VACCINE DELIVERY RESEARCH DIGEST

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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Details of Articles

1. Assessing the value of human papillomavirus vaccination in Gavi-eligible low-income and middle-income countries.

Ochalek J, Abbas K, Claxton K, Jit M, Lomas J.

BMJ Glob Health. 2020 Oct 23;5(10).

PubMed ID: 33082132

ABSTRACT

INTRODUCTION: Estimating the value of providing effective healthcare interventions in a country requires an assessment of whether the improvement in health outcomes they offer exceeds the improvement in health that would have been possible if the resources required had, instead, been made available for other healthcare activities in that country. This potential alternative use of the same resources represents the health opportunity cost of providing the intervention. Without such assessments, there is a danger that blanket recommendations made by international organisations will lead to the adoption of healthcare interventions that are not cost effective in some countries, even given existing donor mechanisms intended to support their affordability.

METHODS: We assessed the net health impact to 46 Gavi-eligible countries of achieving one of the WHO's proposed 90-70-90 targets for cervical cancer elimination, which includes 90% coverage of human papillomavirus (HPV) vaccination among girls by 15 years of age, using published estimates of the expected additional benefits and costs in each country and estimates of the marginal productivity of each healthcare system. We calculated the maximum price each country could afford to pay for HPV vaccination to be cost effective by assessing the net health impact that would be expected to be generated at different potential prices.

RESULTS: At Gavi negotiated prices, HPV vaccination offers net health benefits across most Gavi-eligible countries included in this study. However, if Gavi-eligible countries faced the average price faced by non-Gavi eligible countries, providing HPV vaccination would result in reduced overall population health in most countries.

CONCLUSION: Estimates of the net health impact of providing a healthcare intervention can be used to assess the benefit (or lack of) to countries of adhering to global guidance, inform negotiations with donors, as well as pricing negotiations and the value of developing new healthcare interventions.

WEB: 10.1136/bmjgh-2020-003006
IMPACT FACTOR: 4.280
CITED HALF-LIFE: 1.9

START COMMENTARY

Ochalek *et al.* explore health opportunity costs of providing human papillomavirus (HPV) vaccination in Gavi-eligible low-income and middle-income countries. Though the WHO provides global recommendation for 90% coverage of HPV vaccination among girls by 15 year of age, and traditional cost-effective thresholds (e.g. 1x GDP per-capita) indicate HPV vaccines are highly cost effective in nearly every country, HPV vaccination is not implemented globally. This article fills a critical gap in the literature by providing country-specific health opportunity costs to ensure that all countries can determine the benefit of HPV vaccine on population health, as well as understand the maximum price that they can pay relevant to this net health impact.

Ochalek *et al.* provide health opportunity costs across several potential policy options, including achieving the WHO recommendation at the average market price per dose (USD 25) and at current Gavi-negotiated per dose prices (USD 4.50) with and without current Gavi support. *Table 1* presents each country's net health impact and net monetary impact at each price. Overall, authors conclude that the average market price (USD 25 per dose) would result in net health losses in most countries (20 of 22 low-income countries and 13 of 24 lower middle-income countries) and result in a burden of 38 million DALYs globally, making this policy option likely infeasible. However, with the Gavi-negotiated price (USD 4.50 per dose), nearly all countries had positive net health benefits. The authors also assess what procurement prices would generate a health benefit for each country, and more broadly, for country income groups (e.g. low-income, lower-middle income). *Table 2* presents the price reductions required for each country and each country income group. This article can inform country-level decision-making by providing guidance on HPV vaccination relative to other healthcare system interventions to determine which is likely to generate the greatest health gains. Further, it highlights the positive public health impact of Gavi's price negotiations in facilitating cervical cancer elimination goals through cost-effective HPV vaccination.

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2. Assessing coverage of essential maternal and child health interventions using health-facility data in Uganda.

Simmons E, Singh K, Mpiima J, Kumar M, Weiss W.

Popul Health Metr. 2020 Nov 03;18(1):26.

PubMed ID: 33036626

ABSTRACT

BACKGROUND: Nationally representative household surveys are the gold standard for tracking progress in coverage of life-saving maternal and child interventions, but often do not provide timely information on coverage at the local and health facility level. Electronic routine health information system (RHIS) data could help provide this information, but there are currently concerns about data quality. This analysis seeks to improve the usability of and confidence in electronic RHIS data by using adjustments to calculate more accurate numerators and denominators for essential interventions.

METHODS: Data from three sources (Ugandan Demographic and Health (UDHS) survey, electronic RHIS, and census) were used to provide estimates of essential maternal (> 4 antenatal care visits (ANC), skilled delivery, and postnatal care visit (PNC)) and child health interventions (diphtheria, pertussis, tetanus, and hepatitis B and Haemophilus influenzae type b and polio vaccination series, measles vaccination, and vitamin A). Electronic RHIS data was checked for quality and both numerators and denominators were adjusted to improve accuracy. Estimates were compared between the three sources.

