VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

PRODUCED BY: ARAKAKI L, BABIGUMIRA JB

FEBRUARY 2020

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1. [Quantifying the success of measles vaccination campaigns in the Rohingya refugee camps.](#)

Chin T, Buckee C, Mahmud A.
Epidemics. 2020 Jan 21;30:100385.
PubMed ID: 31951876

ABSTRACT

In the wake of the Rohingya population's mass migration from Myanmar, one of the world's largest refugee settlements was constructed in Cox's Bazar, Bangladesh to accommodate nearly 900,000 new refugees. Refugee populations are particularly vulnerable to infectious disease outbreaks due to many population and environmental factors. A large measles outbreak, with over 1700 cases, occurred among the Rohingya population between September and November 2017. Here, we estimate key epidemiological parameters and use a dynamic mathematical model of measles transmission to evaluate the effectiveness of the reactive vaccination campaigns in the refugee camps. We also estimate the potential for subsequent outbreaks under different vaccination coverage scenarios. Our modeling results highlight the success of the vaccination campaigns in rapidly curbing transmission and emphasize the public health importance of maintaining high levels of vaccination in this population, where high birth rates and historically low vaccination coverage rates create suitable conditions for future measles outbreaks.

START COMMENTARY

Chin et al. conducted a study to assess the impact of the measles and rubella vaccination campaign following a measles outbreak in the Cox Bazar refugee settlement in 2017 and the potential for another outbreak. Authors used the serial interval distribution and incident cases to estimate the effective reproductive number at time *t,* an approach developed by Wallinga and Teunis (2004). Parameters summarized in Table 1 and case and effective reproductive number data depicted in Figure 2 were used to inform an SIR model to estimate the number of measles cases with and

without vaccination. The authors estimated that about 77,000 cases were averted due to the vaccination campaign (Figure 3) and an additional 4,000 to 19,000 cases over the next two years. Limitations of the study include the potential for biased effective reproductive numbers due to the potential of other interventions during the measles outbreak and the assumption of a constant serial interval distribution, potential bias in number of cases by assuming all confirmed and suspected cases were measles cases early in the outbreak, not factoring in maternal immunity, and the lack of generalizability to other populations. Authors also did not include age-dependent heterogeneities in the model due to the lack of age data. Despite these limitations, Chin et al. provided valuable information on measles dynamics among the Rohinga refugees that could inform public health interventions to prevent future outbreaks.

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2. The impact of vaccination on gender equity: conceptual framework and human papillomavirus (HPV) vaccine case study.

Portnoy A, Clark S, Ozawa S, Jit M.

ABSTRACT

BACKGROUND:

Although the beneficial effects of vaccines on equity by socioeconomic status and geography are increasingly well-documented, little has been done to extend these analyses to examine the linkage between vaccination and gender equity. In this paper, evidence from the published literature is used to develop a conceptual framework demonstrating the potential impact of vaccination on measures of gender equity. This framework is then applied to human papillomavirus (HPV) vaccination in three countries with different economic and disease burden profiles to establish a proof of concept in a variety of contexts.

METHODS:

We conducted a literature review examining evidence on the linkage between health outcomes and dimensions of gender equity. We utilized the Papillomavirus Rapid Interface for Modelling and Economics (PRIME) model to estimate cervical cancer incidence and deaths due to HPV types 16/18 by age in each country. We estimated labor force participation and fertility effects from improvements in health, and converted these into inputs consistent with those used to calculate the United Nations Gender Inequality Index to assess gender equity.

RESULTS:

In our case study, we found that HPV vaccination among girls could help narrow socioeconomic gender disparities by quantifying the main pathways by which HPV vaccination improves health, which enables improvement in gender equity indicators such as labor force participation and maternal mortality ratios. While these improvements are small when averaged over the entire population, the components measured - labor force participation and maternal mortality ratio - account for 50% of the index scores.

CONCLUSIONS:

This proof of concept model is a starting point to inform future health and economic analyses that might incorporate the impact of gender equity as an additional impact of vaccination in improving the health and well-being of the population.

