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DECEMBER 2021

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1. [Assessing the overlap between immunisation and other essential health interventions in 92 low- and middle-income countries using household surveys: opportunities for expanding immunisation and primary health care.](#)

Santos T, Cata-Preta B, Mengistu T, Victora C, Hogan D, Barros A.

EClinicalMedicine. 2021 Nov 23;42:101196.

PubMed ID: 34805814

ABSTRACT

BACKGROUND: Unvaccinated children may live in households with limited access to other primary health care (PHC) services, and routine vaccination services may provide the opportunity to bring caregivers into contact with the health system. We aimed to investigate the overlap between not being vaccinated and failing to receive other PHC services in low- and middle-income countries (LMICs).

METHODS: Using Demographic and Health Surveys (DHS) and Multiple Indicator Cluster Surveys (MICS) data between 2010-2019 from 92 LMICs, we analysed six vaccination indicators based on the bacille Calmette-Guérin (BCG), polio, diphtheria-pertussis-tetanus (DPT) and measles vaccines and their overlap with four other PHC indicators - at least four antenatal care (ANC) visits, institutional delivery, careseeking for common childhood illnesses or symptoms and place for handwashing in the home - in 211,141 children aged 12-23 months. Analyses were stratified according to wealth quintiles and World Bank income levels.

FINDINGS: Unvaccinated children and their mothers were systematically less likely to receive the other PHC interventions. These associations were particularly marked for 4+ ANC visits and institutional delivery and modest for careseeking behaviour. Our stratified analyses confirm a systematic disadvantage of unvaccinated children and their families with respect to obtaining other health services in all levels of household wealth and country income.

INTERPRETATION: We suggested that lack of vaccination goes hand in hand with missing out on other health interventions. This represents an opportunity for integrated delivery strategies that may more efficiently reduce inequalities in health service coverage.

FUNDING: Bill & Melinda Gates Foundation, Gavi, the Vaccine Alliance, The Wellcome Trust, Associação Brasileira de Saúde Coletiva and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior.

WEB: [10.1016/j.eclinm.2021.101196](https://doi.org/10.1016/j.eclinm.2021.101196)

IMPACT FACTOR: N/A

CITED HALF-LIFE: N/A

START COMMENTARY

In this cross sectional study, Santos *et al.* assess the extent to which unvaccinated children and their families are missing key health interventions across 92 low- and middle-income countries (LMICs). This study is impactful as it fills a key gap in understanding the overlap between non-vaccination and primary healthcare (PHC) service coverage across multiple countries. It is critical to understand this association, as child vaccinations could provide an opportunity for families to contact the health system for other PHC services such as institutional delivery, antenatal care, and care seeking for child illness. Data for this analysis was obtained from the most recent Demographic Health Survey (DHS) and Multiple Indicator Cluster Surveys (MICS). Authors calculated six vaccination indicators using vaccine cards or parental recall if cards were unavailable. Vaccination indicators included the proportion of children that failed to receive any doses of an individual vaccine (diphtheria-pertussis-tetanus [DPT], polio, Bacillus-Calmette-Guerin [BCG], measles-containing vaccines [MCV]), the proportion of children who received zero doses for all four vaccines, and the proportion of children who were fully vaccinated (i.e., one dose of BCG, one dose of MCV, three doses of polio, and three doses of DPT). PHC indicators included at least four antenatal care visits, institutional delivery, care seeking for childhood illnesses or symptoms, and place for handwashing at home. Of note, the age of the study population was children aged 12-23 months. However, in eight countries, children aged 18-29 months were included as these countries offer measles vaccine after 12 months of age. A strength of this analysis was that Santos *et al.* investigated between-country differences by stratifying results by country income levels.

Key findings included that PHC coverage was associated with all vaccine indicators (*Table 2*). Santos *et al.* calculated the ratio of coverage between non-vaccinated and vaccinated (i.e., at least one dose) children. For non-vaccinated children, coverages were 51% lower for 4+ antenatal care visits, 47% lower for institutional delivery, 24% lower for care seeking for child illness, and 36% lower for handwashing facility (p -value <0.001 for all). Similar trends were shown for children with no DTP doses or BCG doses. Fully immunized children were more likely to receive any of the four PHC services compared to non-fully immunized children including 15% higher care seeking and 39% higher 4+ antenatal care visits (p -value <0.001). Santos *et al.* Figure 1 shows the prevalence of not receiving a dose of each type of vaccine and not receiving each PHC intervention. PHC coverage increased by country income level regardless of vaccine status. Trends for antenatal care and institutional delivery varied drastically by country income level (*Figure 2*). Overall, this study

underscores the importance of integrated health services, as child immunization is closely related to the utilization of other PHC services.

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2. [Progress Toward Regional Measles Elimination - Worldwide, 2000-2020.](#)

Dixon M, Ferrari M, Antoni S, Li X, Portnoy A, Lambert B, et al.

MMWR Morb Mortal Wkly Rep. 2021 Nov 15;70(45):1563-1569.

PubMed ID: 34758014

ABSTRACT

In 2012, the World Health Assembly endorsed the Global Vaccine Action Plan,* with the objective of eliminating measles in five of the six World Health Organization (WHO) regions by 2020 (1). The Immunization Agenda 2021-2030 (IA2030). uses measles incidence as an indicator of the strength of immunization systems. The Measles-Rubella Strategic Framework 2021-2030. and the Measles Outbreaks Strategic Response Plan 2021-2023** are aligned with the IA2030 and highlight robust measles surveillance systems to document immunity gaps, identify root causes of undervaccination, and develop locally tailored solutions to ensure administration of 2 doses of measles-containing vaccine (MCV) to all children. This report describes progress toward World Health Assembly milestones and measles elimination objectives during 2000-2020 and updates a previous report (2). During 2000-2010, estimated MCV first dose (MCV1) coverage increased globally from 72% to 84%, peaked at 86% in 2019, but declined to 84% in 2020 during the COVID-19 pandemic. All countries conducted measles surveillance, although fewer than one third achieved the sensitivity indicator target of 2 discarded cases per 100,000 population in 2020. Annual reported measles incidence decreased 88% during 2000-2016, from 145 to 18 cases per 1 million population, rebounded to 120 in 2019, before falling to 22 in 2020. During 2000-2020, the annual number of estimated measles deaths decreased 94%, from 1,072,800 to 60,700, averting an estimated 31.7 million measles deaths. To achieve regional measles elimination targets, enhanced efforts are needed to reach all children with 2 MCV doses, implement robust surveillance, and identify and close immunity gaps.

