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Details of Articles

1. Controlled temperature chain for vaccination in low- and middle-income countries: a realist evidence synthesis.

Seaman C, Kahn A, Kristensen D, Steinglass R, Spasenoska D, Scott N, et al.

Bull World Health Organ. 2022 Aug 05;100(8):491-502.

PubMed ID: 35923285

ABSTRACT

OBJECTIVE: To evaluate the evidence describing how the controlled temperature chain approach for vaccination could lead to improved equitable immunization coverage in low- and middle-income countries.

METHODS: We created a theory of change construct from the Controlled temperature chain: strategic roadmap for priority vaccines 2017-2020, containing four domains: (i) uptake and demand for the approach; (ii) compliance and safe use of the approach; (iii) programmatic efficiency gains from the approach; and (iv) improved equitable immunization coverage. To verify and improve the theory of change, we applied a realist review method to analyse published descriptions of controlled temperature chain or closely related experiences.

FINDINGS: We evaluated 34 articles, describing 22 unique controlled temperature chain or closely related experiences across four World Health Organization regions. We identified a strong demand for this approach among service delivery providers; however, generating an equal level of demand among policy-makers requires greater evidence on economic benefits and on vaccination coverage gains, and use case definitions. Consistent evidence supported safety of the approach when integrated into special vaccination programmes. Feasible training and supervision supported providers in complying with protocols. Time-savings were the main evidence for efficiency gains, while cost-saving data were minimal. Improved equitable coverage was reported where vaccine storage beyond the cold chain enabled access to hard-to-reach populations. No evidence indicated an inferior vaccine effectiveness nor increased adverse event rates for vaccines delivered under the approach.

CONCLUSION: Synthesized evidence broadly supported the initial theory of change. Addressing evidence gaps on economic benefits and coverage gains may increase future uptake.

WEB: 10.2471/BLT.21.287696

IMPACT FACTOR: 6.960

CITED HALF-LIFE: 12.4

START COMMENTARY

In this review, Seaman *et al.* evaluate the evidence on controlled temperature chain for vaccination in LMICs. This study is important as it summarizes evidence from 34 studies within a descriptive framework (WHO Controlled temperature chain: strategic roadmap for priority vaccines 2017–2020) to understand existing evidence and future priorities for research and evaluation. Seaman *et al.* developed the framework to include four domains: 1) uptake and demand for the approach; 2) compliance and safe use of the approach; 3) programmatic efficiency gains from the approach; and 4) improved equitable coverage. *Figure 1* shows a context-mechanism-outcome construct for the theory of chain domains. As part of the review, authors aimed to include studies which provided evidence on at least one component of the theory of change and used three quality checklists to assess the rigor of studies, a strength of this work.

In total, 34 articles were eligible for inclusion, most of which discuss the hepatitis B birth dose (41%). *Figure 2* shows the study selection process and *Table 1* shows each study including location, WHO region, vaccine, a summary, and contribution to the theory of change domains. *Figure 3* presents the revised construct along with levels of evidence (strong evidence, some evidence, no evidence) from the review. Key findings for domain 1 included that awareness of cold chain constraints, awareness of the controlled temperature chain as an intervention for immunization programs, and the ability of national/global policy makers to understand controlled temperature chain drove demand and uptake. For theory of change 2 (controlled temperature chain compliance and safe implementation), guidance and training provided to workers, and the understanding of and compliance with cold chain protocols were key approaches shown related to this domain. For the third domain (improved efficiency of vaccination programs), mechanisms such as no source preparation/conditioning of ice packs reduces vaccine freezing risk, reduced dependence on peripheral cold chain capacity, and effort previously required for transportation being shifted to microplanning and vaccination were mechanisms that resulted in cost/time saving of vaccination programs. Lastly, for the fourth domain (improved equitable coverage), mechanisms related to understanding/compliance with controlled temperature chain protocols by health workers, a reduced reliance on cold chain including transport and lower staff, and the evidence of safety and effectiveness all led to improved coverage. Overall, this study showed that existing evidence supported the proposed theory of change and refined the theory to better show the feasibility of controlled temperature chain to improve coverage in LMICs.

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2. Correlates of Zero-Dose Vaccination Status among Children Aged 12-59 Months in Sub-Saharan Africa: A Multilevel Analysis of Individual and Contextual Factors.

Ozigbu C, Olatosi B, Li Z, Hardin J, Hair N.

Vaccines (Basel). 2022 Jul 31;10(7).

PubMed ID: 35891216

ABSTRACT

Despite ongoing efforts to improve childhood vaccination coverage, including in hard-to-reach and hard-to-vaccinate communities, many children in sub-Saharan Africa (SSA) remain unvaccinated. Considering recent goals set by the Immunization Agenda 2030 (IA2030), including reducing the number of zero-dose children by half, research that goes beyond coverage to identify populations and groups at greater risk of being unvaccinated is urgently needed. This is a pooled cross-sectional study of individual- and country-level data obtained from Demographic and Health Surveys Program and two open data repositories. The sample includes 43,131 children aged 12-59 months sampled between 2010 and 2020 in 33 SSA countries. Associations of zero-dose status with individual and contextual factors were assessed using multilevel logistic regression. 16.5% of children had not received any vaccines. Individual level factors associated lower odds of zero-dose status included mother's primary school or high school education, employment, use of antenatal care services and household wealth. Compared to children in countries with lower GDP, children in countries with relatively high GDP had nearly four times greater odds of being unvaccinated. Both individual and contextual factors are correlated with zero-dose status in SSA. Our results can inform efforts to identify and reach children who have not received any vaccines.