START COMMENTARY

Portnoy et al. conducted a proof-of-concept study to explore the association between vaccination and United Nations Gender Inequality Index (GII) Scores. The Gender Inequality Index is comprised of measures of reproductive health, empowerment, and economic status. Figure 1 displays the conceptual framework the authors developed through their literature review, using the human papillomavirus (HPV) vaccine as a case study. They found HPV vaccination associated with higher GII scores, though small, when compared to no HPV vaccination. Furthermore, they found that labor force participation and maternal mortality ratio accounted for 50% of the GII score. A couple notable limitations included the reliance on literature, which was scarce, and the inability to make causal inference on the relationship between vaccination and GII score.

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3. The effectiveness of influenza vaccination in pregnancy in relation to child health outcomes: Systematic review and meta-analysis.

Jarvis J, Dorey R, Warricker F, Alwan N, Jones C.

ABSTRACT

OBJECTIVES:

To determine the effectiveness of influenza vaccination during pregnancy on child health outcomes.

DESIGN:

Systematic review/meta-analysis.

DATA SOURCES:

Clinical Trials.gov, Cochrane Library, EMBASE, Medline, Medline in process, PubMed and Web of Science, from 1st January 1996 to 29th June 2018. An updated Medline search was performed 30th June 2018 to 31st October 2019.

METHODS:

Randomised controlled trials (RCTs) and observational studies reporting health outcomes of infants and children born to women who received inactivated influenza vaccine during pregnancy. The primary outcome was infant laboratory confirmed influenza (LCI). Secondary outcomes included influenza-like illness (ILI), other respiratory illnesses, primary care, clinic visit or hospitalisations due to influenza illness and long-term respiratory childhood outcomes.

RESULTS:

19 studies were included; 15 observational studies and 4 primary RCTs with an additional 3 papers reporting secondary outcomes of these RCTs. In a random effects meta-analysis of 2 RCTs including 5742 participants, maternal influenza vaccination was associated with an overall reduction of LCI in infants of 34% (95% confidence interval 15-50%). However, there was no effect of maternal influenza vaccination on ILI in infants ≤6 months old. Two RCTs were excluded from the meta-analysis for the outcome of LCI in infants (different controls used). Both of these studies showed a protective effect for infants from LCI, with a vaccine efficacy of up to 70%. Overall observational studies showed an inverse (protective) association between maternal influenza vaccination and infant LCI, hospitalisation and clinic visits due to LCI or ILI in infants and other respiratory illness in infants ≤6 months old.

CONCLUSIONS:

This systematic review supports maternal influenza vaccination as a strategy to reduce LCI and influenza-related hospitalisations in young infants. Communicating these benefits to pregnant women may support their decision to accept influenza vaccination in pregnancy and increase vaccine coverage in pregnant women.

REGISTRATION:

PROSPERO CRD42018102776.

START COMMENTARY

Jarvis et al. conducted a systematic review and meta-analysis of the impact of maternal influenza vaccination on infant laboratory confirmed influenza (LCI) and other child health outcomes. This review was an update and expansion of a previous review by Nunes and Madhi published in 2018. Results, summarized in a forest plot in Figure 3, show a protective association between maternal immunization and infant LCI. Authors noted particular challenges when comparing studies because of heterogeneous study outcomes, diagnostic tests, and influenza-like illness definitions. They also highlighted that most studies lacked vaccine composition and circulating virus distribution data, preventing an analysis of the impact of mismatched influenza vaccine and circulating viruses. Jarvis et al. astutely commented on the need to better understand the complexity of gestational timing of maternal influenza vaccination that accounts for optimal antibody transfer, waning infant immunity, and local influenza seasonality. This review provides further evidence to support maternal influenza vaccination, but also raises important questions about the optimization of against influenza for infants.

4. Factors affecting HBV vaccination in a Medical training College in Kenya: A mixed methods Study.

Maina A, Bii L.

ABSTRACT

BACKGROUND:

Hepatitis B Virus (HBV) is highly endemic in Sub-Saharan Africa with 70 to 90% of the population becoming infected before the age of 40 years. Healthcare workers (HCWs) including healthcare students (HCSs) are at an increased risk of contracting HBV due to occupational exposure. HCSs are especially at a high risk because of their inexperience with infection control procedures and insufficient knowledge about the level of risk when dealing with patients. Despite the availability of an effective vaccine, and its recommendation by Kenya's Ministry of Health, few HCW and students are vaccinated. The aim of this study was to evaluate the influence of awareness, attitude, practices, and access factors on hepatitis B vaccination uptake by HCSs at Kenya Medical Training College (KMTC).

