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VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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   - An assessment of polyvalent formulation of gp120 immunogens to improve antibody responses in rabbits.

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9. **Polio immunity and the impacts of mass immunization campaigns in the Democratic Republic of the Congo**
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- A study to assess polio immunity and recommendations for improving the quality of vaccination campaigns in the DRC.

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    - A study to assess rotavirus vaccination coverage and current burden of disease in Niger.

DETAILS OF ARTICLES

1. Assessing the cost-effectiveness of different measles vaccination strategies for children in the Democratic Republic of Congo
   Doshi RH, Eckhoff P, Cheng A, Hoff NA, Mukadi P, Shidi C, et al.
   Vaccine. 2017 35 (45): 6187-6194. 2017 Sept 28.
   PubMed ID: 28966000

ABSTRACT
One of the goals of the Global Measles and Rubella Strategic Plan is the reduction in global measles mortality, with high measles vaccination coverage as one of its core components. While measles mortality has been reduced more than 79%, the disease remains a major cause of childhood vaccine preventable disease burden globally. Measles immunization requires a two-dose schedule and only countries with strong, stable immunization programs can rely on routine services to deliver the second dose. In the Democratic Republic of Congo (DRC), weak health infrastructure and lack of provision of the second dose of measles vaccine necessitates the use of supplementary immunization activities (SIAs) to administer the second dose. We modeled three vaccination strategies using an age-structured SIR (Susceptible-Infectious-Recovered) model to simulate natural measles dynamics along with the effect of immunization. We compared the cost-effectiveness of two different strategies for the second dose of Measles Containing Vaccine (MCV) to one dose of MCV through routine immunization services over a 15-year time period for a hypothetical birth cohort of 3 million children. Compared to strategy 1 (MCV1 only), strategy 2 (MCV2 by SIA) would prevent a total of 5,808,750 measles cases, 156,836 measles-related deaths and save U.S. $199 million. Compared to strategy 1, strategy 3 (MCV2 by RI) would prevent a total of 13,232,250 measles cases, 166,475 measles-related deaths and save U.S. $408 million. Vaccination recommendations should be tailored to each country, offering a framework where countries can adapt to local epidemiological and economical circumstances in the context of other health priorities. Our results reflect the synergistic effect of two doses of MCV and demonstrate that the most cost-effective approach to measles vaccination in DRC is to incorporate the second dose of MCV in the RI schedule provided that high enough coverage can be achieved.

WEB: 10.1016/j.vaccine.2017.09.038
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START EDITORIAL COMMENT: Although widespread vaccination has led to a reduction of approximately 79% in measles mortality in children under the age of five, more than 95% of measles related deaths occur in resource-limited countries. In Sub-Saharan Africa, specifically the DRC, the national measles-containing vaccine (MCV) coverage is only 71.6%, which is below the WHO recommendation of 95% coverage of the two-dose measles vaccine. The DRC's Expanded Program on Immunization proposed to change the administration of MCVs from supplementary immunization activities (SIAs) to a routine immunization (RI) schedule. This study assesses the cost-effectiveness of the different vaccination strategies in the DRC—MCV1 only (strategy1), MCV2 by SIA (strategy 2), and MCV2 by RI (strategy 3). Cost data specific to the healthcare system in DRC were used in this comparison. Three vaccination strategies were modeled (Figure 1) using an age-structured susceptible-exposed-infectious-recovered (SEIR) model in a population of 3 million children divided into five, age-specific cohorts. Total costs for each vaccination program were modeled (Table 3). Strategy 3 was determined to be the most cost-effective scenario. Limitations of this study were the lack of data for cold chain costs and inability to calculate overall additional disease costs.

2. Determinants of defaulting from completion of child immunization in Laelay Adiabo District, Tigray Region, Northern Ethiopia: A case-control study
   Aregawi HG, Gebrehiwot TG, Abebe YG, Meles KG, Wuneh AD.
   PLoS One. 2017 Sep 27;12(9):e0185533. 2017 Sept 27.
   PubMed ID: 28953970