WEB: 10.3390/vaccines10071052

IMPACT FACTOR: 4.086

CITED HALF-LIFE: 3.4

START COMMENTARY

In this study, Ozigbu *et al.* evaluate the multi-level correlates (individual and contextual factors) associated with zero-dose status across 33 sub-Saharan African countries. This study fills an important gap in research as it is the first of its kind to report the prevalence and associated factors in SSA. Data sources included individual and household level data from the DHS. *Table 1* summarizes the eligible SSA countries and survey details (year, sample size). Country-level data obtained from the World Bank included GDP per capita, literacy rate, fertility rate, health expenditure, unemployment rate, and physician density. The global peace index was obtained from the Institute of Economics and Peace.

In total, 43,131 children aged 12-59 months were included. Of these, 16.5% did not receive any vaccines. Detailed baseline and bivariate analysis of individual factors as shown in *Table 2* and bivariate analysis of contextual factors associated with zero-dose vaccination status is shown in *Table 3.* Individual factors significantly associated with zero-dose status included: child's age, mother's education, mother's occupation, antenatal visits, delivery location, and exposure to media. Contextual factors on a household level associated with zero dose status included rural resident, wealth index quintile, and religion. Contextual factors on the national level that were significantly associated with zero-dose status included GDP per capita, female unemployment rate, fertility rate and the global peace index. *Figures 1-3* present detailed results from each of the models. Overall, this study supports the finding that there are many zero-dose children in SSA and the factors leading to this high prevalence are complex multi-level factors.

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3. The Association between Childhood Immunization and Gender Inequality: A Multi-Country Ecological Analysis of Zero-Dose DTP Prevalence and DTP3 Immunization Coverage.

Vidal Fuertes C, Johns N, Goodman T, Heidari S, Munro J, Hosseinpoor A.

Vaccines (Basel). 2022 Jul 31;10(7).

PubMed ID: 35891196

ABSTRACT

This study explores the association between childhood immunization and gender inequality at the national level. Data for the study include annual country-level estimates of immunization among children aged 12-23 months, indicators of gender inequality, and associated factors for up to 165 countries from 2010-2019. The study examined the association between gender inequality, as measured by the gender development index and the gender inequality index, and two key outcomes: prevalence of children who received no doses of the DTP vaccine (zero-dose children) and children who received the third dose of the DTP vaccine (DTP3 coverage). Unadjusted and adjusted fractional logit regression models were used to identify the association between immunization and gender inequality. Gender inequality, as measured by the Gender Development Index, was positively and significantly associated with the proportion of zero-dose children (high inequality AOR = 1.61, 95% CI: 1.13-2.30). Consistently, full DTP3 immunization was negatively and significantly associated with gender inequality (high inequality AOR = 0.63, 95% CI: 0.46-0.86). These associations were robust to the use of an alternative gender inequality measure (the Gender Inequality Index) and were consistent across a range of model specifications controlling for demographic, economic, education, and health-related factors. Gender inequality at the national level is predictive of childhood immunization coverage, highlighting that addressing gender barriers is imperative to achieve universal coverage in immunization and to ensure that no child is left behind in routine vaccination.

WEB: 10.3390/vaccines10071032

IMPACT FACTOR: 4.086

CITED HALF-LIFE: 3.4

START COMMENTARY

In this ecological study, Fuertes *et al.* study the association between childhood immunization and gender inequality at a national level for 165 countries. The study outcomes included: 1) zero-dose diphtheria, tetanus and pertussis vaccine (DTP), a proxy for children missing immunization completely; 2) DTP3 immunization coverage, a proxy for children accessing all immunizations. This study is important as gender inequality is linked to several adverse health outcomes, and this

expands the understanding of the impacts on vaccine coverage. Data included national estimates of gender inequality, immunization, demographic, economic, and social characteristics from 2010 to 2019. Gender inequality was measured using the gender development index (GDI) and the gender inequality index (GII). The GDI is below 1 when men have higher development than women, 1 when it is equal, and above 1 when women have higher development than men. GII has a scale of 0 to 1 with 0 reflecting equality and 1 representing women faring worse than other on dimensions such as reproductive health, empowerment, and the labor market. The inclusion of two measures is a strength of this study. Detailed information on indicators and data sources is presented in *Table 1.*

Overall, the lowest GDI was in Yemen in 2018 (0.482) indicating inequality for women and highest was in Latvia in 2010 (1.042) indicating high equality. On the scale of GII (higher indicating greater inequality), Yemen in 2015 had the highest mean value (0.819) whereas Switzerland in 2019 had the lowest (0.819). When assessing higher levels of gender inequality and zero-dose DTP and lower DTP3, there was an evident relationship (shown in *Table 2*). Among countries with high gender inequality, there was 1.6 times higher odds of zero-dose prevalence (adjusted odds ratio [AOR]: 1.61, 95% CI: 1.13-2.30) compared to those countries without high gender inequality (*Table 3*). DTP3 coverage was 37% lower (AOR: 0.63, 95% CI: 0.46-0.86) for high inequality countries compared to low. Similar results were shown when the GII was used as the predictor for zero-dose children and DTP3 immunization coverage (*Table 4*). In conclusion, this study suggests that the level of gender inequality on a national level is associated with DTP immunization rates, highlighting the need for greater gender equality globally.