METHODS:

This was a concurrent mixed methods study. For the quantitative arm, a structured questionnaire was used to assess the awareness, knowledge, attitudes and practices towards HBV disease and vaccination. Accessibility of the HBV vaccine in the participating campuses was also assessed. Two FGDs were carried out: one comprised of student representatives of the participating campuses while the second comprised of members of staff. Quantitative data was analysed using STATA (version 15) while NVIVO (version 11) was used for qualitative data.

RESULTS:

Out of 634 students invited to participate in the study, 487 participated (response rate 76.8%). Majority of the respondents were from Nairobi Campus (44.2%) and from the Department of Nursing (31.2%). HBV vaccine uptake rate was 85.8% while the non-vaccination rate was 14.3%. Full vaccination was reported by only 20.2% of respondents. The major reason for not receiving the recommended doses was the unavailability of the vaccine when students went for it. The qualitative study revealed challenges in the implementation of the vaccination program at KMTC.

CONCLUSIONS:

Full vaccination rates remained low despite good knowledge of HBV infection and positive attitude towards vaccination. There is therefore need to streamline vaccination programs in medical colleges to ensure availability and accessibility of the vaccine to healthcare students.

START COMMENTARY

Maina et al. conducted a mixed methods study to assess knowledge, attitude, and practices around hepatitis B virus (HBV) among Kenya Medical Training College (KMTC) healthcare students. They found that most students had good knowledge of and positive attitudes towards HBV and were at least partially vaccinated; however, results demonstrated room for improvement. For example, only 59.5% of respondents knew that HBV can cause liver cancer. The study also highlights the role that KMTC plays in providing information about vaccines to its students, with 86% of students reporting course work and KMTC management as important sources of information about vaccines and immunizations (Figure 2). Furthermore, a majority of students expressed preference of receiving HBV vaccine on campus. Since this study was conducted only on campuses with vaccination programs, it is unclear whether these results reflect the larger student population attending campuses without vaccination programs. It is also unclear whether the results will remain the same, given the discontinuation of the vaccination programs in late 2017, after this study was conducted. Authors noted limitations of their study were the reliance of self-report to ascertain student vaccination status and the small number of focus group discussions.

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5. [A cost-effectiveness analysis of traditional and geographic information system-supported microplanning approaches for routine immunization program management in northern Nigeria.](#)

Ali D, Levin A, Abdulkarim M, Tijjani U, Ahmed B, Namalam F, et al.

ABSTRACT

Effective RI microplanning requires accurate population estimates and maps showing health facilities and locations of villages and target populations. Traditional microplanning relies on census figures to project target populations and on community estimates of distances, while GIS microplanning uses satellite imagery to estimate target populations and spatial analyses to estimate distances. This paper estimates the cost-effectiveness of geographical information systems (GIS)-based microplanning for routine immunization (RI) programming in two states in northern Nigeria. For our cost-effectiveness analysis, we captured the cost of all inputs for both approaches to capture the incremental cost of GIS over traditional microplanning and present the incremental cost-effectiveness ratios for each vaccine-preventable illness, death, and disability-adjusted life year (DALY) averted. We considered two scenarios for estimating vaccine requirements for each microplanning approach, one based on administrative vaccination coverage rates and one based on National Nutrition and Health Survey rates. With the administrative rates, GIS microplanning projected approximately 194,000 and 157,000 more required vaccinations than traditional microplanning in Bauchi and Sokoto States; with the survey rates, the additional number of vaccinations required was nearly 113,000 in Bauchi and about 47,000 in Sokoto. For each state under each scenario, we present numbers of and costs per measles and pertussis cases, deaths, and DALYs averted by the additional vaccinations, as well as annual costs. As expected, GIS-based microplanning incurs higher costs than traditional microplanning, due mainly to the additional vaccinations required for populations previously unreached. Our estimates of cost per DALY averted suggest, however, that GIS microplanning is more cost-effective than traditional microplanning in both states under both coverage scenarios and that the higher costs incurred by GIS microplanning are worth adopting.