WEB: [10.15585/mmwr.mm7045a1](https://doi.org/10.15585/mmwr.mm7045a1)

IMPACT FACTOR: 13.606

CITED HALF-LIFE: 4.4

START COMMENTARY

In this retrospective analysis, Dixon *et al.* present progress to the World Health Assembly's milestones and measles elimination objectives from 2000-2020. This study is critical in providing evidence on progress of measles elimination targets which can inform future immunization efforts. Data for this analysis was obtained from the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) which estimate immunization coverage using data from administrative records on the number of doses administered and the estimated target population.

Overall, MCV first dose (MCV1) coverage increased over the time period from 72% to 84% with a peak of 86% in 2019, which has since decreased, likely due to COVID-19 related disruptions. Detailed estimates for the years 2000, 2010, 2016, 2019, and 2020 by region and globally are presented in *Table 1*. Of 194 WHO member states, 39% (75 countries) had $\geq 90\%$ MCV1 coverage, compared to 45% (86 countries) in 2000. Countries with the highest absolute number of infants not receiving MCV1 were Nigeria (3.3 million), India (2.6 million), Democratic Republic of Congo (1.5 million), and Ethiopia (1.4 million). One notable positive finding was that all countries (N=194) conducted measles surveillance in 2020. However, the number of samples sent for sampling was much lower than expected (a total of 222,517 specimens, the lowest since 2010), likely due to COVID-19. In 2020, 26 large outbreaks (defined as ≥ 20 cases per million) were reported from five WHO regions. Overall, 42% (81 countries) had sustained measles elimination in 2020. However, no new countries had achieved elimination in 2020. Similarly, no WHO Africa country, and no overall region had achieved sustained elimination in 2020. Since 2016, 9 countries which had reported elimination had reestablished transmission (Albania, Cambodia, Czechia, Germany, Lithuania, Mongolia, Slovakia, the United Kingdom, and Uzbekistan). This study summarizes the progress of measles elimination and MCV1/MCV2 coverage, highlighting the negative impact of the COVID-19 pandemic on progress.

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3. [Estimating total spending by source of funding on routine and supplementary immunisation activities in low-income and middle-income countries, 2000-17: a financial modelling study.](#)

Ikilezi G, Micah A, Bachmeier S, Cogswell I, Maddison E, Stutzman H, et al.

Lancet. 2021 Nov 22;398(10314):1875-1893.

PubMed ID: 34742369

ABSTRACT

BACKGROUND: Childhood immunisation is one of the most cost-effective health interventions. However, despite its known value, global access to vaccines remains far from complete. Although supply-side constraints lead to inadequate vaccine coverage in many health systems, there is no comprehensive analysis of the funding for immunisation. We aimed to fill this gap by generating estimates of funding for immunisation disaggregated by the source of funding and the type of activities in order to highlight the funding landscape for immunisation and inform policy making.

METHODS: For this financial modelling study, we estimated annual spending on immunisations for 135 low-income and middle-income countries (as determined by the World Bank) from 2000 to 2017, with a focus on government, donor, and out-of-pocket spending, and disaggregated spending for vaccines and delivery costs, and routine schedules and supplementary campaigns. To generate these estimates, we extracted data from National Health Accounts, the WHO-UNICEF Joint Reporting Forms, comprehensive multi-year plans, databases from Gavi, the Vaccine Alliance, and the Institute for Health Metrics and Evaluation's 2019 development assistance for health database. We estimated total spending on immunisation by aggregating the government, donor, prepaid private, and household spending estimates.

FINDINGS: Between 2000 and 2017, funding for immunisation totalled US\$112.4 billion (95% uncertainty interval 108.5-118.5). Aggregated across all low-income and middle-income countries, government spending consistently remained the largest source of funding, providing between 60.0% (57.7-61.9) and 79.3% (73.8-81.4) of total immunisation spending each year (corresponding to between \$2.5 billion [2.3-2.8] and \$6.4 billion [6.0-7.0] each year). Across income groups, immunisation spending per surviving infant was similar in low-income and lower-middle-income countries and territories, with average spending of \$40 (38-42) in low-income countries and \$42 (39-46) in lower-middle-income countries, in 2017. In low-income countries and territories, development assistance made up the largest share of total immunisation spending (69.4% [64.6-72.0]; \$630.2 million) in 2017. Across the 135 countries, we observed higher vaccine coverage and increased government spending on immunisation over time, although in some countries, predominantly in Latin America and the Caribbean and in sub-Saharan Africa, vaccine coverage decreased over time, while spending increased.

INTERPRETATION: These estimates highlight the progress over the past two decades in increasing spending on immunisation. However, many challenges still remain and will require dedication and commitment to ensure that the progress made in the previous decade is sustained and advanced in the next decade for the Immunization Agenda 2030.

FUNDING: Bill & Melinda Gates Foundation.