RESULTS: Estimates of maternal health interventions from adjusted electronic RHIS data were lower than those of the UDHS, while child intervention estimates were typically higher. Adjustment of electronic RHIS data generally improved accuracy compared with no adjustment. There was considerable agreement between estimates from adjusted, electronic RHIS data, and UDHS for skilled delivery and first dose of childhood vaccination series, but lesser agreement for ANC visits and second and third doses of childhood vaccinations.

CONCLUSIONS: Nationally representative household surveys will likely continue being the gold standard of coverage estimates of maternal and child health interventions, but this analysis shows that current approaches to adjusting health facility estimate works better for some indications than others. Further efforts to improve accuracy of estimates from RHIS sources are needed.

WEB: 10.1186/s12963-020-00236-x

IMPACT FACTOR: 3.328

CITED HALF-LIFE: 6.9

START COMMENTARY

Simmons *et al.* compared estimates of key maternal and child health indicators from three sources, including the Ugandan Demographic Health Survey (UDHS), electronic routine health information system (RHIS), and the census, seeking to determine if quality checks and adjustments to numerators and denominators of RHIS data could improve accuracy compared to other data sources. They provide evidence on the usability of RHIS, and more specifically, the District Health Information Software Version 2 (DHIS2), which is used in Uganda, in providing timely local and health facility data on maternal and child health indicators. Authors aggregated DHIS2 data by sub-region, adjusted the data to improve the quality of the numerators, and combined DHIS2 numerators with census-based denominators to estimate coverage of child interventions. Authors reported both unadjusted- and adjusted DHIS2 statistics for child and maternal estimates and compare those to UDHS. They found high agreement for skilled attendance at birth and first doses of DPT-HepB-Hib and polio vaccinations, and moderate agreement for four antenatal care visits and second vaccination of DPT-HepB-Hiv and polio. However, there was less agreement for other indicators (i.e. third vaccination dose, measles, vitamin A, and postnatal care). Key strengths of this study are the methods employed to improve coverage estimates of essential interventions using health facility data such as data quality checks which involved assessing outliers, numeration adjustments, and denominator adjustments (i.e. adjustments for incomplete reporting, non-use of services, and stillbirths). They conclude that nationally representative household surveys occurring every 3-5 years will likely continue as the main source of data regarding the coverage of maternal and child interventions. However, they suggest that using adjusted electronic health records could provide timely data on some indicators and improve the accuracy of routine facility data in estimating vaccine coverage estimates.

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3. Incidence and mortality of pertussis disease in infants <12 months of age following introduction of pertussis maternal universal mass vaccination in Bogotá, Colombia.

Carrasquilla G, Porras A, Martinez S, DeAntonio R, Devadiga R, Caceres D, *et al*.

Vaccine. 2020 Oct 19;38(46):7384-7392.
PubMed ID: 33012607

ABSTRACT

BACKGROUND: Maternal immunization with tetanus, diphtheria, and acellular pertussis (Tdap) vaccine confers protection to young infants. We aimed to describe trends in pertussis incidence and

associated mortality in children aged <12 months before and after introduction of maternal Tdap immunization in Bogotá, Colombia.

METHODS: Data on pertussis-related cases/deaths in infants aged <12 months were collected from SIVIGILA for the period 2005-2016, and compared incidence for the pre-vaccine introduction (2005-2012) and post-maternal Tdap vaccination (2014-2016) periods in infants aged <12 months and in three distinct age-strata; ≤6 weeks, 7-<28 weeks, and 28-52 weeks. Mortality comparisons were performed in all infants <12 months.

RESULTS: From 2005 to 2016, 2315 laboratory or clinically-confirmed pertussis cases were reported in infants <12 months of age (278 cases in young infants aged ≤6 weeks); 55 pertussis deaths were reported in children aged <12 months. No pertussis deaths were reported in the 2014-2016 period. Since maternal Tdap introduction in 2013, a consistent decline in pertussis incidence and mortality was observed. In the time-series analysis, incidence declined from 209.4/100,000 persons (2005-2012) to 49.1/100,000 persons (2014-2016) in all children <12 months; a 87.5% (95%CI: 77.2-93.2%) reduction. For these same period's incidence in young infants ≤6 weeks declined from 196.7 to 89.6/100,000 person-years (an 54.4% [95% CI: 35.4-67.9%] reduction). Greater incidence reductions were observed in older infants; 73.4% (95% CI: 68.4-77.6%) in those aged 7-<28 weeks, and 100% in those aged 28-52 weeks. A 100% reduction in Pertussis mortality in infants <12 months was observed. Since Tdap introduction, maternal vaccine coverage rose from <60% in 2013-2015 to 80% in 2016.

CONCLUSIONS: Implementation of maternal immunization in Bogotá may have contributed to the reduction in pertussis incidence and mortality among infants <12 months of age (ClinicalTrials.gov: NCT02569879). An Audio Summary linked to this article that can be found on Figshare https://doi.org/10.6084/m9.figshare.12943316.