START COMMENTARY

Ali et al. conducted a study to compare traditional and geographic information system (GIS) methods for routine immunization microplanning in six local government areas (LGAs) in two states of Nigeria. Overall, authors found GIS microplanning resulted in a larger target population compared to traditional microplanning, though one LGA (Itas in Bauchi) had a smaller target population (Table 2). Additional vaccines to cover the larger target population was the primary driver of costs. The main study limitation authors identified was uncertainty around some parameter estimates including vaccine coverage, vaccine effectiveness, and costs. Authors also touched on benefits of GIS microplanning beyond those estimated through this analysis including capacity building, primary health center planning, greater equity, and application to other public health programs.

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6. Exploring Factors Influencing Immunization Utilization in Nigeria-A Mixed Methods Study.

Akwataghibe N, Ogunsola E, Broerse J, Popoola O, Agbo A, Dieleman M.

ABSTRACT

BACKGROUND:

In 2005, Nigeria adopted the Reach Every Ward strategy to improve vaccination coverage for children, 0-23 months. By 2015, Ogun state had full coverage in 12 of its 20 local government areas but eight had pockets of unimmunized children, with the highest burden (37%) in Remo-North. This study aimed to identify factors in Remo-North influencing the use of immunization services, in order to inform intervention approaches to tackle barriers to immunization utilization.

METHODS:

We carried out a cross-sectional study using mixed methods including a survey of caregivers of 215 children, 25 semi-structured interviews with stakeholders involved in immunization service delivery and 16 focus group discussions with community men and women (n = 98). Two wards (Ilara and Ipara) were purposively chosen for the study. Data was analyzed using the SAGE Working Group Vaccine Hesitancy model.

RESULTS:

Only 56 children (32.6%) of the 172 children over 9 months of age had immunization cards available for inspection. Of these, 23 (59.6%) were fully immunized, noticeably higher in Ipara than Ilara. However, when immunization status was assessed by card and recall, 84.9% of the children were assessed as fully immunized. Caregivers in the more rural Ilara had less knowledge of vaccine schedules. The importance of all doses was recognized more by Ipara respondents (95.5%) than in Ilara (75.3%) (p < 0.05). Community links to immunization and household decision-making patterns influenced immunization use in both wards. Migrants and those living in hard-to-reach areas were disadvantaged in both wards. Health service factors like absence of delivery services, shortage of health workers, unavailability of vaccines at scheduled times, and indirect costs of immunization contributed to low utilization.

CONCLUSION:

Immunization utilization was influenced by interlinked community and health services issues. Intervention approaches should ensure that communities' priorities are addressed, actors at both levels involved and strategies are adjusted to suit contexts.

START COMMENTARY

Akwataghibe et al. conducted a cross-sectional mixed methods study to identify factors associated with vaccination utilization in Remo-North, Nigeria. Authors adopted a systems approach to their study. Results were organized into three main areas of the SAGE Vaccine Hesitancy model: contextual influences, individual and group influences, and vaccine and vaccination specific issues (Figure 1). Limitations of the study included a small sample size, recall bias, social desirability bias, and lack of precision on immunization coverage estimates (since surveys covered children under 5 years versus 11-23 months).

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7. Potential health impact and cost-effectiveness of bivalent human papillomavirus (HPV) vaccination in Afghanistan.

Anwari P, Debellut F, Vodicka E, Clark A, Farewar F, Zhwak Z, et al.

ABSTRACT

BACKGROUND:

Human papillomavirus (HPV) vaccination has not been introduced in many countries in South-Central Asia, including Afghanistan, despite the sub-region having the highest incidence rate of cervical cancer in Asia. This study estimates the potential health impact and cost-effectiveness of HPV vaccination in Afghanistan to inform national decision-making.

METHODS:

An Excel-based static cohort model was used to estimate the lifetime costs and health outcomes of vaccinating a single cohort of 9-year-old girls in the year 2018 with the bivalent HPV vaccine, compared to no vaccination. We also explored a scenario with a catch-up campaign for girls aged 10-14 years. Input parameters were based on local sources, published literature, or assumptions when no data was available. The primary outcome measure was the discounted cost per disability-adjusted life-year (DALY) averted, evaluated from both government and societal perspectives.

