VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

FEBRUARY 15, 2018

PRODUCED BY: PAUL, S; BABIGUMIRA, JB.

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8. Aiming at the global elimination of viral hepatitis: Challenges along the care continuum.

- An overview of the hepatitis care continuum presented at the Chronic Viral Hepatitis in Africa Conference (Egypt) to inform national and international policy for viral hepatitis programs.


- An outbreak investigation including risk factors, response efforts, prevention, and preparedness based on the 2013-2014 polio outbreak in Ethiopia.


- An analytical study to assess knowledge, attitudes, and practices related to vaccine wastage-rates in health facilities in Nigeria.
DETAILS OF ARTICLES

1. **Spatial clustering of measles vaccination coverage among children in Sub-Saharan Africa.**
   Brownwright TK, Dodson ZM, van Panhuis WG.
   PubMed ID: 29246217

**ABSTRACT**

**BACKGROUND:**
During the past two decades, vaccination programs have greatly reduced global morbidity and mortality due to measles, but recently this progress has stalled. Even in countries that report high vaccination coverage rates, transmission has continued, particularly in spatially clustered subpopulations with low vaccination coverage.

**METHODS:**
We examined the spatial heterogeneity of measles vaccination coverage among children aged 12-23 months in ten Sub-Saharan African countries. We used the Anselin Local Moran's I to estimate clustering of vaccination coverage based on data from Demographic and Health Surveys conducted between 2008 and 2013. We also examined the role of sociodemographic factors to explain clustering of low vaccination.

**RESULTS:**
We detected 477 spatial clusters with low vaccination coverage, many of which were located in countries with relatively high nationwide vaccination coverage rates such as Zambia and Malawi. We also found clusters in border areas with transient populations. Clustering of low vaccination coverage was related to low health education and limited access to healthcare.

**CONCLUSIONS:**
Systematically monitoring clustered populations with low vaccination coverage can inform supplemental immunization activities and strengthen elimination programs. Metrics of spatial heterogeneity should be used routinely to determine the success of immunization programs and the risk of disease persistence.

**WEB:** [10.1186/s12889-017-4961-9](10.1186/s12889-017-4961-9)

**IMPACT FACTOR:** 2.21

**CITED HALF-LIFE:** 4.30

**START EDITORIAL COMMENT:** This study was performed to characterize spatial heterogeneity of measles vaccination coverage in ten countries in sub-Saharan Africa—Democratic Republic of Congo, Rwanda, Burundi, Kenya, Tanzania, Madagascar, Zambia, Zimbabwe, Malawi, and Mozambique. Vaccination coverage was divided into three categories: low, high, and mixed. Researchers identified 477 spatial clusters with low vaccination coverage, many within countries with high nationwide measles vaccination coverage rates. Low vaccination coverage clustering was more likely in populations with low health education, limited access to healthcare, and children not having a health card. Additionally, populations on the border of Malawi and Zambia were found to be more vulnerable to disease outbreak and low vaccination coverage. A surprising finding was that financial barriers to healthcare were associated with higher vaccination rates, a finding which challenges previous notions about the influence of financial barriers on immunization rates. The study suggests that systematic monitoring of clustered populations with low vaccination coverage for targeting with supplemental immunization activities will be critical to measles elimination programs.

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2. Delivery cost analysis of a reactive mass cholera vaccination campaign: a case study of Shanchol™ vaccine in Lake Chilwa, Malawi.
Ilboudo PG, Le Gargasson JB.
PubMed ID: 29258447

ABSTRACT
BACKGROUND:
Cholera is a diarrheal disease that produces rapid dehydration. The infection is a significant cause of mortality and morbidity. Oral cholera vaccine (OCV) has been propagated for the prevention of cholera. Evidence on OCV delivery cost is insufficient in the African context. This study aims to analyze Shanchol vaccine delivery costs, focusing on the vaccination campaign in response of a cholera outbreak in Lake Chilwa, Malawi.

METHODS:
The vaccination campaign was implemented in two rounds in February and March 2016. Structured questionnaires were used to collect costs incurred for each vaccination related activity, including vaccine procurement and shipment, training, microplanning, sensitization, social mobilization and vaccination rounds. Costs collected, including financial and economic costs were analyzed using Choltool, a standardized cholera cost calculator.

RESULTS:
In total, 67,240 persons received two complete doses of the vaccine. Vaccine coverage was higher in the first round than in the second. The two-dose coverage measured with the immunization card was estimated at 58%. The total financial cost incurred in implementing the campaign was US$480275 while the economic cost was US$588637. The total financial and economic costs per fully vaccinated person were US$7.14 and US$8.75, respectively, with delivery costs amounting to US$1.94 and US$3.55, respectively. Vaccine procurement and shipment accounted respectively for 73% and 59% of total financial and economic costs of the total vaccination campaign costs while the incurred personnel cost accounted for 13% and 29% of total financial and economic costs. Cost for delivering a single dose of Shanchol was estimated at US$0.97.