WEB: 10.1016/j.vaccine.2020.07.046
IMPACT FACTOR: 3.143
CITED HALF-LIFE: 7.3

START COMMENTARY

Carrasquilla *et al.* conducted an interrupted time-series analysis controlling for seasonality and existing trends to estimate the impact of maternal pertussis immunization on monthly and annual pertussis incidence and deaths among infants. This article is impactful as it provides evidence of protection from pertussis by maternal immunization with the tetanus, diphtheria, and acellular pertussis (Tdap) vaccine. The study found substantial decreases in incidence among the most vulnerable infants, those ≤6 weeks, and among infants <12 months. Further, there were decreases in mortality with no deaths reported from 2013, indicating that maternal immunization may have had

a positive impact on these trends. A key strength of this study was the controlling of existing trends, which is particularly relevant for pertussis which has a cyclical epidemiology with significant variations in incidence across time and age groups. Further, the authors considered existing spikes in incidence in Bogotá and nationally in Colombia. However, the study was missing some data (i.e., information on specific components of maternal immunizations, detailed child vaccination data, and monthly incidence data for some age groups) which could have strengthened the analysis.

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4. Co-detection of Bordetella pertussis and other respiratory organisms in children hospitalised with lower respiratory tract infection.

Muloiwa R, Dube F, Nicol M, Hussey G, Zar H.

Sci Rep. 2020 Nov 03;10(1):16412.

PubMed ID: 33009451

ABSTRACT

Multiple potential pathogens are frequently co-detected among children with lower respiratory tract infection (LRTI). Evidence indicates that *Bordetella pertussis* has an important role in the aetiology of LRTI. We aimed to study the association between *B. pertussis* and other respiratory pathogens in children hospitalised with severe LRTI, and to assess clinical relevance of co-detection. Nasopharyngeal (NP) swabs and induced sputa (IS) were tested with a *B. pertussis* specific PCR; additionally, IS was tested for other pathogens using a multiplex PCR. We included 454 children, median age 8 months (IQR 4-18), 31 (7%) of whom tested positive for *B. pertussis*. Children with *B. pertussis* had more bacterial pathogens detected (3 versus 2; $P < 0.001$). While *B. pertussis* showed no association with most pathogens, it was independently associated with *Chlamydia pneumoniae*, *Mycoplasma pneum*oniae and parainfluenza viruses with adjusted risk ratios of 4.01 (1.03-15.64), 4.17 (1.42-12.27) and 2.13 (1.03-4.55), respectively. There was a consistent increased risk of severe disease with *B. pertussis*. Patterns indicated even higher risks when *B. pertussis* was co-detected with any of the three organisms although not statistically significant. Improving vaccine coverage against B. pertussis would impact not only the incidence of pertussis but also that of severe LRTI generally.

WEB: 10.1038/s41598-020-73462-w

IMPACT FACTOR: 3.998

CITED HALF-LIFE: 3.1

START COMMENTARY

Muloiwa *et al.* conducted a prospective cohort study with children hospitalized with cough and WHO defined age specific tachypnoea, or apnoea to assess *B. pertussis* co-detection in South Africa. Children's vaccination status was determined using the vaccination booklets and most study participants with known vaccination status (N=44, 98%) were up to date with their vaccinations including, 72.1% (n=321) that were up to date with pertussis and *Haemophilus influenzae type b* vaccine doses for age. Further, another 71% (n=312) were up to date with PCV13. About 93% (n=418) had received at least one dose of the combination of pertussis and *Haemophilus influenzae type b* vaccine and about 87% (n=385) had received one dose of PCV13. *B. pertussis* was isolated in 5 (18.5%) of the 27 who did not get any pertussis vaccine dose compared to 26 (6.2%) of the 418

who received at least one vaccine dose, which was significant ($p = 0.032$). Muloiwa *et al.* found *C. pneumoniae, M. pneumoniae and parainfluenza* isolation were independently associated with isolation of *B. pertussis.* This article is impactful as it highlights that receiving one dose of the pertussis vaccine is significantly associated with decreased risk of *B. pertussis*, and potentially an indirect reduction of risk of other pathogens that cause severe lower respiratory tract infections.

5. Identifying Perceived Barriers to Human Papillomavirus Vaccination as a Preventative Strategy for Cervical Cancer in Nigeria.

Nguyen N, Okeke E, Anglemyer A, Brock T.

Ann Glob Health. 2020 Oct 23;86(1):118.

PubMed ID: 32983914

ABSTRACT

BACKGROUND: Cervical cancer deaths are disproportionately higher in developing countries depicting one of the most profound health disparities existing today and is ranked as the second most frequent cancer among women in Nigeria. The Human Papillomavirus (HPV) vaccine as a primary prevention strategy is not widely used in Nigeria. This study investigated perceived barriers to HPV vaccination in a Nigerian community, targeting health workers' perceptions.