RESULTS:

Vaccinating a single cohort of 9-year-old girls against HPV in Afghanistan could avert 1718 cervical cancer cases, 125 hospitalizations, and 1612 deaths over the lifetime of the cohort. The incremental cost-effectiveness ratio was US$426 per DALY averted from the government perspective and US$400 per DALY averted from the societal perspective. The estimated annual cost of the HPV vaccination program (US$3,343,311) represents approximately 3.53% of the country's total immunization budget for 2018 or 0.13% of total health expenditures.

CONCLUSIONS:

In Afghanistan, HPV vaccine introduction targeting a single cohort is potentially cost-effective (0.7 times the GDP per capita of $586) from both the government and societal perspective with additional health benefits generated by a catch-up campaign, depending on the government's willingness to pay for the projected health outcomes.

START COMMENTARY

To inform national decision-making in a country where no national cervical cancer screening program exists, Anwari et al. conducted a modelling study to assess the impact and cost-effectiveness of human papillomavirus (HPV) vaccination in Afghanistan. Authors used the static cohort model, UNIVAC, and disease burden estimates from GLOBOCAN to model several scenarios, including those accounting for uncertainty and variation in vaccination coverage, vaccine price, and healthcare utilization. Tables 1–3 and 6 outline model parameters and tables 4 and 5 summarize the impact and costs of HPV vaccination. In sensitivity analyses, authors found the main drivers of the results were vaccine price and incremental health system costs. Authors concluded that implementation of HPV vaccination would be cost-effective depending on government willingness-to-pay threshold. There were several limitations to this study including the inability to account for other preventive interventions, using GLOBOCAN estimates as a proxy for disease burden data, lack of data on health-seeking behavior among cervical cancer patients, and making assumptions for a vaccination strategy not included in the current national immunization schedule. Despite these limitations, Anwari et al. provided important information to consider as Afghanistan sets prioritizes and makes national healthcare decisions.

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8. Comparing alternative cholera vaccination strategies in Maela refugee camp: using a transmission model in public health practice.

Havumaki J, Meza R, Phares C, Date K, Eisenberg M.

ABSTRACT

BACKGROUND:

Cholera is a major public health concern in displaced-person camps, which often contend with overcrowding and scarcity of resources. Maela, the largest and longest-standing refugee camp in Thailand, located along the Thai-Burmese border, experienced four cholera outbreaks between 2005 and 2010. In 2013, a cholera vaccine campaign was implemented in the camp. To assist in the evaluation of the campaign and planning for subsequent campaigns, we developed a mathematical model of cholera in Maela.

METHODS:

We formulated a Susceptible-Infectious-Water-Recovered-based transmission model and estimated parameters using incidence data from 2010. We next evaluated the reduction in cases conferred by several immunization strategies, varying timing, effectiveness, and resources (i.e., vaccine availability). After the vaccine campaign, we generated case forecasts for the next year, to inform on-the-ground decision-making regarding whether a booster campaign was needed.

RESULTS:

We found that preexposure vaccination can substantially reduce the risk of cholera even when <50% of the population is given the full two-dose series. Additionally, the preferred number of doses per person should be considered in the context of one vs. two dose effectiveness and vaccine availability. For reactive vaccination, a trade-off between timing and effectiveness was revealed, indicating that it may be beneficial to give one dose to more people rather than two doses to fewer people, given that a two-dose schedule would incur a delay in administration of the second dose. Forecasting using realistic coverage levels predicted that there was no need for a booster campaign in 2014 (consistent with our predictions, there was not a cholera epidemic in 2014).

CONCLUSIONS:

Our analyses suggest that vaccination in conjunction with ongoing water sanitation and hygiene efforts provides an effective strategy for controlling cholera outbreaks in refugee camps. Effective preexposure vaccination depends on timing and effectiveness. If a camp is facing an outbreak, delayed distribution of vaccines can substantially alter the effectiveness of reactive vaccination, suggesting that quick distribution of vaccines may be more important than ensuring every individual

receives both vaccine doses. Overall, this analysis illustrates how mathematical models can be applied in public health practice, to assist in evaluating alternative intervention strategies and inform decision-making.