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4. The status of refrigeration solutions for last mile vaccine delivery in low-income settings.

Cattin M, Jonnalagedda S, Makohliso S, Sch..nenberger K.

Vaccine X. 2022 Jul 16;11:100184.

PubMed ID: 35800134

ABSTRACT

Recommendations for storage of most vaccines imply a continuous exposure to a temperature range between 0 C and 10 C, from the production to the administration to beneficiaries. According to the World Health Organization, more than 50% of vaccines are wasted around the world. Discontinuities of the cold chain in low-income settings where electricity is scarce contributes to this wastage. Recently, several advances have been made in cooling technologies to store and transport vaccines. This paper presents an overview of refrigeration technologies based on scientific publications, industry white papers and other grey literature. With a focus on vaccine transport, we briefly describe each refrigeration method, its best performing available devices as well as the outstanding research challenges in order to further improve its performance.

WEB: 10.1016/j.jvacx.2022.100184

IMPACT FACTOR: N/A

CITED HALF-LIFE: N/A

START COMMENTARY

In this review article, Cattin *et al.* present an overview of refrigeration technologies with a focus on vaccine transport. This study is important as it describes technology used during the last mile delivery of vaccines, which are essential for maintaining the quality and potency of vaccines. Current estimates indicate that more than half of all vaccines are wasted globally, partially due to cold chain challenges. *Figure 1* is a graphic of the cold chain process from manufacturing to beneficiaries. Cattin *et al.* describe three major methods of cooling used for last mile vaccine delivery: 1) Insulated box and coolant packs-based systems, 2) Sorption refrigeration 3) and Thermoelectric refrigeration. Within each type, the authors present an overall assessment include the state of development, advantages, disadvantages, and research challenges. Detailed findings are presented in *Table 1*. Within passive systems, there are several categories based on cold storage capacity (shown in *Table 2*) according to the World Health Organization (WHO). In summary, passive refrigerator methods are generally low cost and low maintenance but may have some challenges including that freezing coolant requires active refrigeration, they have limited storage, and they pose a risk of vaccines freezing if used incorrectly. Existing research related to passive refrigerator is focused on improving the performance and storage capacity through thermal insulation (i.e., vacuum insulated

panels, aerogels) or different phase change materials. The next method, sorption refrigeration is a method of refrigerator which uses low-grade heat, rather than electricity, with a fluid mixture of absorbate and absorbent. *Figure 2* presents a single absorption process. Although these systems have a great deal of potential, only a few are in development (e.g., the Bill and Melinda Gates funded Indigo Cooler; a cooling solution developed by the Coolar company in Germany). Overall, research challenges are focused on developing absorption and adsorption solutions with heat and mass transfer properties. Lastly, thermoelectric cooling systems are compact, lightweight, and environmentally friendly. However, they rely on batteries and have a low coefficient of performance. Current research is focused on improving the efficiency of the thermoelectric material while reducing costs. Overall, Cattin *et al.* conclude that technologies and future technologies and improvements in these technologies need to consider cost, durability, and efficiency in order to improve last mile vaccine delivery.

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5. Financing COVID-19 vaccination in sub-Saharan Africa: lessons from a nation-wide willingness to pay (WTP) survey in Ghana.

Alhassan R, Nketiah-Amponsah E, Immurana M, Abuosi A.

BMC Public Health. 2022 Jul 04;22(1):1273.

PubMed ID: 35773637

ABSTRACT

BACKGROUND: Over 13 million doses of the corona virus disease, 2019 (COVID-19) vaccines have been administered in Ghana as at March, 2022; 28.5% of the population have received one dose while 16.3% have been fully vaccinated. Cost associated with COVID-19 vaccinations in low- and middle-income countries (LMICs) requires rethinking on sustainable funding arrangements to consolidate gains made towards containing the COVID-19 pandemic.

OBJECTIVE: Ascertain the determinants of willingness to pay (WTP) for COVID-19 vaccination among adult eligible population in Ghana, and prefer evidence-based policy recommendations on sustainable financing regime for COVID-19 vaccination in the global south.

METHODS: Setting/design: A cross-sectional web-based survey was..conducted among adult population aged 18 years and above across the sixteen (16) administrative regions of Ghana.

PARTICIPANTS: A sub-sample of 697 participants willing to receive the COVID-19 vaccine was used as the unit of analysis.

OUTCOME MEASURES: main outcome measures of interests were willingness to pay for COVID-19 vaccination and the specific amount respondents were..willing to pay. The odds of WTP and specific amount were predicted using the step-wise backward logistic regression and backward step-wise OLS, respectively.