ABSTRACT
BACKGROUND: Globally 2.5 million children under five years of age die every year due to vaccine preventable diseases. In Tigray Region in Northern Ethiopia, full vaccination coverage in children is low. However, the determinants of defaulting from completion of immunization have not been studied in depth. This study aimed to identify the determinants of defaulting from child immunization completion among children aged 9-23 months in the Laelay Adiabo District, North Ethiopia. METHODS: An unmatched community based case-control study design was conducted among children aged 9-23 months in the Laelay Adiabo District from February-March 2015. A survey was conducted to identify the existence of cases and controls. Two hundred and seventy children aged 9-23 months (90 cases and 180 controls) were recruited from 11 kebeles (the smallest administrative units) by a simple random sampling technique using computer based Open Epi software. Cases were children aged 9-23 months who missed at least one dose of the recommended vaccine. Controls were children aged 9-23 months who had received all recommended vaccines. Data were collected from mothers/care givers using structured pretested questionnaire. The data were entered into Epi Info version 3.5.1 and analyzed using Statistical Package for Social Sciences (SPSS) version 21. Bivariate and Multiple logistic regression analysis were used to identify the predictors of the outcome variable. The degree of association was assessed by using odds ratio with 95% Confidence Interval (CI). RESULT: This study shows that mothers who take >30 minutes to reach the vaccination site (Adjusted Odds Ratio (AOR) = 3.56,95%CI:1.58-8.01); households not visited by health extension workers at least monthly (AOR = 2.68,95%CI:1.30-5.51); poor participation in women's developmental groups (AOR = 3.3,95%CI 1.54-7.08); no postnatal care follow-up (AOR = 5.2,95%CI:2.36-11.46); and poor knowledge of child immunization (AOR = 3.3,95%CI:1.87-7.43) were predictors of defaulting from completion of child immunization. CONCLUSION: Postnatal care follow-up, household visits by health extension workers and maternal participation in women's development groups are important mediums for disseminating information and increasing knowledge to mothers about child immunization. To reduce the rate of defaulters, health providers should motivate and counsel mothers to attend postnatal care. Health extension workers should visit households at least once per month and strengthen mothers' participation in the women's development groups.

WEB: 10.1371/journal.pone.0185533
IMPACT FACTOR: 3.23
CITED HALF-LIFE: 2.70

START EDITORIAL COMMENT: This study aimed to identify facilitators and determinants of defaulting from completion of child immunizations among children aged 9-23 months in Tigray Region of Northern Ethiopia. Using an unmatched community-based case-control study design, researchers identified the following reasons for defaulting: (1) child sickness during the scheduled appointment time (21.1% of cases), (2) mother's failure to attended vaccination schedules (17.8% of cases), and vaccine vials not being opened because the number of children was too small (10% of cases). The main limitation of this study was recall bias.

3. Impact of rotavirus vaccines in low and middle-income countries
   Sindhu KNC1, Babji S, Ganesan SK.
   Curr Opin Infect Dis. 2017 Oct;30(5):473-481. 2017 Oct 01.
   PubMed ID: 28719399

ABSTRACT
Rotavirus vaccines are playing a pivotal role in improving lives of infants and young children in low and middle-income countries (LMICs). Many of these countries have adopted the vaccine into their routine immunization, whereas others are considering introduction. This article provides an update on the impact of rotavirus vaccines in LMICs on morbidity and mortality in children aged less than 5 years, and their cost-effectiveness. The WHO, in 2013, updated its recommendation to prioritize introduction of rotavirus vaccines in the routine immunization schedule, without age restrictions. Despite the decreased efficacy of the vaccines in LMICs, data from Sub-Saharan Africa have demonstrated a decrease in rotavirus-related morbidity, with some sites reporting an indirect protective effect on children age ineligible to receive the vaccine. Even with improvements in sanitation, nutritional status in children, and other health-related indices in LMICs, the use of rotavirus vaccines will play an important role in preventing rotavirus-related gastroenteritis. Economic models predict a reduction in economic burden because of rotavirus-related health costs, making vaccine introduction cost-effective in resource-constrained settings. Increasing evidence from impact studies shows the significant impact of rotavirus vaccination on hospitalizations and economic burden because of rotavirus gastroenteritis in LMICs. Universal rotavirus vaccination is recommended, and introductions should be monitored by robust surveillance systems to measure effectiveness and impact.