START COMMENTARY

Havumaki et al. used a susceptible-infectious-water-recovered transmission model to examine various cholera vaccination campaign strategies in Maela. Authors used 2010 cholera incidence data, an identifiability analysis, and 2013 campaign coverage data to estimate model parameters summarized in Tables 1 and 2. Figures 3, 5, and 7 show estimated cumulative cholera cases given different vaccination scenarios, including percentage of one-dose vaccination versus two-dose vaccination, varying one-dose effectiveness values, and timing of vaccination delay. As with any modelling study, the results were limited by the uncertainty of the data used to inform the model. Specifically, 2010 data may not appropriately represent 2013 and 2014 scenarios. Furthermore, results may also be limited by the assumptions made. For example, authors did not account for stochastic dynamics, hyperinfectiousness, or any variation of human-human or human-water transmission by demographic groups. However, there were many strengths of this study including the inclusion of the environmental transmission dynamics, the use of identifiability and sensitivity analyses, and the use of real-world data to inform public health decision-making. Of note, Havumaki et al. highlighted the importance of considering one-dose vaccine effectiveness, availability of vaccines, and timing/logistics of vaccine deployment when planning vaccination campaigns to prevent or respond to outbreaks.

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9. [Using Data to Keep Vaccines Cold in Kenya: Remote Temperature Monitoring with Data Review Teams for Vaccine Management.](#)

Lutukai M, Bunde E, Hatch B, Mohamed Z, Yavari S, Some E, et al.

ABSTRACT

BACKGROUND:

Global vaccination coverage rates have remained around 85% for the past several years. Increasing immunization coverage rates requires an effective cold chain to maintain vaccine potency. Remote temperature monitoring (RTM) technology for vaccine refrigerators has shown promise for improving the ability of supply systems to maintain optimal temperature conditions to ensure potent vaccines reach the end users.

METHODS:

A pilot study of RTM technology and data use teams was implemented in 36 study sites in Kenya. Data were collected at baseline and endline points over a 3-month baseline and 7-month implementation period. Data included 44 qualitative interviews, process logs, meeting minutes from data use team meetings, and quantitative temperature and power data from the RTM devices.

RESULTS:

The ability of cold chain equipment to maintain World Health Organization-recommended temperatures in study sites improved markedly between the baseline and implementation periods, resulting in an improvement in total time spent in the correct range from 83.9% in the baseline period to 90.9% in the intervention period and an improvement in time spent in the too cold range from 6.5% to 1.5%. Friedman tests revealed that differences in time spent in the correct range and time spent in the too cold range during the course of the study were statistically significant (P<.001 and P=.04, respectively). Qualitative and quantitative data suggest that this improvement was due to a combination of improved responsiveness to temperature excursions at the facility level, resulting from SMS alarms for temperature excursion periods, and improved ability at the management level to recognize and address recurring problems.

CONCLUSIONS:

The combination of using RTM technology with a structured data review process by a management team is a promising approach for improving cold chain outcomes. Future research examining the added value of each of the technological and behavioral components separately is needed.

START COMMENTARY

Maintaining the cold chain is paramount to ensuring effective vaccines. Lutukai et al. conducted a nonrandomized pre-/post-assessment of the impact of a remote temperature monitoring (RTM) intervention to improve cold chain practices. The intervention comprised of two components: an RTM data collection system and a structured approach for team data review. Authors found a higher average percentage of time that refrigerators were in the correct temperature range in the intervention period compared to the baseline period. However, whether the intervention can be attributed to the improvements in cold chain practices is limited by the study design. Differences observed between baseline and intervention periods may be a result of secular trends or an already occurring upward trend, as demonstrated by the increasing "correct range" proportion in two of the three baseline period months (Figure 1). Inclusion of comparison sites or a longer baseline period could help address these biases. However, the qualitative findings show promise of the impact of the intervention. A strength of this study is the focus on the behavioral component of implementing a new technology as data that become available through technological advancements are only valuable if integrated into decision-making or informing health practice.

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10. Quantifying risks and interventions that have affected the burden of lower respiratory infections among children younger than 5 years: an analysis for the Global Burden of Disease Study 2017.

ABSTRACT

BACKGROUND:

Despite large reductions in under-5 lower respiratory infection (LRI) mortality in many locations, the pace of progress for LRIs has generally lagged behind that of other childhood infectious diseases. To better inform programmes and policies focused on preventing and treating LRIs, we assessed the contributions and patterns of risk factor attribution, intervention coverage, and sociodemographic development in 195 countries and territories by drawing from the Global Burden of Diseases, Injuries, and Risk Factors Study 2017 (GBD 2017) LRI estimates.