RESULTS: A total of 2,107 adult respondents aged 18..years and above were reached out to answer the questionnaire; 1,556 successfully completed the questionnaire, representing 74% response rate. Out of the 1,556 valid responses, 697 said they will receive the COVID-19 vaccine. Out of the 697 sub-sample willing to accept the vaccine, 386 (55%) were willing to pay an average of US$6.00 for the vaccine. Positive predictors of WTP were: being an educated male (OR=0.55, 95% [CI=0.366, 0.826], p = 0.004), married and educated (OR=2.19, 95% [CI=1.077, 4.445], p=0.030), being a married health worker (OR=0.43, 95% [CI=0.217, 0.845], p=0.015), and having positive perception of the vaccine (OR=2.40, 95% [CI=1.144, 5.054], p=0.021). High WTP amounts correlated positively with adherence to COVID-19 prevention protocols (Coef=10.30, 95% [CI=0.463, 20.137], p=0.040) and being a health worker with tertiary education (Coef=56.339, 95% [CI=8.524,

104.154], p=0.021). Christians who are also health workers by occupation were less likely to pay higher amounts for the vaccine.(Coef=-71.431, 95% [CI=118.821, -24.040], p=0.003).

CONCLUSIONS: WTP for COVID-19 vaccination in Ghana is low relative to comparative studies in the sub-region. There is the need for accelerated, advocacy and public education on the benefits of vaccination. Likewise, there should be broader stakeholder engagement and national dialogue..on sustainable financing options for COVID-19 vaccination as donor support continues to dwindle for LIMCs like Ghana.

WEB: 10.1186/s12889-022-13602-1
IMPACT FACTOR: 2.521
CITED HALF-LIFE: 6.0

START COMMENTARY

In this cross-sectional study, Alhassan *et al.* assess determinants of willingness to pay (WTP) for COVID-19 vaccination among eligible adults in Ghana. This study is important as it is important to develop sustainable vaccine models for COVID-19 as levels of free/donated vaccines from high income countries and subsidies from the GAVI Alliance and similar partners are decreasing. As such, there is a need to understand WTP for vaccines in Ghana and similar low- and middle-income countries. Further, in Ghana, the National Health Insurance Scheme (NHIS) does not cover vaccines. A non-probability sampling technique was used to recruit participants to complete a web-based survey prior to the first deployment of COVID-19 vaccines in the country. The survey included questions on demographics, views on COVID-19 and the vaccines and willingness to pay.

In total, 2,107 were approaches and 74% (n=1,556) completed the questionnaire. A total of 697 people stated that they were willing to accept vaccinations. Of these, 55% were willing to pay $6.00 USD (38 Ghana Cedis) for the vaccine. *Table 1* presents detailed characteristics about the study population and *Table 2* shows results from a bivariate analysis on socio-demographic factors and willingness to pay. Factors associated with willingness to pay included being married and education (Odds Ratio [OR]: 2.19, 95% CI =Confidence Interval] 1.077, 4.445, being an educated male (OR = 0.55, 95% CI = 0.366, 0.826), and being a married health worker (OR: 0.43, 95% CI: 0.217, 0.845). In backward step-wise regression (presented in *Table 3*), willingness to pay for higher amounts of vaccine were significantly associated with those who adhered to prevention protocols and those who were health workers with at least tertiary education. Overall, the study shows that 55% of people accepting the vaccine stated they would be willing to pay for it and that willingness to pay was related to levels of education, occupation, religion, and perceptions of COVID-19. This demonstrates that it might be feasible for countries and people would be willing to pay for vaccines, which is critical in an era of dwindling donor support.

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6. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study.

Watson O, Barnsley G, Toor J, Hogan A, Winskill P, Ghani A.

Lancet Infect Dis. 2022 Jul 16.

PubMed ID: 35753318

ABSTRACT

BACKGROUND: The first COVID-19 vaccine outside a clinical trial setting was administered on Dec 8, 2020. To ensure global vaccine equity, vaccine targets were set by the COVID-19 Vaccines Global Access (COVAX) Facility and WHO. However, due to vaccine shortfalls, these targets were not achieved by the end of 2021. We aimed to quantify the global impact of the first year of COVID-19 vaccination programmes.

METHODS: A mathematical model of COVID-19 transmission and vaccination was separately fit to reported COVID-19 mortality and all-cause excess mortality in 185 countries and territories. The impact of COVID-19 vaccination programmes was determined by estimating the additional lives lost if no vaccines had been distributed. We also estimated the additional deaths that would have been averted had the vaccination coverage targets of 20% set by COVAX and 40% set by WHO been achieved by the end of 2021.

FINDINGS: Based on official reported COVID-19 deaths, we estimated that vaccinations prevented 14..4 million (95% credible interval [Crl] 13.7-15.9) deaths from COVID-19 in 185 countries and territories between Dec 8, 2020, and Dec 8, 2021. This estimate rose to 19..8 million (95% Crl 19.1-20..4) deaths from COVID-19 averted when we used excess deaths as an estimate of the true extent of the pandemic, representing a global reduction of 63% in total deaths (19..8 million of 31..4 million) during the first year of COVID-19 vaccination. In COVAX Advance Market Commitment countries, we estimated that 41% of excess mortality (7.4 million [95% Crl 6..8-7.7] of 17..9 million deaths) was averted. In low-income countries, we estimated that an additional 45% (95% Crl 42-49) of deaths could have been averted had the 20% vaccination coverage target set by COVAX been met by each country, and that an additional 111% (105-118) of deaths could have been averted had the 40% target set by WHO been met by each country by the end of 2021.