WEB: 10.1097/QCO.0000000000000397
IMPACT FACTOR: 4.24
CITED HALF-LIFE: 5.40

START EDITORIAL COMMENT: The report summarized the impact of rotavirus vaccination in low- and middle-income countries (LMICs), provided current data on rotavirus diarrhea-associated mortality and morbidity, and discussed the challenges to scale-up of rotavirus vaccination in LMICs. While rotavirus vaccines have been utilized in national immunization programs in 90 countries globally, challenges that remain include competing demands on available resources, incomplete monitoring to measure population immunity, and the emergence of new rotavirus genotypes. Nevertheless, there has been progress in countries such as Brazil, El Salvador, Mexico, Panama, and South Africa, which have reported declines in rotavirus-related hospitalizations of 22–40% in children aged less than 5 years, as seen in Table 1. Other countries that introduced the Rotarix vaccine between 2012 and 2014 (Armenia, Botswana, Malawi, Moldova, Tanzania, Togo, Yemen, and Zambia) reported 22–69% reduction in rotavirus-related diarrheal hospitalizations. Modeling studies and cost-effectiveness studies are assessing the impact of the vaccine, specifically in Southeast and Central Asia. These countries have projected annual reductions in rotavirus-associated hospitalizations and mortality ranging from 33 to 91% and 30–65%, respectively (Sindhu, et al.). Similarly, projections for rotavirus-associated hospitalizations and mortality from Africa, Central and South American regions range between 18–70% and 23–88%; and 27–88% and 27–79%, respectively (Sindhu, et al). Tools such as impact assessments and cost-effectiveness studies can be useful to vaccination efforts by providing insight into vaccine performance and can inform policy decisions in many LMICs.

4. Developments in the formulation and delivery of spray dried vaccines
   Kanojia G, Have RT, Soema PC, Frijlink H, Amorij JP, Kersten G
   Hum Vaccin Immunother. 2017 Oct 3;13(10):2364-2378. 2017 Sept 19.
   PubMed ID: 28925794

ABSTRACT
Spray drying is a promising method for the stabilization of vaccines, which are usually formulated as liquids. Usually, vaccine stability is improved by spray drying in the presence of a range of excipients. Unlike freeze drying, there is no freezing step involved, thus the damage related to this step is avoided. The edge of spray drying resides in its ability for particles to be engineered to desired requirements, which can be used in various vaccine delivery methods and routes. Although several spray dried vaccines have shown encouraging preclinical results, the number of vaccines that have been tested in clinical trials is limited, indicating a relatively new area of vaccine stabilization and delivery. This article reviews the current status of spray dried vaccine formulations and delivery methods. In particular it discusses the impact of process stresses on vaccine integrity, the application of excipients in spray drying of vaccines, process and formulation optimization strategies based on Design of Experiment approaches as well as opportunities for future application of spray dried vaccine powders for vaccine delivery.

WEB: 10.1080/21645515.2017.1356952
IMPACT FACTOR: 2.15
CITED HALF-LIFE: 2.30

START EDITORIAL COMMENT: This review discussed the status of and new developments in spray drying as a method for vaccine delivery, and potential limitations of powder vaccines. The technology of spray-dried vaccines, as explained in Figure 1, can be delivered via spray freeze drying and supercritical drying using CO_2 assisted nebulization. Various risks, such as shear stress (reduces vaccine quality) and dehydration stress are limitations to the integrity of the vaccine using this delivery method. Additionally, temperature, the presence of oxygen, water activity, humidity, and exposure to light can deleteriously affect the shelf life of powder vaccines. Sugars and polysaccharides, divalent cations and proteins can improve the stability of vaccines against several viruses. Currently, there are no marketed spray-dried vaccines, but this technology has great potential for use in a measles powder vaccine.

5. Microneedle-mediated delivery of viral vectored vaccines
   Zaric M, Ibarzo Yus B, Kalcheva PP, Klavinskis LS
   Expert Opin Drug Deliv. 2017 Oct;14(10):1177-1187. 2016 Sept 07.
   PubMed ID: 27591122

ABSTRACT
Microneedle array platforms are a promising technology for vaccine delivery, due to their ease of administration with no sharp waste generated, small size, possibility of targeted delivery to the specified skin depth and efficacious delivery of different vaccine formulations, including viral vectors. Areas covered: Attributes and challenges of the most promising viral vector candidates that have advanced to the clinic and that have been leveraged for skin delivery by microneedles; The importance of understanding the immunobiology of antigen-presenting cells in the skin, in particular dendritic cells, in order to generate further improved skin vaccination strategies; recent studies where viral vectors expressing various antigens have been coupled with microneedle technology to examine their potential for improved vaccination. Expert opinion: Simple, economic and efficacious vaccine delivery methods are needed to improve health outcomes and manage possible outbreaks of new emerging viruses. Understanding what innate/inflammatory signals are required to induce both immediate and long-term responses remains a major hurdle in the development of the effective vaccines. One approach to meet these needs is microneedle-mediated viral vector vaccination. In order for this technology to fulfil this potential the industry must invest significantly to further develop its design, production, biosafety, delivery and large-scale manufacturing.