WEB: [10.1016/S0140-6736\(21\)01591-9](https://doi.org/10.1016/S0140-6736(21)01591-9)

IMPACT FACTOR: 60.390

CITED HALF-LIFE: 8.6

START COMMENTARY

In this financial modelling study, Ikilezi *et al.* estimate annual spending on immunizations for 135 LMICs from 2000-2017. Estimates were calculated for government, donor, and out-of-pocket spending. This analysis is important as it provides standardized estimates of spending on immunization which can inform strategies to improve public financing schemes. This analysis is the first of its kind to capture spending comprehensively across many LMICs (135) and years (2000-2017), and to disaggregate spending by activity and component (e.g., vaccines, delivery, routine expenditure from supplementary immunization efforts). Data on government spending was obtained from sources including the Joint-Reporting Form, WHO-UNICEF comprehensive multi-year plans and financial sustainability plans (i.e., those funded by Gavi, the Vaccine Alliance and the Immunization Delivery Cost Catalog). Data on development assistance was obtained from disbursement data from Gavi and the Global Burden of Diseases, Injuries, and Risk Factors Study 2019. Out-of-pocket spending was estimated using information on the number of doses administered from the Decade of Vaccine Economics Project at Johns Hopkins University whereas delivery costs were obtained from the Immunization Delivery Cost Catalog. Covariates related to each outcome are presented in *Table 1* and include infant population, MCV1 coverage, and health access. Outcomes include total government spending on immunization, government spending on routine immunization, government spending on supplementary immunization, government spending on vaccines, and government spending on delivery.

Key findings include that most countries (132 of 135) increased spending over the study period. Overall immunization funding was \$112.4 billion (95% Uncertainty Interval [UI]: 108.5-118.5 billion). Government spending comprised the largest portion (between 60.0-79.3%, an estimated 2.5-6.4 billion, over the study period) of spending, which is demonstrated in *Figure 1*. Development assistance accounted for 28.2% (\$31.7 billion) of the total spending. Gavi, followed by UN agencies provided the most development assistance funding. The amount of out-of-pocket spending was similar from 2000-2010, and then dramatically increased from 2010-2017. This trend is

demonstrated in *Figure 2*. In conclusion, despite substantial increases in aid and out-of-pocket expenditures, governments are responsible for the majority of immunization services, underscoring the importance of continuing to increase domestic resources for immunization to reach coverage targets.

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4. [Insights into vaccine hesitancy from systems thinking, Rwanda.](#)

Decouttere C, Banzimana S, Davidsen P, Van Riet C, Vandermeulen C, Mason E, et al.

Bull World Health Organ. 2021 Nov 08;99(11):783-794D.

PubMed ID: 34737471

ABSTRACT

OBJECTIVE: To investigate vaccine hesitancy leading to underimmunization and a measles outbreak in Rwanda and to develop a conceptual, community-level model of behavioural factors.

METHODS: Local immunization systems in two Rwandan communities (one recently experienced a measles outbreak) were explored using systems thinking, human-centred design and behavioural frameworks. Data were collected between 2018 and 2020 from: discussions with 11 vaccination service providers (i.e. hospital and health centre staff); interviews with 161 children's caregivers at health centres; and nine validation interviews with health centre staff. Factors influencing vaccine hesitancy were categorized using the 3Cs framework: confidence, complacency and convenience. A conceptual model of vaccine hesitancy mechanisms with feedback loops was developed.

FINDINGS: A comparison of service providers' and caregivers' perspectives in both rural and peri-urban settings showed that similar factors strengthened vaccine uptake: (i).high trust in vaccines and service providers based on personal relationships with health centre staff; (ii).the connecting role of community health workers; and (iii).a strong sense of community. Factors identified as increasing vaccine hesitancy (e.g. service accessibility and inadequate follow-up) differed between service providers and caregivers and between settings. The conceptual model could be used to explain drivers of the recent measles outbreak and to guide interventions designed to increase vaccine uptake.

CONCLUSION: The application of behavioural frameworks and systems thinking revealed vaccine hesitancy mechanisms in Rwandan communities that demonstrate the interrelationship between immunization services and caregivers' vaccination behaviour. Confidence-building social structures and context-dependent challenges that affect vaccine uptake were also identified.

WEB: [10.2471/BLT.20.285258](#)

IMPACT FACTOR: 6.960

CITED HALF-LIFE: 12.4

START COMMENTARY

In this qualitative study, Decouttere *et al.* explore mechanisms underlying vaccine hesitancy in Rwanda, a country with a strong immunization system that continues to face challenges related to

hesitancy contributing to under immunization for measles and subsequent outbreaks. This study makes an important contribution as it takes a systems thinking approach to understanding provider and patient perspectives related to hesitancy to understand the phenomenon in the Rwandan context. This is of utmost importance as vaccine hesitancy is highly context-dependent and can be utilized to inform future vaccine coverage efforts. In-depth qualitative interviews were conducted with 11 vaccinators and staff in the Expanded Program on Immunization and 161 caregivers from an urban and rural community, which are described in *Table 1*. The inclusion of participants in urban and rural areas is a strength of this study.

Factors (both positive and negative) affecting vaccine hesitancy are organized within the three Cs framework (Confidence, Complacency, and Convenience) in *Table 2 and 3*. For caregivers, confidence-related positive factors included trust in the effectiveness and safety of vaccines and their manufacturers and trust in and personal experiences with the health system and health professionals. However, some parents had negative experiences such as their children not being given the vaccine (due to issues with staff not wanting to open vials for one child) or getting fined for being late, not getting the child vaccinated, or not engaging with health system after a delivery. In terms of complacency, positive factors such as the role of influential leaders, historical influences, and social norms related to immunization were identified. Negative factors related to the facility included lack of water and electricity, long wait times, limited space, and few nurses, which could contribute to hesitancy. One notable negative factor included fear of adverse effects or illness related to vaccines, which arose among a few participants. Lastly, in terms of convenience, positive factors that were observed included availability of the service and ability to understand information on vaccine cards. However, factors which could negatively contribute to hesitancy included far distances, poor roads to the clinic due to rainfall, caregivers being sent away if they do not have an appointment, the desired vaccine was not being given that day, or if staff did not want to open a multi-dose vial. *Box 1* compares perspectives of caregivers and service providers regarding strengths and challenges. Decouttere *et al.* summarize findings in two conceptual models, one of which is relevant for factors affecting hesitancy broadly (*Figure 3*) and during a measles outbreak (*Figure 4*).