CONCLUSION:
This study provides new evidence on economic and financial costs of a reactive campaign implemented by international partners in collaboration with MoH. It shows that involvement of international partners' personnel may represent a substantial share of campaign's costs, affecting unit and vaccine delivery costs.

WEB: 10.1186/s12879-017-2885-8
IMPACT FACTOR: 2.61
CITED HALF-LIFE: 3.80

START EDITORIAL COMMENT: This study was performed to assess the financial and economic costs of providing the oral cholera (Shanchol™) vaccine in the setting of a campaign following a cholera outbreak in Malawi. The campaign reached over 67,000 individuals with two rounds of vaccination, a coverage rate of 58%. The financial and economic costs per vaccinated person were $7.14 and $8.75 respectively with the bulk of the costs (59% - 73%) going to vaccine procurement and shipment. Campaign, personnel, and delivery costs accounted for a smaller percentage of the cost per vaccinated person. However, the economic costs of personnel were driven by costs of international partners. In other
LMICs underestimation of the true costs of cholera vaccine delivery may occur if economic costs and incurred international personnel costs are not accounted for. Additional research is necessary to analyze household-level private costs for oral cholera vaccine delivery, estimate costs from the societal perspective, and estimate the costs of monitoring adverse events following immunization.

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3. Maternal influenza immunization in Malawi: Piloting a maternal influenza immunization program costing tool by examining a prospective program.

ABSTRACT
BACKGROUND:
This costing study in Malawi is a first evaluation of a Maternal Influenza Immunization Program Costing Tool (Costing Tool) for maternal immunization. The tool was designed to help low- and middle-income countries plan for maternal influenza immunization programs that differ from infant vaccination programs because of differences in the target population and potential differences in delivery strategy or venue.

METHODS:
This analysis examines the incremental costs of a prospective seasonal maternal influenza immunization program that is added to a successful routine childhood immunization and antenatal care program. The Costing Tool estimates financial and economic costs for different vaccine delivery scenarios for each of the major components of the expanded immunization program.

RESULTS:
In our base scenario, which specifies a donated single dose pre-filled vaccine formulation, the total financial cost of a program that would reach 2.3 million women is approximately $1.2 million over five years. The economic cost of the program, including the donated vaccine, is $10.4 million over the same period. The financial and economic costs per immunized pregnancy are $0.52 and $4.58, respectively. Other scenarios examine lower vaccine uptake, reaching 1.2 million women, and a vaccine purchased at $2.80 per dose with an alternative presentation.

CONCLUSION:
This study estimates the financial and economic costs associated with a prospective maternal influenza immunization program in a low-income country. In some scenarios, the incremental delivery cost of a maternal influenza immunization program may be as low as some estimates of childhood vaccination programs, assuming the routine childhood immunization and antenatal care systems are capable of serving as the platform for an additional vaccination program. However, purchasing influenza vaccines at the prices assumed in this analysis, instead of having them donated, is likely to be challenging for lower-income countries. This result should be considered as a starting point to understanding the costs of maternal immunization programs in low- and middle-income countries.

WEB: 10.1371/journal.pone.0190006
IMPACT FACTOR: 3.23
CITED HALF-LIFE: 2.70

START EDITORIAL COMMENT: The WHO recommends prioritization of pregnant women over other high-risk groups for receipt of the influenza vaccine on account of elevated risk for severe infection and the efficiency gains associated with vaccination in the setting of already existing antenatal care infrastructure. This study was a first evaluation of the Maternal Influenza Immunization Program Costing Tool, an excel spreadsheet created to assist low- and middle-income countries to estimate the incremental costs of maternal immunization against influenza, and enable planning. The tool estimates financial and economic costs of different vaccine strategies. The tool was used to estimate $1.2 million in financial costs and $10.4 million in economic costs (including costs of donated vaccine) to reach 2.3 million women in Malawi. Although the tool provided valuable data for planning a possible maternal
influenza immunization program, the large difference in financial and economic costs, particularly the true opportunity cost of vaccines, means that Malawi is unlikely to afford such a program.