METHODS: This descriptive study captured responses from a cross-sectional, convenience sample of adult health workers within Anambra State, Nigeria. An anonymous 42-item survey with multiple validated scales was developed based on the Theory of Planned Behavior model and previous studies. The self-administered survey was distributed by research assistants at study sites within Anambra State which were identified through local constituents by the regional zones Adazi-Ani, Onitsha, and Awka. Data analyses were performed using Microsoft Excel for descriptive statistics and R software for the logistic regression, with a statistical significance level of 5%. Subgroup analysis was performed for the baseline knowledge questionnaire to determine if there were any differences in correct responses based on demographics such as: Institution type, profession, age, sex, religion and parental status.

RESULTS: Responses were collected from 137 Nigerian health workers; 44% nurses, 14% physicians, 6% pharmacists and 31% other health workers. The majority of respondents were female (69%), between 18 and 39 years of age (78%), from urban settings (82%), and identified as having Christian religious beliefs (97%). The most significant barriers identified were lack of awareness (39%), vaccine availability (39%), and cost (13%). When asked baseline knowledge questions regarding HPV, females were more likely to answer incorrectly as compared to males. Significant differences were found for statements: (1) HPV is sexually transmitted (p = 0.008) and (2) HPV is an infection that only affects women (p = 0.004).

CONCLUSIONS: Perceived barriers to HPV vaccination identified by Nigerian health workers include lack of awareness, vaccine availability/accessibility, cost, and concerns about acceptability. Ongoing efforts to subsidize vaccine costs, campaigns to increase awareness of HPV vaccine, and interventions to improve attainability could advance administration rates in Nigeria, and ultimately improve death rates due to cervical cancer in this population.

WEB: 10.5334/aogh.2890
IMPACT FACTOR: 1.192
CITED HALF-LIFE: 4.1

START COMMENTARY

Nguyen *et al*. describe barriers to HPV vaccination identified through self-administered surveys of health workers (n=137) in Anambra State, Nigeria. The study found most perceived barriers among health workers were due to vaccine availability (39%), lack of awareness (39%), and cost (13%). Only 12% of health workers had HPV vaccine available in their clinical setting, however the majority believed the vaccine should be offered. While patient acceptability of vaccine ranked low as a significant barrier, free text comments highlighted some vaccine misconceptions. Initial findings also show that knowledge of HPV infection and transmission may be lower among female health workers as compared to males (correct knowledge of infection: 26% vs. 46%, $p = 0.004$; correct knowledge of transmission: 54% vs. 78%, $p = 0.008$), however further research is needed as the study was not powered to detect differences. An important limitation of the study was its small convenience sample, which was not representative of populations in northern Nigeria (with different religious views) or those who work in federal institutions (where a vaccine may first be widely available). While national plans for largescale vaccination in Nigeria are not yet established, this study can inform vaccine introduction and tailor interventions to decrease key barriers, such as education campaigns (among patients and healthcare professionals) and programs to improve accessibility.

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6. Recent Progress in the Development of Liver Fluke and Blood Fluke Vaccines.

McManus D.

Vaccines (Basel). 2020 Nov 03;8(3).
PubMed ID: 32971734

ABSTRACT

Liver flukes (*Fasciola* spp*., Opisthorchis* spp., *Clonorchis sinensis*) and blood flukes (*Schistosoma* spp.) are parasitic helminths causing neglected tropical diseases that result in substantial morbidity afflicting millions globally. Affecting the world's poorest people, fasciolosis, opisthorchiasis, clonorchiasis and schistosomiasis cause severe disability; hinder growth, productivity and cognitive development; and can end in death. Children are often disproportionately affected. *F. hepatica* and *F. gigantica* are also the most important trematode flukes parasitising ruminants and cause substantial economic losses annually. Mass drug administration (MDA) programs for the control of these liver and blood fluke infections are in place in several countries but treatment coverage is often low, re-infection rates are high and drug compliance and effectiveness can vary. Furthermore, the spectre of drug resistance is ever-present, so MDA is not effective or sustainable long term. Vaccination would provide an invaluable tool to achieve lasting control leading to elimination. This review summarises the status currently of vaccine development, identifies some of the major scientific targets for progression and briefly discusses future innovations that may provide effective protective immunity against these helminth parasites and the diseases they cause.

WEB: 10.3390/vaccines8030553
IMPACT FACTOR: 4.086
CITED HALF-LIFE: 3.4

START COMMENTARY

In this article, McManus reviews the state of research for liver fluke (*Fasciola spp., Opisthorchis spp., Clonorchis sinensis)* and blood flukes (*Schistosoma spp.*) which is highly relevant for millions living in low- and lower-middle income countries (LMICs). Vaccines are urgently needed for liver and blood flukes given the high burden of disease, low treatment coverage of mass drug administration programs, and high re-infection rates. The author provides updates on each liver and blood fluke, concluding that despite advances on several fronts (e.g., genomics, proteomics, vaccinomics, etc.), identifying novel targets for disease prevention efforts, the complicated immunology and limited funding and effort in this area have been obstacles to successful vaccine development.