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5. [Projections of human papillomavirus \(HPV\) vaccination impact in Ethiopia, India, Nigeria and Pakistan: a comparative modelling study.](#)

Portnoy A, Abbas K, Sweet S, Kim J, Jit M.

BMJ Glob Health. 2021 Dec 04;6(11).

PubMed ID: 34725040

ABSTRACT

INTRODUCTION: Cervical cancer is the second most common cancer among women in Ethiopia, India, Nigeria and Pakistan. Our study objective was to assess similarities and differences in vaccine-impact projections through comparative modelling analysis by independently estimating the potential health impact of human papillomavirus (HPV) vaccination.

METHODS: Using two widely published models (Harvard and Papillomavirus Rapid Interface for Modelling and Economics (PRIME)) to estimate HPV vaccination impact, we simulated a vaccination scenario of 90% annual coverage among 10 cohorts of 9-year-old girls from 2021 to 2030 in Ethiopia, India, Nigeria and Pakistan. We estimated potential health impact in terms of cervical cancer cases, deaths and disability-adjusted life years averted among vaccinated cohorts from the time of vaccination until 2100. We harmonised the two models by standardising input data to comparatively estimate HPV vaccination impact.

RESULTS: Prior to harmonising model assumptions, the range between PRIME and Harvard models for number of cervical cancer cases averted by HPV vaccination was: 262000 to 270000 in Ethiopia; 1640000 to 1970000 in India; 330000 to 336000 in Nigeria and 111000 to 133000 in Pakistan. When harmonising model assumptions, alignment on HPV type distribution significantly narrowed differences in vaccine-impact estimates.

CONCLUSION: Despite model differences, the Harvard and PRIME models yielded similar vaccine-impact estimates. The main differences in estimates are due to variation in interpretation around data on cervical cancer attribution to HPV-16/18. As countries make progress towards WHO targets for cervical cancer elimination, continued explorations of underlying differences in model inputs, assumptions and results when examining cervical cancer prevention policy will be critical.

WEB: [10.1136/bmjgh-2021-006940](https://doi.org/10.1136/bmjgh-2021-006940)

IMPACT FACTOR: 4.280

CITED HALF-LIFE: 1.9

START COMMENTARY

Portnoy *et al.* conducted a comparative modeling study of two models – the Harvard model and the Papillomavirus Rapid Interface for Modelling and Economics (PRIME) model to project the health impact of HPV vaccination in Nigeria and Pakistan. This article is impactful as it provides information on the differences and similarities between HPV vaccination impact predicted by different models. Key features of the Harvard model include that it is a static, multi-cohort proportional impact model which estimates the impact of HPV vaccination on cases and deaths of cervical cancer. Cancer progression is described using country-specific distributions of cancer stages (i.e., two years lived with disability, five-year survival). Key features of the PRIME model are that it is static, open, multi-cohort with proportional outcomes, with cancer progression based on the Global Burden of Disease (GBD) durations and phases. Both models use the Globocan 2020 database of the International Agency for Research on Cancer (IARC) to describe incidence. A notable difference between the models is that HPV-16/18 proportion is estimated by meta-analysis in the Harvard model and by a combination of meta-analyses and retrospective cohort study in the PRIME model. Outcomes include cervical cancer deaths, cases, and disability-adjusted life years (DALYs) averted. Vaccination scenarios assumed 90% coverage of annual routine vaccination of nine-year old girls and 100% vaccine protection against HPV-16/18.

Key findings included that the Harvard model estimated a greater number of cases averted in all countries (Ethiopia, India, Nigeria, and Pakistan). The PRIME model estimated a greater number of DALYs averted compared to the Harvard model by 8% in Ethiopia. However, the Harvard model showed greater DALY aversion in the remaining countries. One key strength of this study is that Portnoy *et al.* harmonized model assumptions around population demography to project the number of cervical cancer cases averted per 1,000 vaccinated individuals in both models, which found similar projected results. When harmonizing assumptions around HPV-16/18 distribution, the differences in impact were negligible. Overall, this study shows that HPV-type distribution plays a critical role in understanding both the burden of HPV and the impact of HPV immunization. Overall, both models project that HPV will be impactful in reducing the burden of all four of these countries that are yet to introduce HPV vaccination.

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6. [The impact of the timely birth dose vaccine on the global elimination of hepatitis B.](#)

de Villiers M, Nayagam S, Hallett T.

Nat Commun. 2021 Nov 17;12(1):6223.

PubMed ID: 34711822

ABSTRACT

In 2016 the World Health Organization set the goal of eliminating hepatitis B globally by 2030. Horizontal transmission has been greatly reduced in most countries by scaling up coverage of the infant HBV vaccine series, and vertical transmission is therefore becoming increasingly dominant. Here we show that scaling up timely hepatitis B birth.dose vaccination to 90% of new-borns in 110 low- and middle-income countries by 2030 could prevent 710,000 (580,000 to 890,000) deaths in the 2020 to 2030 birth cohorts compared to status quo, with the greatest benefits in Africa. Maintaining this could lead to elimination by 2030 in the Americas, but not before 2059 in Africa. Drops in coverage due to disruptions in 2020 may lead to 15,000 additional deaths, mostly in South-East Asia and the Western Pacific. Delays in planned scale-up could lead to an additional 580,000 deaths globally in the 2020 to 2030 birth cohorts.

