuals in the selected risk groups (\$140.9 million/\$270.5 million), individuals aged 5–64 years with underlying medical conditions (UMC) accounted for the highest proportion (42.4%; \$59.8 million), with the highest mean cost per illness episode among those with tuberculosis (TB) for medically attended severe illness (\$1,117). Individuals 5-64 years in selected risk groups also contributed the highest proportion of mean annual absenteeism (39.7%; 2.0 million days/5.1 million days). Of the mean annual YLL due to influenza-associated death among risk groups (262,069 /304,867 years), individuals aged 5–64 with HIV accounted for the highest proportion of YLL (57.3%; 150,075 years). Costs and productivity losses may be underestimated, as the study was underpowered to parametrize some costs among certain risk groups and estimation approach for productivity losses only used minimum wages. The authors suggest future studies build off this economic analysis to evaluate the cost-effectiveness of influenza immunization among risk groups in order to inform decisions around vaccine investment and prioritization.

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10. [Impact of COVID-19 pandemic response on uptake of routine immunizations in Sindh, Pakistan: An analysis of provincial electronic immunization registry data.](#)

Chandir S, Siddiqi D, Mehmood M, Setayesh H, Siddique M, Mirza A, et al.

Vaccine. 2020 Oct 22;38(45):7146-7155.

PubMed ID: 32943265

ABSTRACT

BACKGROUND: COVID-19 pandemic has affected routine immunization globally. Impact will likely be higher in low and middle-income countries with limited healthcare resources and fragile health systems. We quantified the impact, spatial heterogeneity, and determinants for childhood immunizations of 48 million population affected in the Sindh province of Pakistan.

METHODS: We extracted individual immunization records from real-time provincial Electronic Immunization Registry from September 23, 2019, to July 11, 2020. Comparing baseline (6 months preceding the lockdown) and the COVID-19 lockdown period, we analyzed the impact on daily

immunization coverage rate for each antigen by geographical area. We used multivariable logistic regression to explore the predictors associated with immunizations during the lockdown.

RESULTS: There was a 52.5% decline in the daily average total number of vaccinations administered during lockdown compared to baseline. The highest decline was seen for Bacille Calmette Guérin (BCG) (40.6% (958/2360) immunization at fixed sites. Around 8438 children/day were missing immunization during the lockdown. Enrollments declined furthest in rural districts, urban sub-districts with large slums, and polio-endemic super high-risk sub-districts. Pentavalent-3 (penta-3) immunization rates were higher in infants born in hospitals (RR: 1.09; 95% CI: 1.04-1.15) and those with mothers having higher education (RR: 1.19-1.50; 95% CI: 1.13-1.65). Likelihood of penta-3 immunization was reduced by 5% for each week of delayed enrollment into the immunization program.

CONCLUSION: One out of every two children in Sindh province has missed their routine vaccinations during the provincial COVID-19 lockdown. The pool of un-immunized children is expanding during lockdown, leaving them susceptible to vaccine-preventable diseases. There is a need for tailored interventions to promote immunization visits and safe service delivery. Higher maternal education, facility-based births, and early enrollment into the immunization program continue to show a positive association with immunization uptake, even during a challenging lockdown.

WEB: [10.1016/j.vaccine.2020.08.019](https://doi.org/10.1016/j.vaccine.2020.08.019)

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

In this analysis of immunization registry data from children 0-23 months old across Sindh province, Pakistan, *Chandir et al.* measure changes in vaccination coverage of the Expanded Program on Immunizations (EPI) recommended vaccines, pre-and post-COVID-19 lockdown period. To explore associations of immunization predictors on the outcome of three doses of pentavalent vaccine (penta-3), multivariable regression analysis was used with a backward stepwise approach for final multivariable model selection with adjustment for gender as a lockterm. The authors found a 51.0% decrease in average daily immunizations during the lockdown compared to baseline, with heterogeneous reduction across districts and union councils. During the lockdown only 30.7% of children due for follow-up were vaccinated (172,228/561,826), compared to 70.5% (1,142,915/1,620,896) at baseline. District West Karachi had the highest number of missed children (6.8%; 26,620/389,598), and overall 29.4% (114,442/389,598) of the missed children were concentrated in five districts: West Karachi, Hyderabad, Badin, Sanghar and Naushero Feroz.