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7. Operability, Usefulness, and Task-Technology Fit of an mHealth App for Delivering Primary Health Care Services by Community Health Workers in Underserved Areas of Pakistan and Afghanistan: Qualitative Study.

Zaidi S, Kazi A, Riaz A, Ali A, Najmi R, Jabeen R, *et al*.

J Med Internet Res. 2020 Oct 20;22(9):e18414.

PubMed ID: 32940612

ABSTRACT

BACKGROUND: The recent proliferation of digital health technology in low- and middle-income countries has made it possible for community health workers (CHWs) to use mobile health (mHealth) to perform tasks such as data collection and training. Although most studies focus on the prospect of digital apps to motivate and connect CHW, only a few have captured end-user experiences with mobile-based apps. We examined the experience of frontline health workers with a move towards digitalized real-time data to record maternal and childcare services in remote areas of Afghanistan and Pakistan.

OBJECTIVE: Our study aimed to explore CHW perceptions on the operability of the mHealth app in a community setting, usefulness of the app in the delivery of assigned maternal and childcare functions, and the task-technology fit with monitoring information systems.

METHODS: The Hayat app, designed to digitalize and facilitate electronic record keeping, was evaluated to be embedded into mainstream health systems. The app had 2 components: smartphone app for data entry and web dashboard for visualization of the maternal, newborn, and child health reports. Using a qualitative exploratory study design, we conducted a total of 8 focus group discussions with purposively selected lady health workers (LHWs) and CHWs in 3 districts of Pakistan and 3 hamlets of Afghanistan, respectively. Focus group discussions were conducted in the local language, audio recorded, and converted into expanded notes for thematic analysis.

RESULTS: Although a majority of LHWs used the app with ease, some initially faced difficulties in operating it and requested a longer duration of training. Contrary to LHWs, the CHWs were able to use the app without difficulty, as they were using it only to register clients. Overall, use of the mHealth app in both countries resulted in a positive impact on health education sessions, easier communication with parents or clients, tracking of routine immunization defaulters and follow-ups, improved data validity, easily accessible vaccination schedules, and faster registration. In addition to building up their image in the community and personal development, the improved reporting and monitoring mechanisms also set the stage for the LHWs to get recognized for their hard work. CHWs in Afghanistan also reported the app provided immediate access to information when requested by their supervisor. Although the Hayat app eliminates the need to carry multiple registers and helps in

recalling client information at the touch of a button, technical issues around connectivity and data inputting tabs were highlighted by the participants.

CONCLUSIONS: The digitization of records not only provided CHWs support in their daily routine but also strengthened monitoring mechanisms and improved motivation. We recommend conducting end user experience studies before embedding apps into mainstream health systems as high acceptability does not always result in high uptake of digital technology.

WEB: 10.2196/18414
IMPACT FACTOR: 5.034
CITED HALF-LIFE: 4.8

START COMMENTARY

In this qualitative study, Zaidi *et al.* explore community health worker (CHW) and lady health worker (LHW) perceptions of a mobile health application, the Hayat app. This article is impactful as it provides reflections from frontline workers that administer routine immunizations in Pakistan and Afghanistan and who would serve as the end users for this application in communities. This is particularly relevant for vaccination given the reliance on CHWs and LHWs for polio campaigns in the two countries. The authors explored three key outcomes in qualitative interviews: 1) Operability, defined as the perceptions and barriers (i.e. ease of use, technical competency, and accessibility); 2) Usefulness, defined as the perceived satisfaction of users (including results and consequences); and 3) Task-technology fit, defined as the ability of the app to facilitate the required tasks of end users and how the technology interacts with the management system interface. Key findings included that LHWs noted that the digitization made vaccination procedures easier as it allowed them to enter data into one mobile device, rather than multiple registers. LHWs reported that the app told them which children were defaulters with a specific color and presented the vaccination schedule, allowing them to refer parents to health facilities when required. However, healthcare workers highlighted some concerns about the application, as the lack of certain features that they would typically find in their registers (e.g. total population, number of kids, death/birth records) and limited options for outcomes, indicating that this technology could be improved further to meet the needs of CHWs and LHWs. A key strength of this study is the inclusion of end users, who are critical for the successful integration of technology into existing programs in LMICs.

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8. Spatial access inequities and childhood immunisation uptake in Kenya.

Joseph N, Macharia P, Ouma P, Mumo J, Jalang'o R, Wagacha P, *et al*.

BMC Public Health. 2020 Oct 01;20(1):1407.
PubMed ID: 32933501

ABSTRACT

BACKGROUND: Poor access to immunisation services remains a major barrier to achieving equity and expanding vaccination coverage in many sub-Saharan African countries. In Kenya, the extent to which spatial access affects immunisation coverage is not well understood. The aim of this study was to quantify spatial accessibility to immunising health facilities and determine its influence on immunisation uptake in Kenya while controlling for potential confounders.