WEB: [10.1038/s41467-021-26475-6](https://doi.org/10.1038/s41467-021-26475-6)

IMPACT FACTOR: 14.919

CITED HALF-LIFE: 3.7

START COMMENTARY

In this modelling study, de Villiers *et al.* describe the impact of scaling up timely Hepatitis B Birth Dose (HepB-BD) vaccine on incident chronic Hepatitis B (HBV) cases and Hepatitis B Antigen (HBsAg) prevalence across 110 Gavi-eligible LMICs and all six WHO regions. This study is important as it describes the importance of timely HepB-BD vaccine in contributing to HBV elimination. Although HepB vaccines have been implemented for 40+ years, HBV still poses a substantial burden to populations globally and uptake of timely HepB-BD coverage is low in many places. Model input data were obtained from the United Nations 2019 World Population Prospects, the WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) and prior studies. Key input parameters included country-specific demographic information (fertility, male-to-female sex ratios, population size, migration, and all-cause mortality), vaccine coverage, and HbsAg prevalence. One key strength of the HBV model is the risk of vertical transmission was calibrated to each country whereas the risk of horizontal transmission was age-dependent (e.g., much higher in young children than adults). Another notable strength of this analysis is the inclusion of several vaccine scenarios for both HepB3 and HepB-BD vaccines, which are described in detail in *Table 1*.

Overall, the analysis projects that it will not be possible to achieve the WHO goal of elimination by 2030. By scaling up timely birth dose to $\geq 90\%$ by 2030, the model projects substantial reduction in chronic HBsAg incidence and the prevalence of HBsAg among five-year olds. De Villiers *et al.* find that it would not be possible to reach the elimination target (defined as 0.1% HBsAg prevalence in five-year olds) earlier than 2100 without scaling up HepB-BD. By scaling up timely HepB-BD to $\geq 90\%$ by 2030, 41 million (36-46 million) chronic HBV infections could be averted compared to the status quo. Even if the birth dose is scaled up, DALYs and deaths are projected to continue to rise until 2030-2040 given the lag between HBV infection and death. *Figure 2* demonstrates the modelled impact of scaling up HepB-BD and *Figure 3* describes the populations in which the effect of timely HepB-BD scale-up is most strongly concentrated. Detailed results for each WHO region and country are presented for selected scenarios in *Supplementary Tables 3–6*. This study highlights the critical role of scaling up timely HepB-BD, particularly in LMICs to achieve global HBV elimination in this century.

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7. [Factors that influence parents' and informal caregivers' views and practices regarding routine childhood vaccination: a qualitative evidence synthesis.](#)

Cooper S, Schmidt B, Sambala E, Swartz A, Colvin C, Leon N, et al.

Cochrane Database Syst Rev. 2021 Nov 24;10:CD013265.

PubMed ID: 34706066

ABSTRACT

BACKGROUND: Childhood vaccination is one of the most effective ways to prevent serious illnesses and deaths in children. However, worldwide, many children do not receive all recommended vaccinations, for several potential reasons. Vaccines might be unavailable, or parents may experience difficulties in accessing vaccination services; for instance, because of poor quality health services, distance from a health facility, or lack of money. Some parents may not accept available vaccines and vaccination services. Our understanding of what influences parents' views and practices around childhood vaccination, and why some parents may not accept vaccines for their children, is still limited. This synthesis links to Cochrane Reviews of the effectiveness of interventions to improve coverage or uptake of childhood vaccination.

OBJECTIVES: - Explore parents' and informal caregivers' views and practices regarding routine childhood vaccination, and the factors influencing acceptance, hesitancy, or nonacceptance of routine childhood vaccination. - Develop a conceptual understanding of what and how different factors reduce parental acceptance of routine childhood vaccination. - Explore how the findings of this review can enhance our understanding of the related Cochrane Reviews of intervention effectiveness.

SEARCH METHODS: We searched MEDLINE, Embase, CINAHL, and three other databases for eligible studies from 1974 to June 2020.

SELECTION CRITERIA: We included studies that: utilised qualitative methods for data collection and analysis; focused on parents' or caregivers' views, practices, acceptance, hesitancy, or refusal of routine vaccination for children aged up to six years; and were from any setting globally where childhood vaccination is provided.

DATA COLLECTION AND ANALYSIS: We used a pre-specified sampling frame to sample from eligible studies, aiming to capture studies that were conceptually rich, relevant to the review's phenomenon of interest, from diverse geographical settings, and from a range of income-level settings. We extracted contextual and methodological data from each sampled study. We used a meta-ethnographic approach to analyse and synthesise the evidence. We assessed methodological limitations using a list of criteria used in previous Cochrane Reviews and originally based on the

Critical Appraisal Skills Programme quality assessment tool for qualitative studies. We used the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative research) approach to assess our confidence in each finding. We integrated the findings of this review with those from relevant Cochrane Reviews of intervention effectiveness. We did this by mapping whether the underlying theories or components of trial interventions included in those reviews related to or targeted the overarching factors influencing parental views and practices regarding routine childhood vaccination identified by this review.