During lockdown, hospital births had 1.09 times (95% CI: 1.04, 1.15) and presence of maternal education 1.19 to 1.50 times (95% CI: 1.13, 1.65) higher probability of penta-3 completion. This analysis demonstrates impact of COVID-19 lockdown restrictions on immunization coverage and discusses issues with immunization service availability and demand. The authors highlight the importance of leveraging real-time registry data for better allocation of scarce resources, using tailored approaches targeted at known high-risk areas and geographies with the highest numbers of missed children.

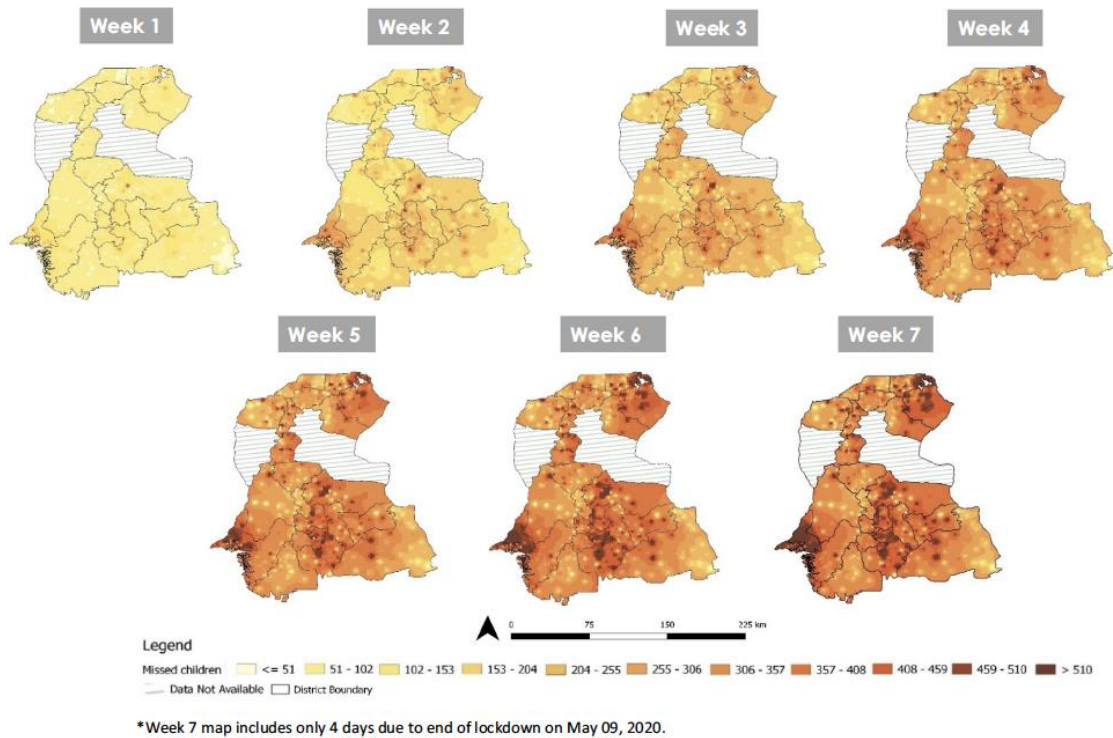


Figure Map of weekly cumulative distribution of 0-23 months old children (geocoded at enrollment visit) who missed immunization follow-up visits across Sindh Province during the COVID-19 lockdown. *Figure 2* in manuscript.

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Appendix

The literature search for the December 2020 Vaccine Delivery Research Digest was conducted on November 17, 2020. We searched English language articles indexed by the US National Library of Medicine and published between October 15, 2020 and November 14, 2020. The search resulted in 375 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]) (“2020/10/15”[PDAT] : “2020/11/14”[PDAT]))