INTERPRETATION: COVID-19 vaccination has substantially altered the course of the pandemic, saving tens of millions of lives globally. However, inadequate access to vaccines in low-income countries has limited the impact in these settings, reinforcing the need for global vaccine equity and coverage.

FUNDING: Schmidt Science Fellowship in partnership with the Rhodes Trust; WHO; UK Medical Research Council; Gavi, the Vaccine Alliance; Bill & Melinda Gates Foundation; National Institute for Health Research; and Community Jameel.

WEB: 10.1016/S1473-3099(22)00320-6
IMPACT FACTOR: 24.446
CITED HALF-LIFE: 4.7

START COMMENTARY

In this modelling study, Watson *et al.* projects the impacts of the first year of COVID-19 vaccination programs. This study is important as it provides a benchmark of the estimated impact of vaccinations and provides guidance on how to improve and increase the impact of vaccines globally. Watson *et al.* report some of the impressive COVID-19 statistics from the first year of vaccine implementation including that 55.5% of the global population have received one dose of the vaccine in the first year, and another 45.5% had received two doses. Despite this progress, more than 3.5 million deaths have been reported in the same period. This study expands our understanding of the direct and indirect effects of the first year of COVID-19 vaccinations. *The Appendix* provides details on the COVID-19 transmission model, vaccination, variants, and model fitting. Model-based estimates for all-cause excess mortality were obtained from The Economist and COVID-19 deaths were obtained from the Johns Hopkins University COVID-19 Data Repository. Alternative scenarios were included: 1) the impact of fully vaccinating 40% of the eligible population in each country by the end of 2021 (the WHO target); 2) the impact of fully vaccinating 20% of the eligible population in the COVAX Advance Market Commitment countries by the end of 2021.

Watson *et al.* estimate that without vaccinations, 18.1 million (95% credible interval (CrI): 17.4-19.7) deaths would have occurred due to COVID-19. The vaccines are estimated to have prevented 79% of deaths globally. *Table 1* presents the estimated deaths averted worldwide by World Bank income group and WHO region. Overall, 31.1 million deaths (95% CrI: 30.6-32.1) would have occurred without COVID vaccinations. These results are shown in *Table 2* and are particularly pronounced in low-income countries. Lastly, in scenarios where WHO and COVAX targets were met, many deaths could have been averted. A total of 96 countries did not meet the WHO target of 40%, which would have saved nearly 600,000 lives. Shortfalls in the COVAX goal resulted in an additional 156,900 deaths (95% CrI: 147,800-165,400). This study shows the remarkable direct and indirect impacts of COVID-19 vaccination in its first year.

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7. Mapping BCG vaccination coverage in Ethiopia between 2000 and 2019.

Atalell K, Alemayehu M, Teshager N, Belay G, Alemu T, Anlay D, et al.

BMC Infect Dis. 2022 Jun 27;22(1):569.

PubMed ID: 35739462

ABSTRACT

INTRODUCTION: The Bacille-Calmette-Guerin (BCG) vaccination remains the primary strategy to prevent severe disseminated TB in young children, particularly in high TB-burden countries such as Ethiopia. Accurate knowledge of vaccination coverage in small geographical areas is critically important to developing targeted immunization campaigns. Thus, this study aimed to investigate the spatiotemporal distributions and ecological level determinants of BCG vaccination coverage in Ethiopia.

METHOD: Bacille-Calmette-Guerin immunization coverage and geographical information data were obtained from five different Demographic and Health Surveys, conducted in Ethiopia between 2000 and 2019. Data for independent variables were obtained from publicly available sources. Bayesian geostatistical models were used to predict the spatial distribution of BCG vaccination coverage in Ethiopia.

RESULT: The overall national BCG vaccination coverage between 2000 and 2019 was 65.5%. The BCG vaccine coverage was 53.5% in 2000, 56.9% in 2005, 64.4% in 2011, 79.6% in 2016, and 79.0% in 2019. BCG vaccination coverage increased by 47.6% in Ethiopia from 2000 to 2019, but substantial geographical inequalities in BCG coverage remained at sub-national and local levels. High vaccination coverage was observed in northern, western, and central parts of Ethiopia. Climatic and demographic factors such as temperature, altitude, and population density were positively associated with BCG vaccination coverage. Whereas, healthcare access factors such as distance to health facilities and travel time to the nearest cities were negatively associated with BCG vaccine coverage in Ethiopia.

CONCLUSION: Despite substantial progress in national BCG vaccination coverage, marked spatial variation in BCG coverage persists throughout the country at sub-national and local levels. Healthcare access and climatic and demographic factors determined the spatial distribution of BCG vaccination coverage. Maintaining a high level of vaccination coverage across geographical areas is important to prevent TB in Ethiopia.

WEB: 10.1186/s12879-022-07547-4

IMPACT FACTOR: 2.688

CITED HALF-LIFE: 5.0

START COMMENTARY

In this ecological study, Atalell *et al.* use Demographic Health Surveys (DHS) and publicly available data sources to develop Bayesian geostatistical methods to map the spatial distribution of Bacille-Calmette–Guerin (BCG) vaccination coverage in Ethiopia. This study is important as it provides insight into areas and populations that should be targeted for immunization campaigns, which is of critical importance in high tuberculosis (TB) countries such as Ethiopia. Immunization coverage was obtained from five DHS surveys between 2000-2019. Geospatial covariates included mean monthly temperature, mean monthly precipitation, altitude, travel time to cities in minutes, access to health care facilities, population density, and distance to waterbody. All were obtained from public data sources and were selected based on potential association with vaccine coverage.