MAIN RESULTS: We included 145 studies in the review and sampled 27 of these for our analysis. Six studies were conducted in Africa, seven in the Americas, four in South-East Asia, nine in Europe, and one in the Western Pacific. Studies included urban and rural settings, and high-, middle-, and low-income settings. Many complex factors were found to influence parents' vaccination views and practices, which we divided into four themes. Firstly, parents' vaccination ideas and practices may be influenced by their broader ideas and practices surrounding health and illness generally, and specifically with regards to their children, and their perceptions of the role of vaccination within this context. Secondly, many parents' vaccination ideas and practices were influenced by the vaccination ideas and practices of the people they mix with socially. At the same time, shared vaccination ideas and practices helped some parents establish social relationships, which in turn strengthened their views and practices around vaccination. Thirdly, parents' vaccination ideas and practices may be influenced by wider political issues and concerns, and particularly their trust (or distrust) in those associated with vaccination programmes. Finally, parents' vaccination ideas and practices may be influenced by their access to and experiences of vaccination services and their frontline healthcare workers. We developed two concepts for understanding possible pathways to reduced acceptance of childhood vaccination. The first concept, 'neoliberal logic', suggests that many parents, particularly from high-income countries, understood health and healthcare decisions as matters of individual risk, choice, and responsibility. Some parents experienced this understanding as in conflict with vaccination programmes, which emphasise generalised risk and population health. This perceived conflict led some parents to be less accepting of vaccination for their children. The second concept, 'social exclusion', suggests that some parents, particularly from low- and middle-income countries, were less accepting of childhood vaccination due to their experiences of social exclusion. Social exclusion may damage trustful relationships between government and the public, generate feelings of isolation and resentment, and give rise to demotivation in the face of public services that are poor quality and difficult to access. These factors in turn led some parents who were socially excluded to distrust vaccination, to refuse vaccination as a form of resistance or a way to bring about change, or to avoid vaccination due to the time, costs, and distress it creates. Many of the overarching factors our review identified as influencing parents' vaccination views and practices were underrepresented in the interventions tested in the four related Cochrane Reviews of intervention effectiveness.

AUTHORS' CONCLUSIONS: Our review has revealed that parents' views and practices regarding childhood vaccination are complex and dynamic social processes that reflect multiple webs of influence, meaning, and logic. We have provided a theorised understanding of the social processes contributing to vaccination acceptance (or not), thereby complementing but also extending more individualistic models of vaccination acceptance. Successful development of interventions to promote acceptance and uptake of childhood vaccination will require an understanding of, and then tailoring to, the specific factors influencing vaccination views and practices of the group(s) in the target setting. The themes and concepts developed through our review could serve as a basis for gaining this understanding, and subsequent development of interventions that are potentially more aligned with the norms, expectations, and concerns of target users.

WEB: [10.1002/14651858.CD013265.pub2](https://doi.org/10.1002/14651858.CD013265.pub2)

IMPACT FACTOR: 7.890

CITED HALF-LIFE: 6.1

START COMMENTARY

In this systematic review, Cooper *et al.* explore caregivers' views and practices related to routine childhood vaccination for children up to six years of age. This study is impactful as it summarizes qualitative findings from 1974 to 2020 on the factors that influence acceptance, hesitancy, and non-acceptance of childhood vaccines globally, a research area that is of high importance and relevance, particularly during the ongoing COVID-19 pandemic. Although 145 studies were identified for inclusion in the study, it was decided that this number was too large to summarize findings in detail. Instead, 27 studies were selected based on conceptual richness, geographic spread, and relevance. *Figure 2* describes the process of extracting data and mapping findings. Broadly, the key steps were to extract findings to develop study summaries, determine how studies were related, develop overarching second order findings, develop third order findings, grade each finding based on a standardized approach (the GRADE-CERQual approach), map findings in a standardized framework (the Cochrane Review of Effectiveness) and development of prompts for immunization decision-makers. A key strength of this study is assessing the confidence in each finding utilizing the GRADE-CERQual approach. This allowed the Cooper *et al.* to consider the methodological limitations and study relevance to inform each finding.

Overall, 11 of 27 studies were conducted in LMICs. The main themes that emerged included: 1) ideas and practices surrounding child health and illness (i.e., religious beliefs, the perceptive that infants are fragile, views on the primacy of nature, individualized health, immunity, and vaccine responses, views on parental expertise, and personal choice); 2) social communities and networks, and 3) political events, relations and processes (i.e., distrust in systems, declining trust in authority, marginalization), 4) access-supply-demand interactions (i.e., socioeconomic challenges, undesirable

features of the logistics and vaccination process, interactions with healthcare workers). Cooper *et al.* describe two potential pathways to reduced acceptance of vaccines. The first arose in studies from high-income countries and was described as neoliberal logic, in which parents believe that health decisions should be made by an individual who weighs their own risks and benefits. This view is at odds with many vaccination messages focused on social responsibility and community health. The second mechanism arose in studies of LMICs and was defined as social exclusion. Many caregivers experienced structural social exclusion through economic disadvantage, segregation, and a lack of rights or political representation. Such structural challenges led caregivers to distrust or refuse vaccines or to avoid immunizations because of the time, effort, and cost required. Overall, this study provides a summary of evidence across settings and populations of caregivers which can contribute to an understanding of childhood vaccine acceptance, hesitancy, and non-acceptance, which is foundational for improving vaccine uptake globally.

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8. [Estimation of health impact from digitalizing last-mile Logistics Management Information Systems \(LMIS\) in Ethiopia, Tanzania, and Mozambique: A Lives Saved Tool \(LiST\) model analysis.](#)

Fritz J, Herrick T, Gilbert S.

PLoS One. 2021 Nov 23;16(10):e0258354.

PubMed ID: 34695158

ABSTRACT

BACKGROUND: Digital health has become a widely recognized approach to addressing a range of health needs, including advancing universal health coverage and achieving the Sustainable Development Goals. At present there is limited evidence on the impact of digital interventions on health outcomes. A growing body of peer-reviewed evidence on digitalizing last-mile electronic logistics management information systems (LMIS) presents an opportunity to estimate health impact.

METHODS: The impact of LMIS on reductions in stockouts was estimated from primary data and peer-reviewed literature, with three scenarios of impact: 5% stockout reduction (conservative), 10% stockout reduction (base), and 15% stockout reduction (optimistic). Stockout reduction data was inverted to stock availability and improved coverage for vaccines and essential medicines using a 1:1 conversion factor. The Lives Saved Tool (LiST) model was used to estimate health impact from lives saved in newborns and children in Mozambique, Tanzania, and Ethiopia between 2022 and 2026 across the three scenarios.