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Sarker AR, Sultana M, Mahumud RA, Van Der Meer R, Morton A.
Hum Vaccin Immunother. 2018 Jan 2;14(1):189-198.
PubMed ID: 29099653

ABSTRACT
Diarrhea is one of the world's leading killers of children, and globally, rotavirus is the most common cause of severe diarrhea among under 5 children. In Bangladesh, rotavirus kills nearly 6,000 under 5 children in each year. To reduce the burden of childhood rotavirus diseases, universal rotavirus vaccination is recommended by World Health Organization. The objective of this study is to assess the cost-effectiveness of introducing universal childhood rotavirus vaccination with the newly developed ROTAVAC vaccine in national Expanded Programme of Immunization in Bangladesh. We developed a decision model to examine the potential impact of vaccination in Bangladesh and to examine the effect if the vaccination is applied in the nationwide immunization program schedule. Introduction of childhood universal rotavirus vaccination in Bangladesh scenario appears as highly cost-effective and would offer substantial future benefits for the young population if vaccinated today. The cost per DALY averted of introducing the rotavirus vaccine compared with status quo is approximately US$ 740.27 and US$ 728.67 per DALY averted from the health system and societal perspective respectively which is "very cost-effective" using GDP threshold level according to World Health Organization definition. The results of this analysis seek to contribute to an evidence-based recommendation about the introduction of universal rotavirus vaccination in national Expanded Programme of Immunization (EPI) in Bangladesh.

WEB: 10.1080/21645515.2017.1356962
IMPACT FACTOR: 2.15
CITED HALF-LIFE: 2.30

START EDITORIAL COMMENT: This study is the first cost-effectiveness analysis of rotavirus vaccination in Bangladesh. Researchers found that universal childhood rotavirus vaccination, with incremental cost-effectiveness ratios of US$ 740 and US$ 729 per DALY averted from the health system and societal perspectives respectively, would be highly cost-effective and would reduce childhood illness and death due to rotavirus vaccination in Bangladesh. Vaccine price was the key driver of cost-effectiveness in the study—universal rotavirus vaccination is no longer cost-effective when the price of the vaccine is over US$ 10. Although the study argues for introduction of universal rotavirus vaccination into the EPI in Bangladesh on account of cost-effectiveness, it is silent on the potential budget impact (affordability) of such a policy from the perspective of the Bangladesh health system.

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5. Potential for a booster dose of rotavirus vaccine to further reduce diarrhea mortality.
Burnett E, Lopman BA, Parashar UD.
PubMed ID: 29169893

ABSTRACT
Concern has grown that children vaccinated against rotavirus in developing countries may be vulnerable to rotavirus diarrhea in the second year of life due to waning immunity. Adding a booster dose of rotavirus vaccine at 9 or 12 months of age with measles vaccine has been suggested as a strategy to address this. We evaluated the hypothetical potential benefits of a booster dose on reduction of rotavirus mortality. The projected number of deaths averted were calculated using national level full series vaccination coverage, estimated national rotavirus deaths by week of age, and VE at <12 months of age and ≥12 months of age derived from the published literature. We assumed three functional forms of waning based on the VE estimates: stepwise, linear, and logarithmic. We modeled three potential boosting scenarios: (a) reduced VE waning in the second year of life by 50%, (b) reestablished second year of life VE to the levels in the first year of life, and (c) boosted first year VE by 50% of the difference between VE in the first and second years. To express uncertainty resulting from the parameters, each of the nine models were run 1000 times using a random sample of input values. Across all WHO regions, with the stepwise models we estimated a median of 9800 (95%CI: 9400, 10,200), 19,600 (95%CI: 18,800, 20,400), and 29,400 (95%CI: 28,200, 30,700) additional rotavirus deaths averted in the reduced VE waning, reestablished VE, and boosted VE scenarios. These estimates were highly sensitive to the assumed functional form of waning with approximately 65-80% fewer deaths averted if immunity waned in a linear or logarithmic fashion compared to the stepwise model. While these projections will benefit from improved input data points, our results inform consideration of booster doses of rotavirus vaccine.

WEB: 10.1016/j.vaccine.2017.10.027
IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START EDITORIAL COMMENT: There are concerns that due to waning immunity, children vaccinated against rotavirus in their first year become susceptible in the second year of life. This study estimated 9,800 to 29,400 additional rotavirus deaths averted with a booster dose of rotavirus vaccine during the second year in all WHO regions, depending on analytic scenario. The results were highly-sensitive to the functional form of vaccine efficacy waning, suggesting a need for improved input data to inform modeling projections. Despite this and other limitations, the study provides evidence to support serious consideration of booster doses of rotavirus vaccination during the second year of life in WHO member countries.