Overall, coverage improved from 2000 to 2019 (53.5% in 2000 and 79% in 2019). Detailed findings for each period are presented for the nation and each region in *Table 1*. Although overall trends demonstrate improvement, there were substantial spatial variations (as shown in *Figure 2*). *Figure 3* presents the predicted BCG vaccine coverage, which shows the highest predicted BCG coverage in Northern, Northwestern, and central parts of the country, and the lowest in Southern, Eastern, and Northeastern regions. Temperature, altitude, and population density were positively associated with vaccination coverage whereas travel time to nearest cities and distance to health facilities was negatively associated with coverage. Overall, this study demonstrates substantially spatial variations in coverage in Ethiopia, underscoring the need for targeted immunization campaigns.

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8. Healthcare provider perspectives on delivering next generation rotavirus vaccines in five low-to-middle-income countries.

Mooney J, Price J, Bain C, Bawa J, Gurley N, Kumar A, et al.

PLoS One. 2022 Jul 19;17(6):e0270369.

PubMed ID: 35737718

ABSTRACT

BACKGROUND: Live oral rotavirus vaccines (LORVs) have significantly reduced rotavirus hospitalizations and deaths worldwide. However, LORVs are less effective in low- and middle-income countries (LMICs). Next-generation rotavirus vaccines (NGRVs) may be more effective but require administration by injection or a neonatal oral dose, adding operational complexity. Healthcare providers (HPs) were interviewed to assess rotavirus vaccine preferences and identify delivery issues as part of an NGRV value proposition.

OBJECTIVE: Determine HP vaccine preferences about delivering LORVs compared to injectable (iNGRV) and neonatal oral (oNGRV) NGRVs.

METHODS: 64 HPs from Ghana, Kenya, Malawi, Peru, and Senegal were interviewed following a mixed-method guide centered on three vaccine comparisons: LORV vs. iNGRV; LORV vs. oNGRV; oNGRV vs. iNGRV. HPs reviewed attributes for each vaccine in the comparisons, then indicated and explained their preference. Additional questions elicited views about co-administering iNGRV+LORV for greater public health impact, a possible iNGRV-DTP-containing combination vaccine, and delivering neonatal doses.

RESULTS: Almost all HPs preferred oral vaccine options over iNGRV, with many emphasizing an aversion to additional injections. Despite this strong preference, HPs described challenges delivering oral doses. Preferences for LORV vs. oNGRV were split, marked by disparate views on rotavirus disease epidemiology and the safety, need, and feasibility of delivering neonatal vaccines. Although overwhelmingly enthusiastic about an iNGRV-DTP-containing combination option, several HPs had concerns. HP views were divided on the feasibility of co-administering iNGRV+LORV, citing challenges around logistics and caregiver sensitization.

CONCLUSION: Our findings provide valuable insights on delivering NGRVs in routine immunization. Despite opposition to injectables, openness to co-administering LORV+iNGRV to improve efficacy suggests future HP support of iNGRV if adequately informed of its advantages. Rationales for LORV vs. oNGRV underscore needs for training on rotavirus epidemiology and stronger service integration. Expressed challenges delivering existing LORVs merit further examination and indicate need for improved delivery.

WEB: 10.1371/journal.pone.0270369
IMPACT FACTOR: 2.740
CITED HALF-LIFE: 5.6

START COMMENTARY

In this qualitative study, Mooney *et al.* interviewed 64 health providers (HPs) to understand their rotavirus preferences (i.e., live oral vaccines [LORVs] versus injectable or oral NGRV [iNGRV and oNGRV, respectively) and delivery issues that may arise with next-generation rotavirus vaccines (NGRVs). This study is important as NGRVs (including injectable and oral) are currently in development and may be better or safer than LORVs. To understand the acceptance and potential issues before implementation, 64 HPs were interviewed across Ghana, Kenya, Malawi, Peru, and Senegal. Countries were purposively selected to represent the geographies of Gavi. Country characteristics are presented in *Table 1.* The route of administration, schedule and doses, and cold chain volume per fully immunized child were reported. Detailed information for each vaccine is presented in *Table 2.*

Most HPs considered rotavirus to be a “very serious problem” (56%) or a “serious problem” (33%) in their countries. Overall, HPs greatly preferred oral vaccines (either LORV or oNGRV) over injectables. Only a small number of people preferred the oNGRV over LORB (n=37 versus n=27, respectively). HPs stated that their preference was related to concerns of delivery by injection, including that mothers dislike injection, HPs felt it inflicted pain on children. However, other providers noted there were some benefits to injectable vaccines including fewer risks of children spitting up the vaccine or vomiting. Detailed preference drivers are presented in *Table 5*. When asked about providing a birth dose of rotavirus vaccines, challenges highlighted included that vaccines would not be able to be integrated into existing practice, educating mothers would be difficult, neonates cannot handle it, home and weekend births would pose a challenge, and there may be safety issues. In terms of delivering iNGRV in a DTP-containing combination vaccine, key concerns included caregiver acceptability (that caregivers already accept LORV so there is no need to change); safety concerns (i.e., increased pain), potential reactions with other DTP-containing vaccines (*Table 7*). Overall, the HPs provided important insights into vaccine preferences and potential issues that may arise during the scale up of NGRVs.