RESULTS: Improving coverage of vaccines with a digital LMIS intervention in the base scenario (conservative, optimistic) could prevent 4,924 (2,578-6,094), 3,998 (1,621-4,915), and 17,648 (12,656-22,776) deaths in Mozambique, Tanzania, and Ethiopia, respectively over the forecast timeframe. In addition, scaling up coverage of non-vaccine medications could prevent 17,044 (8,561-25,392), 21,772 (10,976-32,401), and 34,981 (17,543-52,194) deaths in Mozambique, Tanzania, and Ethiopia, respectively. In the base model scenario, the maximum percent reduction in deaths across all geographies was 1.6% for vaccines and 4.1% for non-vaccine medications.

INTERPRETATION: This study projects that digitalization of last-mile LMIS would reduce child mortality by improving coverage of lifesaving health commodities. This analysis helps to build the evidence base around the benefits of deploying digital solutions to address health challenges. Findings should be interpreted carefully as stockout reduction estimates are derived from a small number of studies.

WEB: [10.1371/journal.pone.0258354](https://doi.org/10.1371/journal.pone.0258354)

IMPACT FACTOR: 2.740

CITED HALF-LIFE: 5.6

START COMMENTARY

In this modelling study, the Lives Saved Tool (LiST) was used to estimate the impact of logistics management information systems (i.e., systems that address inventory management, provide stock level notification and distribution information) on deaths in Mozambique, Tanzania, and Ethiopia. This study contributes to a body of knowledge linking digital health interventions to health outcomes. *Figure 1* describes the impact model connecting digital health to improved health outcomes. For example, interventions that can provide stock out notifications would result in quicker replenishment of supplies, contributing to improved inventory, which contributes to improved coverage, and lastly, better health outcomes (lives saved). Three scenarios were included in this analysis: conservative (5% reduction in stock outs), base (10% reduction in stockouts), and optimistic (15% reduction in stock outs). These scenarios were informed by estimates in prior studies (shown in *Table 1*), which is a strength of this analysis. Scenarios were compared to the status quo, which was no change in stock outs. Data for other inputs (i.e., mortality rates, health status, intervention effectiveness) were obtained from the United Nations Population Division, DHS, and MICS. *Table 2* describes country-specific coverage estimates for each medical commodity or intervention included in the analysis.

Key findings included that scaling up coverage over five years with the base scenario (e.g., 10% reduction in stock outs) could prevent approximately 4,924 under-five deaths (2,578-6,094) in Mozambique, 3,988 (1,621-4,915) in Tanzania, and 17,648 (12,656-22,776) in Ethiopia. Scaling up the coverage of non-vaccine medications would save the greatest number of lives across each country (shown in *Table 3*). Similarly, non-vaccine interventions that had the largest impact on under-five mortality were the treatment of neonatal sepsis/pneumonia and antibiotics for pneumonia. Scaling up vaccine coverage had a smaller impact on mortality when compared to non-vaccine medicines. This modelling study demonstrates that implementation of a digital inventory management system could substantially reduce under-five mortality across scenarios and countries.

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9. [Progress and barriers towards maternal and neonatal tetanus elimination in the remaining 12 countries: a systematic review.](#)

Yusuf N, Raza A, Chang-Blanc D, Ahmed B, Hailegebriel T, Luce R, et al.

Lancet Glob Health. 2021 Dec 03;9(11):e1610-e1617.

PubMed ID: 34678200

ABSTRACT

This systematic review assessed the progress and barriers towards maternal and neonatal tetanus elimination in the 12 countries that are yet to achieve elimination, globally. Coverage of at least 80% (the coverage level required for elimination) was assessed among women of reproductive age for five factors: (1) at least two doses of tetanus toxoid-containing vaccine, (2) protection at birth, (3) skilled birth attendance, (4) antenatal care visits, and (5) health facility delivery. A scoping review of the literature and data from Demographic and Health Surveys and Multiple Indicator Cluster Surveys provided insights into the barriers to attaining maternal and neonatal tetanus elimination. Findings showed that none of the 12 countries attained at least 80% coverage for women of reproductive age receiving at least two doses of tetanus toxoid-containing vaccine or protection at birth according to the data from Demographic and Health Surveys or Multiple Indicator Cluster Surveys. Barriers to maternal and neonatal tetanus elimination were mostly related to health systems and socioeconomic factors. Modification to existing maternal and neonatal tetanus elimination strategies, including innovations, will be required to accelerate maternal and neonatal tetanus elimination in these countries.

WEB: [10.1016/S2214-109X\(21\)00338-7](https://doi.org/10.1016/S2214-109X(21)00338-7)

IMPACT FACTOR: 21.597

CITED HALF-LIFE: 3.1

START COMMENTARY

In this systematic review, Yusuf *et al.*, describe progress and barriers towards maternal and neonatal tetanus elimination in 12 countries that have yet to achieve elimination (defined as having less than one neonatal tetanus case per 1,000 livebirths). Countries included in the systematic review were: Afghanistan, Angola, Central African Republic, Guinea, Mali, Nigeria, Pakistan, Papua New Guinea, Somalia, South Sudan, Sudan and Yemen. Data sources include estimates from the WHO/UNICEF, DHS, and MICS.

Table 1 describes the trend of coverage with Tetanus toxoid-containing vaccine (TTCV) and protection at birth (PAB) in the twelve countries that have yet to achieve elimination. Only two of the countries (Afghanistan and Guinea) reported the target of at least 80% TTCV2+ coverage. Yemen

reported the lowest coverage (25%) and Central African Republic and Nigeria had the lowest percentage of PAB (60% each). Supplementary immunization activities resulted in TTCV2+ coverage as high as 86% in Sudan. Children born to educated mothers residing in urban areas were more likely to be protected at birth. Barriers to immunization included money for treatment, distance to health facilities, lack of permission, and not wanting to go alone. One notable finding was that competing priorities of other infectious disease outbreaks was a key impediment to immunization efforts. This study summarizes key issues affecting neonatal tetanus elimination which should be urgently addressed in these 12 countries that are yet to achieve elimination.