METHODS: Spatial databases of immunising facilities, road network, land use and elevation were used within a cost friction algorithim to estimate the travel time to immunising health facilities. Two travel scenarios were evaluated; (1) Walking only and (2) Optimistic scenario combining walking and motorized transport. Mean travel time to health facilities and proportions of the total population living within 1-h to the nearest immunising health facility were computed. Data from a nationally representative cross-sectional survey (KDHS 2014), was used to estimate the effect of mean travel time at survey cluster units for both fully immunised status and third dose of diphtheria-tetanus-pertussis (DPT3) vaccine using multi-level logistic regression models.

RESULTS: Nationally, the mean travel time to immunising health facilities was 63 and 40 min using the walking and the optimistic travel scenarios respectively. Seventy five percent of the total population were within one-hour of walking to an immunising health facility while 93% were within one-hour considering the optimistic scenario. There were substantial variations across the country with 62%(29/47) and 34%(16/47) of the counties with < 90% of the population within one-hour from an immunising health facility using scenarios 1 and 2 respectively. Travel times > 1-h were significantly associated with low immunisation coverage in the univariate analysis for both fully immunised status and DPT3 vaccine. Children living more than 2-h were significantly less likely to be fully immunised [AOR:0.56(0.33-0.94) and receive DPT3 [AOR:0.51(0.21-0.92) after controlling for household wealth, mother's highest education level, parity and urban/rural residence.

CONCLUSION: Travel time to immunising health facilities is a barrier to uptake of childhood vaccines in regions with suboptimal accessibility (> 2-h). Strategies that address access barriers in the hardest to reach communities are needed to enhance equitable access to immunisation services in Kenya.

WEB: 10.1186/s12889-020-09486-8
IMPACT FACTOR: 2.521
CITED HALF-LIFE: 6.0

START COMMENTARY

In this geospatial analysis, Joseph *et al.* determine travel time to 6,135 public and private immunizing health facilities in Kenya in both a walking only and walking + motorized transport (optimistic) scenario. The authors constructed a population distribution map using asymmetric spatial modelling techniques, with weights of population density used in a random forest technique adjusting for rural-urban differences to obtain population at 100m square grids. To extract travel times, geographical coordinates for sampled clusters in the Kenya Demographic Health Survey 2014 (KDHS 2014) were used. The proportion of the population within one hour to an immunization facility was 75% in the walking only scenario and 93% in the optimistic scenario; however there was high heterogeneity at the county level, with ranges from 21%-100% and 38%-100% in each scenario, respectively. Children living in regions with a mean travel time less than one hour had significantly higher immunization coverage for both DPT3 (91%) and fully immunized status (78%) compared to those who lived greater than one hour from the immunizing health facility with coverage of 82% and 60% respectively (p value< 0.001). Limitations of the study include potential recall bias of immunization status due to respondent-based reporting and that travel time did not account for seasonality nor traffic delays due to lack of data availability. This analysis demonstrates substantial inequities that persist in spatial access to vaccination in Kenya and provides a basis for better-informed resource allocation to mitigate inequalities and reach marginalized populations. Governments and implementing agencies can use such spatial access outputs to enhance new WHO and Gavi targets that focus on addressing immunization equity.

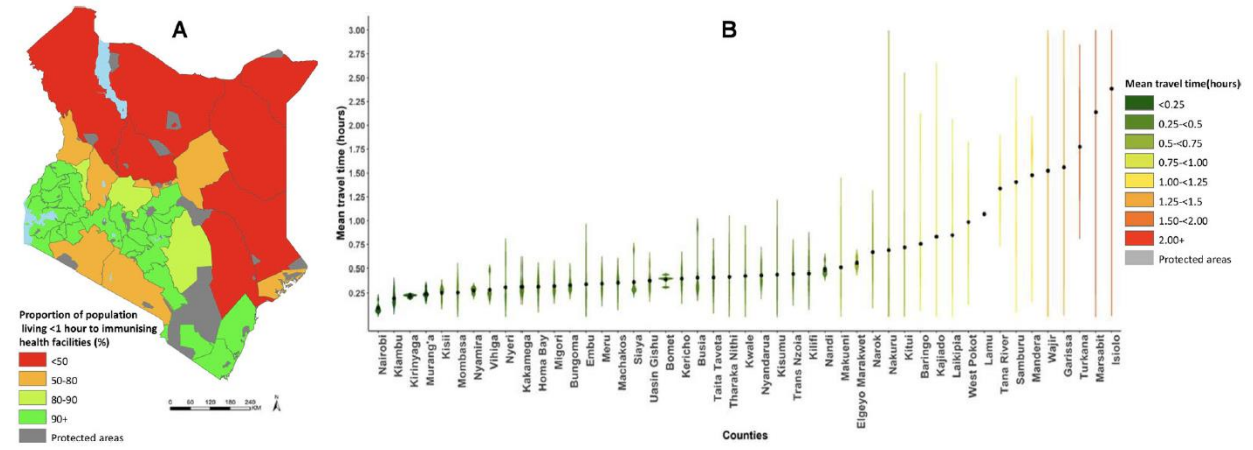

Figure Map of proportion of population within one-hour to immunizing health facilities and distribution of time based on optimistic travel scenario by county. Figure 2 in manuscript.