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9. Incidence of typhoid and paratyphoid fever in Bangladesh, Nepal, and Pakistan: results of the Surveillance for Enteric Fever in Asia Project.

Garrett D, Longley A, Aiemjoy K, Yousafzai M, Hemlock C, Yu A, et al.

Lancet Glob Health. 2022 Jul 16;10(7):e978-e988.

PubMed ID: 3571464835714634

ABSTRACT

BACKGROUND: Precise enteric fever disease burden data are needed to inform prevention and control measures, including the use of newly available typhoid vaccines. We established the Surveillance for Enteric Fever in Asia Project (SEAP) to inform these strategies.

METHODS: From September, 2016, to September, 2019, we conducted prospective clinical surveillance for Salmonella enterica serotype Typhi (S Typhi) and Paratyphi (S Paratyphi) A, B, and C at health facilities in predetermined catchment areas in Dhaka, Bangladesh; Kathmandu and Kavrepalanchok, Nepal; and Karachi, Pakistan. Patients eligible for inclusion were outpatients with 3 or more consecutive days of fever in the last 7 days; inpatients with suspected or confirmed enteric fever; patients with blood culture-confirmed enteric fever from the hospital laboratories not captured by inpatient or outpatient enrolment and cases from the laboratory network; and patients with non-traumatic ileal perforation under surgical care. We used a hybrid surveillance model, pairing facility-based blood culture surveillance with community surveys of health-care use. Blood cultures were performed for enrolled patients. We calculated overall and age-specific typhoid and paratyphoid incidence estimates for each study site. Adjusted estimates accounted for the sensitivity of blood culture, the proportion of eligible individuals who consented and provided blood, the probability of care-seeking at a study facility, and the influence of wealth and education on care-seeking. We additionally calculated incidence of hospitalisation due to typhoid and paratyphoid.

FINDINGS: A total of 34,747 patients were enrolled across 23 facilitates (six tertiary hospitals, surgical wards of two additional hospitals, and 15 laboratory network sites) during the study period. Of the 34, 303 blood cultures performed on enrolled patients, 8705 (26%) were positive for typhoidal Salmonella. Adjusted incidence rates of enteric fever considered patients in the six tertiary hospitals. Adjusted incidence of S Typhi, expressed per 100, 000 person-years, was 913 (95% CI 765-1095) in Dhaka. In Nepal, the adjusted typhoid incidence rates were 330 (230-480) in Kathmandu and 268 (202-362) in Kavrepalanchok. In Pakistan, the adjusted incidence rates per hospital site were 176 (144-216) and 103 (85-126). The adjusted incidence rates of paratyphoid (of which all included cases were due to S Paratyphi A) were 128 (107-154) in Bangladesh, 46 (34-62) and 81 (56-118) in the Nepal sites, and 23 (19-29) and 1 (1-1) in the Pakistan sites. Adjusted incidence of hospitalisation was high across sites, and overall, 2804 (32%) of 8705 patients with blood culture-confirmed enteric fever were hospitalised.

INTERPRETATION: Across diverse communities in three south Asian countries, adjusted incidence exceeded the threshold for “high burden” of enteric fever (100 per 100…000 person-years). Incidence was highest among children, although age patterns differed across sites. The substantial disease burden identified highlights the need for control measures, including improvements to water and sanitation infrastructure and the implementation of typhoid vaccines.

FUNDING: Bill & Melinda Gates Foundation.

WEB: 10.1016/S2214-109X(22)00119-X
IMPACT FACTOR: 21.597
CITED HALF-LIFE: 3.1

START COMMENTARY

In this prospective clinical surveillance study, Garrett *et al.* calculate overall and age-specific typhoid and paratyphoid incidence. This study is part of the newly established Surveillance for Enteric Fever in Asia Project (SEAP) an makes an important contribution as it quantifies the incidence and burden of typhoid, providing evidence that the typhoid conjugate vaccine may be needed in these settings. This study was conducted in 23 facilities across Bangladesh, Nepal, and Pakistan. Eligible participants were any individuals with febrile illness. Patients were recruited from outpatient facilities, inpatient units, from hospital laboratory records, and surgery units with specific exclusion/inclusion criteria for each. Blood cultures were used to confirm enteric fever.

From September 2016 to September 2019, a total of 41,244 were deemed eligible. Of these, 99% (n=34,303) had blood cultures performed. *Figure 1* shows the recruitment, eligibility, study consent, and laboratory culture positivity for the study. A total of 26% of persons (n=8,706) were positive for enteric fever (28% in Bangladesh; 23% in Nepal; 23% in Pakistan). *Salmonella Typhi* was the most common isolate (85% in Bangladesh; 85% in Nepal, and 94% in Pakistan). *Table 1* presents detailed demographics of all enrolled patients within each country and overall. Crude incidence rates of typhoid from a low of 12 (10-14) per 100,000 person years to 103 (95% CI: 97-109) per 100,000 per-years. *Figure 2* presents unadjusted and adjusted incidence rates of laboratory-confirmed typhoid and paratyphoid cases per 100,000 person-years. Incidence varied by age; the highest incidence was shown among children 2-4 years old in Bangladesh and Pakistan and among 5-25 year olds in Nepal. Overall, this surveillance study indicates a high prevalence and burden of typhoid in SEAP, indicating the need for TCV introduction in each of these settings.