WEB: 10.1080/17425247.2017.1230096
IMPACT FACTOR: 3.75
CITED HALF-LIFE: 4.40

START EDITORIAL COMMENT: Current challenges to vaccination campaigns, such as insufficient vaccine supply, or production limitations, have proven problematic for mass vaccination in many LMICs. Because most conventional vaccines require optimal temperature to maintain their potency, 'cold chains' are necessary for vaccine maintenance. This further complicated by cost: the global cold-chain-related cost of vaccine programs is $200–300 million per year. The overall success of a vaccine can be determined by understanding the main characteristics of a viral vector and vaccine delivery methods. New vaccine platforms and improved delivery methods are emerging, specifically those that target antigen to dendritic cells (DCs). Microneedle development and design is one such technique (Figure 3). This article discussed the methods of microneedle vaccine release, thermostability of microneedle vaccines, physical parameters of solid microneedle arrays (MAs) (as they influence immune response), dissolvable microneedles for viral vector delivery, durability of immune responses induced by viral-vectored microneedles, and skin DC subsets mobilized by viral-vectored microneedles. Problems concerning viral vector vaccines include preexisting patient immunity, immunogenicity, genetic stability, and genotoxicity. Clinical trials are necessary to address these challenges. MAs technology has the potential to replace older, more traditional methods once challenges are addressed and research studies are conducted to optimize the method.

6. Screening of primary gp120 immunogens to formulate the next generation polyvalent DNA prime-protein boost HIV-1 vaccines
   Wang S, Chou TH, Hackett A, Efros V, Wang Y, Han D, et al.
   Hum Vaccin Immunother. 2017 Sep 21:1-14. 2017 Sept 21.
   PubMed ID: 28933684

ABSTRACT
Our previous preclinical studies and a Phase I clinical trial DP6-001 have indicated that a polyvalent Env formulation was able to elicit broadly reactive antibody responses including low titer neutralizing antibody responses against viral isolates of subtypes A, B, C and AE. In the current report, a panel of 62 gp120 immunogens were screened in a rabbit model to identify gp120 immunogens that can elicit improved binding and neutralizing antibody responses and some of them can be included in the next polyvalent formulation. Only about 19% of gp120 immunogens in this panel were able to elicit neutralizing antibodies against greater than 50% of the viruses included in a high throughput PhenoSense neutralization assay when these immuongens were tested as a DNA prime followed by a fixed 5-valent gp120 protein vaccine boost. The new polyvalent formulation, using five gp120 immunogens selected from this subgroup, elicited improved quality of antibody responses in rabbits than the previous DP6-001 formulation. More significantly, this new polyvalent formulation elicited higher antibody responses against a panel of gp70V1V2 antigens expressing V1V2 sequences from diverse subtypes. Bioinformatics analysis supports the design of a 4-valent or 5-valent formulation using gp120 immunogens from this screening study to achieve a broad coverage against 16 HIV-1 subtypes.

WEB: 10.1080/21645515.2017.1380137
IMPACT FACTOR: 2.15
CITED HALF-LIFE: 2.30

START EDITORIAL COMMENT: This study investigated methods to develop improved protective antibody responses using a new polyvalent formulation. The study found that, while the sera elicited by the new polyvalent formulation still could not neutralize the standard panel of viral isolates, the improvement on neutralizing antibodies against other viruses was clear. However, the new polyvalent formulation was able to elicit a better antibody reaction than the original. In addition, the new polyvalent formulation was also able to elicit higher antibody responses against a diverse group of antigens.

7. Progress Stalls in Improving Vaccine Coverage Rates
   Friedrich MJ
   JAMA. 2017 Sep 19;318(11):995. 2017 Sept 19.
   PubMed ID: 28975313

ABSTRACT
About 1 in 10 or nearly 12.9 million infants around the world received no vaccinations in 2016, according to a recent report from the World Health Organization and United Nations Children's Fund (UNICEF). The report, "Progress and Challenges With Achieving Universal Immunization Coverage: 2016 Estimates of Immunization Coverage," focused primarily on the diphtheria-tetanuspertussis (DTP) vaccine, which has protected children since 1949. The new data also showed that last year an additional 6.6 million infants who received their first dose of the DTP vaccine did not complete the full 3-dose immunization series, called DTP3. Coverage rates for DTP3 shots were below 50% in 8 countries: Central African Republic, Chad, Equatorial Guinea, Nigeria, Somalia, South Sudan, Syrian Arab Republic, and Ukraine. Millions of children remain undervaccinated in countries that are especially vulnerable to outbreaks due to poverty and conflict.