METHODS:

We used four strategies to model LRI burden: the mortality due to LRIs was modelled using vital registration data, demographic surveillance data, and verbal autopsy data in a predictive ensemble modelling tool; the incidence of LRIs was modelled using population representative surveys, health-care utilisation data, and scientific literature in a compartmental meta-regression tool; the attribution of risk factors for LRI mortality was modelled in a counterfactual framework; and trends in LRI mortality were analysed applying changes in exposure to risk factors over time. In GBD, infectious disease mortality, including that due to LRI, is among HIV-negative individuals. We categorised locations based on their burden in 1990 to make comparisons in the changing burden between 1990 and 2017 and evaluate the relative percent change in mortality rate, incidence, and risk factor exposure to explain differences in the health loss associated with LRIs among children younger than 5 years.

FINDINGS:

In 2017, LRIs caused 808 920 deaths (95% uncertainty interval 747 286-873 591) in children younger than 5 years. Since 1990, there has been a substantial decrease in the number of deaths (from 2 337 538 to 808 920 deaths; 65·4% decrease, 61·5-68·5) and in mortality rate (from 362·7 deaths [330·1-392·0] per 100 000 children to 118·9 deaths [109·8-128·3] per 100 000 children; 67·2% decrease, 63·5-70·1). LRI incidence declined globally (32·4% decrease, 27·2-37·5). The

percent change in under-5 mortality rate and incidence has varied across locations. Among the risk factors assessed in this study, those responsible for the greatest decrease in under-5 LRI mortality between 1990 and 2017 were increased coverage of vaccination against Haemophilus influenza type b (11·4% decrease, 0·0-24·5), increased pneumococcal vaccine coverage (6·3% decrease, 6·1-6·3), and reductions in household air pollution (8·4%, 6·8-9·2).

INTERPRETATION:

Our findings show that there have been substantial but uneven declines in LRI mortality among countries between 1990 and 2017. Although improvements in indicators of sociodemographic development could explain some of these trends, changes in exposure to modifiable risk factors are related to the rates of decline in LRI mortality. No single intervention would universally accelerate reductions in health loss associated with LRIs in all settings, but emphasising the most dominant risk factors, particularly in countries with high case fatality, can contribute to the reduction of preventable deaths.

FUNDING:

Bill & Melinda Gates Foundation.

WEB: 10.1016/S1473-3099(19)30410-4
IMPACT FACTOR: 27.516
CITED HALF-LIFE: 6.7

START COMMENTARY

The GBD 2017 Lower Respiratory Infections Collaborators conducted a study to estimate lower respiratory infection (LRI) morbidity and mortality among children under 5 years of age globally and for 195 countries and territories. Authors divided countries into the following categories: high mortality/high incidence, high mortality/low incidence, low mortality/high incidence, and low mortality/low incidence. Figure 1 shows country categorizations in 1990 (Figure 1A) and changes of those categorizations from 1990 to 2017 (Figure 1B). As authors mentioned, LRI mortality has dramatically decreased over time, but to varying degrees on the country level. An examination of the risk factors associated with morbidity and mortality revealed the relationships between these risk factors and changes in LRI mortality are not uniform (Figure 4); however, increased Haemophilus influenza type b and pneumococcal vaccination coverage was positively associated with decreases in LRI burden. The lack of consistent risk factor patterns in Figure 4 highlights the importance of understanding the country-specific context. As with all modelling studies, this study was limited by the quantity and quality of data available to inform models. Authors noted data for some countries, including countries with high LRI burden, were scarce and thus had large uncertainty intervals. Authors also commented that certain healthcare variables that may impact LRI mortality, such as health-seeking behavior and treatment practices, were not directly accounted for in this analysis.

Despite these limitations, this framework allows for comparison of LRI burden across locations and time, and identification of potential areas for intervention.

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Appendix

The literature search for the February 2020 Vaccine Delivery Research Digest was conducted on January 25, 2019. We searched English language articles indexed by the US National Library of Medicine and published between December 15, 2019 and January 14, 2020. The search resulted in 209 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]) ("2019/12/15"[PDAT] : "2020/01/14"[PDAT]))