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9. Routine childhood immunisation during the COVID-19 pandemic in Africa: a benefit-risk analysis of health benefits versus excess risk of SARS-CoV-2 infection.

Abbas K, Procter S, van Zandvoort K, Clark A, Funk S, Mengistu T, *et al*.

Lancet Glob Health. 2020 Oct 02;8(10):e1264-e1272.

PubMed ID: 3268779232979934

ABSTRACT

BACKGROUND: National immunisation programmes globally are at risk of suspension due to the severe health system constraints and physical distancing measures in place to mitigate the ongoing COVID-19 pandemic. We aimed to compare the health benefits of sustaining routine childhood immunisation in Africa with the risk of acquiring severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection through visiting routine vaccination service delivery points.

METHODS: We considered a high-impact scenario and a low-impact scenario to approximate the child deaths that could be caused by immunisation coverage reductions during COVID-19 outbreaks. In the high-impact scenario, we used previously reported country-specific child mortality impact estimates of childhood immunisation for diphtheria, tetanus, pertussis, hepatitis B, Haemophilus influenzae type b, Streptococcus pneumoniae, rotavirus, measles, meningitis A, rubella, and yellow fever to approximate the future deaths averted before 5 years of age by routine childhood vaccination during a 6-month COVID-19 risk period without catch-up campaigns. In the low-impact scenario, we approximated the health benefits of sustaining routine childhood immunisation on only the child deaths averted from measles outbreaks during the COVID-19 risk period. We assumed that contact-reducing interventions flattened the outbreak curve during the COVID-19 risk period, that 60% of the population will have been infected by the end of that period, that children can be infected by either vaccinators or during transport, and that upon child infection the whole household will be infected. Country-specific household age structure estimates and age-dependent infection-fatality rates were applied to calculate the number of deaths attributable to the vaccination clinic visits. We present benefit-risk ratios for routine childhood immunisation, with 95% uncertainty intervals (UIs) from a probabilistic sensitivity analysis.

FINDINGS: In the high-impact scenario, for every one excess COVID-19 death attributable to SARS-CoV-2 infections acquired during routine vaccination clinic visits, 84 (95% UI 14-267) deaths in children could be prevented by sustaining routine childhood immunisation in Africa. The benefit-risk ratio for the vaccinated children is 85 000 (4900-546 000), for their siblings (<20 years) is 75 000 (4400-483 000), for their parents or adult carers (aged 20-60 years) is 769 (148-2700), and for older adults (>60 years) is 96 (14-307). In the low-impact scenario that approximates the health benefits to only the child deaths averted from measles outbreaks, the benefit-risk ratio to the households of

vaccinated children is 3 (0-10); if the risk to only the vaccinated children is considered, the benefit-risk ratio is 3000 (182-21 000).

INTERPRETATION: The deaths prevented by sustaining routine childhood immunisation in Africa outweigh the excess risk of COVID-19 deaths associated with vaccination clinic visits, especially for the vaccinated children. Routine childhood immunisation should be sustained in Africa as much as possible, while considering other factors such as logistical constraints, staff shortages, and reallocation of resources during the COVID-19 pandemic.

FUNDING: Gavi, the Vaccine Alliance; Bill & Melinda Gates Foundation.

WEB: 10.1016/S2214-109X(20)30308-9
IMPACT FACTOR: 5.034
CITED HALF-LIFE: 4.8

START COMMENTARY

Abbas *et al*. report this is the first benefit–risk analysis examining sustaining routine childhood immunization in African countries during the COVID-19 pandemic. The study looked at high and low impact scenarios of a 6-month disruption to immunization and tracked health benefits of children and contacts. The high impact scenario accounted for vaccine averted deaths of children up to five years of age with no catch-up campaign conducted at the end of the SARS-CoV-2 outbreak, whereas the low impact scenario accounted only for measles vaccine averted deaths (assuming herd immunity protection for all other vaccine preventable diseases) and catch-up campaigns immediately following the 6-month disruption. Routine immunization in the high impact scenario prevented 702,000 child deaths (95% Uncertainty Interval [UI] 635 000–782 000), with about two-thirds of deaths attributable to measles and pertussis alone and led to 8,300 (95% UI 1,300–25,000) excess deaths attributable to additional SARS-CoV-2. In addition to overall household and age benefit–risk ratios, the authors provide these broken down by country. These household benefit-risk ratios ranged from 34 (95% UI 4–124) in Morocco to 180 (95% UI 28–598) in Angola in the high-impact scenario, and from 0 (95% UI 0–1) in Tunisia to 9 (95% UI 1–29) in the Republic of the Congo in the low-impact scenario . The findings are largely similar across all 54 African countries, with the benefit of routine childhood immunization programs found to be greater than the COVID-19 risk associated with vaccination clinic visits. *Figure 3* shows a sensitivity analysis for uncertainty in the benefit–risk ratio estimates, which are largely due to variation in the estimated number of contacts and infection fatality rate for older adults. However, even at upper bounds of these fatality rates, sustaining routine childhood vaccination is beneficial. These findings reinforce current global guidance to sustain routine immunization services where operationally safe and feasible.