WEB: 10.1001/jama.2017.11783
IMPACT FACTOR: 7.48
CITED HALF-LIFE: 0.00

START EDITORIAL COMMENT: This article discusses the 2016 WHO/UNICEF report on achieving universal immunization coverage. According to the report, approximately 1 in 10 or nearly 12.9 million infants around the world received no vaccinations in 2016. In 2016, an additional 6.6 million infants did not complete the full 3-dose immunization series after receiving their first dose of the DTP vaccine. The paper also highlights the suboptimal coverage for vaccines in the first and second years of life—85% and 64% respectively. While much progress has been made, coverage is not sufficient to prevent outbreaks as global coverage for vaccines such as the rotavirus vaccine and the pneumococcal conjugate vaccine has not reached 50%.

8. Estimating the full public health value of vaccination
   Gessner BD, Kaslow D, Louis J, Neuzil K, O'Brien KL, Picot V, et al.
   Vaccine. 2017 Nov 1;35(46):6255-6263. 2017 Oct 03.
   PubMed ID: 28986035

ABSTRACT
There is an enhanced focus on considering the full public health value (FPHV) of vaccination when setting priorities, making regulatory decisions and establishing implementation policy for public health activities. Historically, a therapeutic paradigm has been applied to the evaluation of prophylactic vaccines and focuses on an individual benefit-risk assessment in prospective and individually-randomized phase III trials to assess safety and efficacy against etiologically-confirmed clinical outcomes. By contrast, a public health paradigm considers the population impact and encompasses measures of community benefits against a range of outcomes. For example, measurement of the FPHV of vaccination may incorporate health inequity, social and political disruption, disruption of household integrity, school absenteeism and work loss, health care utilization, long-term/on-going disability, the development of antibiotic resistance, and a range of non-etiologically and etiologically defined clinical outcomes. Following an initial conference at the Fondation Mérieux in mid-2015, a second conference (December 2016) was held to further describe the efficacy of using the FPHV of vaccination on a variety of prophylactic vaccines. The wider scope of vaccine benefits, improvement in risk assessment, and the need for partnership and coalition building across interventions has also been discussed during the 2014 and 2016 Global Vaccine and Immunization Research Forums and the 2016 Geneva Health Forum, as well as in numerous publications including a special issue of Health Affairs in February 2016. The December 2016 expert panel concluded that while progress has been made, additional efforts will be necessary to have a more fully formulated assessment of the FPHV of vaccines included into the evidence-base for the value proposition and analysis of unmet medical need to prioritize vaccine development, vaccine licensure, implementation policies and financing decisions. The desired outcomes of these efforts to establish an alternative framework for vaccine evaluation are a more robust vaccine pipeline, improved appreciation of vaccine value and hence of its relative affordability, and greater public access and acceptance of vaccines.

WEB: 10.1016/j.vaccine.2017.09.048
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START EDITORIAL COMMENT: This paper argues for a more comprehensive measure—full public health value (FPHV)—for vaccines to inform vaccine investments, development, and vaccine interventions. Researchers developed a summary of current measures to assess vaccine benefits, seen in Table 1. Case studies of vaccine adoption (rotavirus, maternal immunization with influenza vaccine, dengue, vaccines under evaluation, and the vaccine pipeline) were also used to illustrate how the application of FPHV could impact decision-making. More efforts are needed to include wider parameters sets for modern cost-benefit studies of vaccines. Consideration should be given to concepts such as local and national economic issues and outbreak control, among other factors, in the evaluation of the public health value of vaccination.

9. Polio immunity and the impacts of mass immunization campaigns in the Democratic Republic of the Congo
   Voorman A, Hoff NA, Doshi RH, Alfonso V, Mukadi P, Muyembe-Tamfum JJ, et al.
   Vaccine. 2017 Oct 9;35(42):5693-5699. 2017 Sept 04.
   PubMed ID: 28882442

ABSTRACT
Background: In order to prevent outbreaks from wild and vaccine-derived poliovirus, maintenance of population immunity in non-endemic countries is critical. Methods: We estimated population seroprevalence using dried blood spots collected from 4893 children 6-59months olds in the 2013-2014 Demographic and Health Survey in the Democratic Republic of the Congo (DRC). Results: Population immunity was 81%, 90%, and 70% for poliovirus types 1, 2, and 3, respectively. Among 6-59-month-old children, 78% reported at least one dose of polio in routine immunization, while only 15% had three doses documented on vaccination cards. All children in the study had been eligible for at least two trivalent oral polio vaccine campaigns at the time of enrollment; additional immunization campaigns seroconverted 5.0%, 14%, and 5.5% of non-immune children per-campaign for types 1, 2, and 3, respectively, averaged over relevant campaigns for each serotype. Conclusions: Overall polio immunity was high at the time of the study, though pockets of low immunity cannot be ruled out. The DRC still relies on supplementary immunization campaigns, and this report stresses the importance of the quality and coverage of those campaigns over their quantity, as well as the importance of routine immunization.