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10. A cross-sectional survey to evaluate prescribers' knowledge and understanding of safety messages following Dengvaxia.. product information update.

Almas M, Toussi M, Valero E, Moureau A, Marcelon L.

Pharmacoepidemiol Drug Saf. 2022 Jul 31;31(7):758-768.

PubMed ID: 35505623

ABSTRACT

PURPOSE: We evaluated the effectiveness of additional risk minimisation measures (aRMMs; i.e., educational materials) distributed to prescribers to ensure that only individuals with evidence of prior dengue infection (PDI, i.e., dengue seropositive) would be vaccinated with the tetravalent dengue vaccine (CYD-TDV; Dengvaxia..).

METHODS: A survey was conducted in 2020 among 300 CYD-TDV prescribers in Brazil and Thailand to ascertain three success criteria: prescribers' awareness of the materials (receiving and reading them); knowledge of the key messages; and whether their self-reported behaviour regarding practice-related scenarios was aligned with the updated guidance.

RESULTS: The aRMMs were not generally effective as <80% of prescribers in both countries met two of the three predefined success criteria. In Brazil, 98.7% were aware of the aRMMs whereas in Thailand this criterion was fulfilled by 74.0%. Almost all prescribers knew that CYD-TDV was recommended only in individuals with PDI (98.7% and 96.7% in Brazil and Thailand, respectively). In Brazil, where vaccination was restricted to those with a documented history of PDI, 11.3% considered that confirmation should be done through a blood test. More than 75% in both countries considered additional signs of dengue, as early warning signs, and not only those regarded as such by the 2009 WHO guidelines.

CONCLUSIONS: These results do not support that the aRMMs were effective as the predefined success criteria were not met. The use of reliable rapid diagnosis tests together with the revised prescribing information and educational materials will facilitate the implementation and compliance with pre-vaccination screening for CYD-TDV eligibility.

WEB: 10.1002/pds.5447

IMPACT FACTOR: N/A

CITED HALF-LIFE: N/A

START COMMENTARY

In this cross-sectional study in Brazil and Thailand, Almas *et al.* evaluate prescribers' awareness and knowledge of safety messages after the dengue vaccine product information update (Dengvaxia).

This study is important as long-term safety studies indicate that the live, attenuated, tetravalent dengue vaccine (CYD-TDV) results in a higher risk of hospitalization and severe dengue among those without history of prior infection. Prescribing information for CYD-TDV was updated to limit the use of vaccines to those previously exposed to the virus. In addition, Sanofi Pasteur updated the international Risk Management Plan through additional risk minimisation measures (aRMMs). aRMMs included an educational guide targeting health care providers (HCPs) which was distributed through email in Brazil. In Thailand, the Paediatric Infectious Disease Society of Thailand and the Infectious Disease Association of Thailand developed a document and posted it on their websites. This study aimed to understand how effective these materials were by assessing prescribers' awareness and knowledge of the materials, safety messages, and subsequent behaviour. Participants includes all prescribers of CYD-TDV in Brazil and Thailand that were wiling to participate.

Of the 929 invited to participate in an online survey in Brazil], 69.3% (n=644) agreed to participate. Among these, 463 were deemed ineligible, largely due to conflicts of interest or never having prescribed the vaccine. In total, 150 prescribers were included. A limitation of the study is that only 16.1% of those invited were enrolled. *Figure 1* presents a graphic of awareness, knowledge, and behaviour outcomes among different types of clinicians (internal medicine, paediatrics, infectious disease, allergy/immunology, and all). Awareness of the aRMM was very high (98.7% of prescribers received and read the aRMM). Although knowledge of the recommended prescribing practices was high (98.7% stating that only those who were previously exposed should be given the vaccine), only 1.3% knew about the increased risk of hospitalization or more severe dengue among seronegative patients. Nearly all participants (96%) incorrectly identified scenarios as eligible for CYD-TDV. Similarly, 78% of clinicians incorrectly identified rash and bone pain as early warning signs of dengue.

In Thailand, of 386 invited prescribers that were invited, 72.8% (n=281) agreed to participate. However, 126 were deemed ineligible. *Figure 2* presents a graphic of awareness, knowledge, and behaviour outcomes among different types of clinicians in Thailand (internal medicine, paediatrics, infectious disease, and all). The vast majority of knew that CYD-TDV should be given to individuals with prior exposure to dengue viruses, and 78% knew it should not be given to seronegative individuals. Early dengue signs were correctly identified 37.3-69.3% of participants depending on the clinical sign. In terms of behaviour, many clinicians incorrectly identified scenarios in which vaccines were recommended. Overall, this study indicates that the aRMMS were not successful in improving clinician knowledge or behaviour, even with high awareness (particularly in Brazil). This indicates that there needs to be further clarification and communication of CYC-TDV vaccine guidelines.

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Appendix

The literature search for the August 2022 Vaccine Delivery Research Digest was conducted on August 8, 2022. We searched English language articles indexed by the US National Library of Medicine and published between June 15, 2022 and July 14, 2022. The search resulted in 624 items.

SEARCH TERMS

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