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10. Global Impact of Rotavirus Vaccination on Diarrhea Hospitalizations and Deaths Among Children <5 Years Old: 2006-2019.

Burnett E, Parashar U, Tate J.

J Infect Dis. 2020 Oct 14;222(10):1731-1739.

PubMed ID: 32095831

ABSTRACT

BACKGROUND: Since 2006, more than 100 countries have introduced rotavirus vaccine into their immunization programs. We reviewed published data on relative reductions of rotavirus hospitalizations, acute gastroenteritis (AGE) hospitalizations, and AGE deaths among children <5 years old.

METHODS: Articles published from January 1, 2006 to December 31, 2019 with at least 12 months of data before and after rotavirus vaccine introduction were included. Relative reductions were abstracted into a standardized form. Descriptive statistics are presented as medians and interquartile ranges (IQRs).

RESULTS: We reviewed 1827 total records and included 105 articles from 49 countries. Among children <5 years old, there was a median reduction of 59% (IQR, 46-74) in rotavirus hospitalizations, 36% (IQR, 23-47) in AGE hospitalizations, and 36% (IQR, 28-46) AGE mortality. Reductions were larger in countries with low child mortality, among younger age groups, and in countries with higher coverage. The median percentage of specimens that tested positive for rotavirus among children <5 years old hospitalized for diarrhea was 40% (IQR, 28-45) before rotavirus vaccine introduction and 20% (IQR, 20-20) 4 years after introduction.

CONCLUSIONS: Overall, we found sustained impact on rotavirus and AGE hospitalizations and deaths. These results should encourage countries still considering rotavirus vaccine implementation.

WEB: 10.1093/infdis/jiaa081
IMPACT FACTOR: 5.022
CITED HALF-LIFE: 9.8

START COMMENTARY

In this literature review, Burnett *et al.* present ecological impacts of rotavirus vaccines on rotavirus hospitalizations, all-cause acute gastroenteritis (AGE) hospitalizations, and AGE deaths of <5-year-old children across 105 articles and 49 countries that have implemented rotavirus vaccine. This article is impactful as it presents evidence to support the development of routine rotavirus vaccination programs and for those programs to aim to achieve high coverage to see the most

significant declines in hospitalizations and deaths. Nearly all included observations (90%) were from countries with universal rotavirus introduction, whereas two observations (2%) were from countries in demonstration and 11 other observations (9%) took place where rotavirus could be purchased privately. Studies were categorized based on child mortality, with 52% of observations from countries in low child mortality strata, 16% from the medium child mortality strata and 33% from high child mortality strata. Burnett *et al.* present the overall reductions in rotavirus and AGE hospitalization and AGE mortality by mortality strata (*Figure 3-4*), annul percentage positive for rotavirus by age group (*Figure 5*), reductions by year and age group (*Figure 6),* and rate reduction by coverage (*Supplementary Figure 2A-2B*). Key strengths of this study are the inclusion of a sensitivity analysis, and analysis comparing outcomes across varied child mortality strata, age groups, and coverage.

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Appendix

The literature search for the November 2020 Vaccine Delivery Research Digest was conducted on October 26,2020. We searched English language articles indexed by the US National Library of Medicine and published between September 15, 2020 and October 14, 2020. The search resulted in 343 items.

SEARCH TERMS

(((((vaccine[tiab] OR vaccines[tiab] OR vaccination[tiab] OR immunization[tiab] OR immunisation[tiab] OR vaccine[mesh] OR immunization[mesh]) AND (logistics[tiab] OR supply[tiab] OR “supply chain”[tiab] OR implementation[tiab] OR expenditures[tiab] OR financing[tiab] OR economics[tiab] OR “Cost effectiveness”[tiab] OR coverage[tiab] OR attitudes[tiab] OR belief[tiab] OR beliefs[tiab] OR refusal[tiab] OR “Procurement”[tiab] OR timeliness[tiab] OR systems[tiab])) OR (“vaccine delivery”[tiab])) NOT (“in vitro”[tiab] OR “immune response”[tiab] OR gene[tiab] OR chemistry[tiab] OR genotox*[tiab] OR sequencing[tiab] OR nanoparticle*[tiab] OR bacteriophage[tiab] OR exome[tiab] OR exogenous[tiab] OR electropor*[tiab] OR “systems biology”[tiab] OR “animal model”[tiab] OR cattle[tiab] OR sheep[tiab] OR goat[tiab] OR rat[tiab] OR pig[tiab] OR mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR rodent[tiab] OR fish[tiab])) AND (English[LA]) (“2020/9/15”[PDAT] : “2020/10/14”[PDAT]))