WEB: 10.1016/j.vaccine.2017.08.063
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START EDITORIAL COMMENT: This study conducted a serologic assessment of populations in the Democratic Republic of Congo (DRC) to measure the effectiveness of polio immunization activities and identify populations with sub-optimal immunity. Researchers used a Demographic and Health Survey (DHS) and a multi-stage stratified cluster design. Dried blood spots were collected from participating children (with parental consent). A stratified analysis was conducted, which resulted in an estimation of the population immunity to each poliovirus serotype at the national level, by subgroups such as age, wealth, maternal education level, birth order, residence (rural or urban), and household size. In addition, an estimate was generated of population immunity to each serotype. Findings showed variability based on demographic characteristics such as age, wealth, and residence. Results also showed that immunity was not associated with the gender of the child, birth order, or household size. Immunity to type 1 poliovirus was 79% and 83% among 6–11 month olds and among 48–59 month olds, respectively. Limitations of the study included poor representation from hard-to-reach populations and missing serology data.

10. An ensemble approach to predicting the impact of vaccination on rotavirus disease in Niger
Park J, Goldstein J, Haran M, Ferrari M
Vaccine. 2017 Oct 13;35(43):5835-5841. 2017 Sept 20.
PubMed ID: 28941619

ABSTRACT
Recently developed vaccines provide a new way of controlling rotavirus in sub-Saharan Africa. Models for the transmission dynamics of rotavirus are critical both for estimating current burden from imperfect surveillance and for assessing potential effects of vaccine intervention strategies. We examine rotavirus infection in the Maradi area in southern Niger using hospital surveillance data provided by Epicentre collected over two years. Additionally, a cluster survey of households in the region allows us to estimate the proportion of children with diarrhea who consulted at a health structure. Model fit and future projections are necessarily particular to a given model; thus, where there are competing models for the underlying epidemiology an ensemble approach can account for that uncertainty. We compare our results across several variants of Susceptible-Infectious-Recovered (SIR) compartmental models to quantify the impact of modeling assumptions on our estimates. Model-specific parameters are estimated by Bayesian inference using Markov chain Monte Carlo. We then use Bayesian model averaging to generate ensemble estimates of the current dynamics, including estimates of R0, the burden of infection in the region, as well as the impact of vaccination on both the short-term dynamics and the long-term reduction of rotavirus incidence under varying levels of coverage. The ensemble of models predicts that the current burden of severe rotavirus disease is 2.6-3.7% of the population each year and that a 2-dose vaccine schedule achieving 70% coverage could reduce burden by 39-42%.

WEB: 10.1016/j.vaccine.2017.09.020
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START EDITORIAL COMMENT: Diarrheal disease is a major source of childhood morbidity and mortality in many LMICs. However, the nature of the disease makes it challenging to investigate total burden of disease or the benefits of new interventions. In this study, researchers used an ensemble of fitted empiric models to predict the short-term and long-term impact of vaccination on rotavirus incidence. Incidence was assessed using a state-space model and non-specific surveillance data. In addition, these tools were used to analyze the underlying dynamics of vaccination campaigns. Data was collected using a cluster survey from clinic admissions and a community-based survey, which resulted in six independent models. The modeling approach predicted a current burden of severe rotavirus disease of 2.6–3.7% of the population each year. The analysis also predicted that a 2-dose vaccine schedule that achieved 70% coverage would reduce disease burden by 39–42%. The modeling approach generated new evidence on transmission in peak months and the impact of population density on transmission. Limitations of the study included difficulties in predicting future dynamics and disease burden and non-specific surveillance data.

APPENDIX

(((((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]) ("2017/9/15"[PDAT] : "2017/10/14"[PDAT]))

* October 30, 2017, this search of English language articles published between September 15, 2017 and October 14, 2017 and indexed by the US National Library of Medicine resulted in 205 unique manuscripts.