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10. [Resource allocation for different types of vaccines against COVID-19: Tradeoffs and synergies between efficacy and reach.](#)

Kim D, Pekgun P, Yildirim ., Keskinocak P.

Vaccine. 2021 Nov 18;39(47):6876-6882.

PubMed ID: 34688498

ABSTRACT

OBJECTIVE: Vaccine shortage and supply-chain challenges have caused limited access by many resource-limited countries during the COVID-19 pandemic. One of the primary decisions for a vaccine-ordering decision-maker is how to allocate the limited resources between different types of vaccines effectively. We studied the tradeoff between efficacy and reach of the two vaccine types that become available at different times.

METHODS: We extended a Susceptible-Infected-Recovered-Deceased (SIR-D) model with vaccination, ran extensive simulations with different settings, and compared the level of infection attack rate (IAR) under different reach ratios between two vaccine types under different resource allocation decisions.

RESULTS: We found that when there were limited resources, allocating resources to a vaccine with high efficacy that became available earlier than a vaccine with lower efficacy did not always lead to a lower IAR, particularly if the former could vaccinate less than 42.5% of the population (with the selected study parameters) who could have received the latter. Sensitivity analyses showed that this result stayed robust under different study parameters.

CONCLUSIONS: Our results showed that a vaccine with lower resource requirements (wider reach) can significantly contribute to reducing IAR, even if it becomes available later in the pandemic, compared to a higher efficacy vaccine that becomes available earlier but requires more resources. Limited resource in vaccine distribution is significant challenge in many parts of the world that needs to be addressed to improve the global access to life-saving vaccines. Understanding the tradeoffs between efficacy and reach is critical for resource allocation decisions between different vaccine types for improving health outcomes.

WEB: [10.1016/j.vaccine.2021.10.025](https://doi.org/10.1016/j.vaccine.2021.10.025)

IMPACT FACTOR: 3.143

CITED HALF-LIFE: 7.3

START COMMENTARY

In this modelling study, Kim *et al.* extend a Susceptible-Infected-Recovered-Deceased (SIR-D) model with COVID-19 vaccination to understand the tradeoffs between reach and efficacy in vaccine procurement and distribution. This study is highly relevant as many countries are facing barriers to COVID-19 resource allocation and implementation. This analysis includes two types of vaccines: 1) a high-efficacy vaccine which is available earlier but requires more resources and 2) a low-efficacy vaccine that is available later with fewer resource requirements. Comparing the impact of resource allocation between the two types of vaccines can inform future vaccine implementation efforts, particularly in LMICs. Model parameters were based on known SARS-CoV-2 characteristics (e.g., infectious period length, recovery rates, infectivity). Outcomes included the infection attack rate (IAR), peak day (defined as the day when the peak infections occur), and peak percentage (defined as the percentage of the population that is newly infected on the peak day). A notable strength of this study was the inclusion of sensitivity analysis, which adjusted input parameters such as infectivity, timing of vaccine availability, and efficacy.

Key findings show that without vaccines, about half of the population (50.18%) would be infected, with a peak day of 38 and peak percentage of 0.65%. *Table 1* and *Figure 2* present the IAR under different resource allocation decisions and reach ratios. Overall, allocating all resources to the low-efficacy vaccine would minimize the IAR. However, the difference between the low- and high-efficacy vaccine decreases as reach increases. The differences in IAR between the low- and high-efficacy range from 4.83-0.293% (16 million to 0.97 million) depending on the reach and resource allocation. Kim *et al.* present additional detailed findings related to the peak percentage and the simulation results in *Table 2*, and the *Supplementary Materials*, respectively. Overall, this study looks at the impact of resource allocation decisions for two types of vaccines and concludes that the preference for vaccines is highly dependent on reach and vaccine efficacy. The determined threshold of deciding between high-and low-efficacy is reach of 42.5%. If the high-efficacy, high-resource requirement vaccine reaches less than 42.5% of people, it would be highly resource intensive and lead to slower decrease in daily infections over time, when compared to an allocation scenario of complete low-efficacy vaccine distribution. This study can inform decision-makers across countries in considering reach, efficacy, and timing when determining the optimal way to vaccinate populations against COVID-19.

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Appendix

The literature search for the December 2021 Vaccine Delivery Research Digest was conducted on November 22, 2021. We searched English language articles indexed by the US National Library of Medicine and published between October 15, 2021 and November 14, 2021. The search resulted in 488 items.

SEARCH TERMS

(((((vaccine[tiab] OR vaccines[tiab] OR vaccination[tiab] OR immunization[tiab] OR immunisation[tiab] OR vaccine[mesh] OR immunization[mesh]) AND (logistics[tiab] OR supply[tiab] OR “supply chain”[tiab] OR implementation[tiab] OR expenditures[tiab] OR financing[tiab] OR economics[tiab] OR “Cost effectiveness”[tiab] OR coverage[tiab] OR attitudes[tiab] OR belief[tiab] OR beliefs[tiab] OR refusal[tiab] OR “Procurement”[tiab] OR timeliness[tiab] OR systems[tiab])) OR (“vaccine delivery”[tiab])) NOT (“in vitro”[tiab] OR “immune response”[tiab] OR gene[tiab] OR chemistry[tiab] OR genotox*[tiab] OR sequencing[tiab] OR nanoparticle*[tiab] OR bacteriophage[tiab] OR exome[tiab] OR exogenous[tiab] OR electropor*[tiab] OR “systems biology”[tiab] OR “animal model”[tiab] OR cattle[tiab] OR sheep[tiab] OR goat[tiab] OR rat[tiab] OR pig[tiab] OR mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR rodent[tiab] OR fish[tiab])) AND (English[LA]) (“2021/10/15”[PDAT] : “2021/11/14”[PDAT]))