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PubMed ID: 29285631

ABSTRACT
Objectives: India has more unvaccinated children than any other country despite provision of free vaccines through the government's Universal Immunization Program. In this study, we calculated the proportion of children aged 12-48 months who were fully vaccinated, under-vaccinated, or who had not received any vaccines. Childhood, household, and sociocultural factors associated with under-vaccination and non-vaccination were evaluated.
Methods: Using data from India's 4th District-level Health and Facility Survey, 2012-2013 (DLHS-4) and the 2012-2013 Annual Health Survey (AHS), we calculated the proportion of children who were non-vaccinated, under-vaccinated, or fully vaccinated with 1 dose of Bacillus Calmette-Guérin, 3 doses of oral polio vaccine, 3 doses of diphtheria-pertussis-tetanus, and 1 dose of measles-containing vaccine. The odds of full vaccination compared to non-vaccination and under-vaccination relative to various factors was assessed using a multivariable, multinomial logistic regression which accounted for survey design.
Results: Of 1,929,580 children aged 12-48 months, 59% were fully vaccinated, 34% were under-vaccinated, and 7% were non-vaccinated. Compared to children born in government institutions, children delivered in non-institutional settings with a skilled birth attendant present had higher odds of non-vaccination (OR 1.66) and those without a skilled attendant present had still greater odds of non-vaccination (OR 2.39) and under-vaccination (OR 1.11).
Conclusions for Practice: India’s vaccination rates among children aged 12-48 months remains unacceptably low. The Indian government should encourage institutional delivery or birthing with a skilled attendant to ensure women receive adequate health education through antenatal care that includes the importance of childhood vaccination.

WEB: 10.1007/s10995-017-2409-6
IMPACT FACTOR: 2.13
CITED HALF-LIFE: 4.70

START EDITORIAL COMMENT: This study explored the factors associated with suboptimal vaccination in India. The study identified female sex, urban locality, low maternal education, non-Hindu religion, scheduled caste/tribe, large family, non-institutional delivery, and non-attendance of antenatal care as being significantly associated with non-vaccination and under-vaccination. Of all the factors, institutional delivery and attendance of antenatal care were the most significant with regard to their association with children being fully vaccinated. The study therefore suggests that, to increase vaccination rates, the Indian government should prioritize antenatal care and facility delivery.

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7. **Increasing full child immunization rates by government using an innovative computerized immunization due list in rural India.**
PubMed ID: 29359630

**ABSTRACT**
Increasing child vaccination coverage to 85% or more in rural India from the current level of 50% holds great promise for reducing infant and child mortality and improving health of children. We have tested a novel strategy called Rural Effective Affordable Comprehensive Health Care (REACH) in a rural population of more than 300,000 in Rajasthan and succeeded in achieving full immunization coverage of 88.7% among children aged 12 to 23 months in a short span of less than 2 years. The REACH strategy was first developed and successfully implemented in a demonstration project by SHARE INDIA in Medchal region of Andhra Pradesh, and was then replicated in Rajgarh block of Rajasthan in cooperation with Bhoruka Charitable Trust (private partners of Integrated Child Development Services and National Rural Health Mission health workers in Rajgarh). The success of the REACH strategy in both Andhra Pradesh and Rajasthan suggests that it could be successfully adopted as a model to enhance vaccination coverage dramatically in other areas of rural India.

**WEB:** 10.1177/0046958017751292

**IMPACT FACTOR:** 0.76

**CITED HALF-LIFE:** 0.00

**START EDITORIAL COMMENT:** This study was performed to evaluate the impact of the Rural Effective Affordable Comprehensive Health Care (REACH) strategy on vaccine coverage in a district in Rajasthan, India. The REACH strategy combines GPS identification, computer-based enumeration and recording of household members, and enhanced health services through provision of immunization (and other services) by additional (supplementary) health workers, in addition to government health services. The rate of full, partial, and none immunization increased from 67.7%, 32.4% and 2.9% at baseline (in 2008) to 88.7%, 10.3%, and 1.0% after 14 months of the REACH intervention. The study suggests that the REACH strategy could be used to increase the rates of full vaccination coverage in other rural areas in India.

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8. **Aiming at the global elimination of viral hepatitis: Challenges along the care continuum.**
   Heffernan A, Barber E, Cook NA, Gomaa AI, Harley YX, Jones CR, et al.
   PubMed ID: 29354656

**ABSTRACT**
A recent international workshop, organized by the authors, analyzed the obstacles facing the ambitious goal of eliminating viral hepatitis globally. We identified several policy areas critical to reaching elimination targets. These include providing hepatitis B birth-dose vaccination to all infants within 24 hours of birth, preventing the transmission of blood-borne viruses through the expansion of national hemovigilance schemes, implementing the lessons learned from the HIV epidemic regarding safe medical practices to eliminate iatrogenic infection, adopting point-of-care testing to improve coverage of diagnosis, and providing free or affordable hepatitis C treatment to all. We introduce Egypt as a case study for rapid testing and treatment scale-up: this country offers valuable insights to policy makers internationally, not only regarding how hepatitis C interventions can be expeditiously scaled-up, but also as a guide for how to tackle the problems encountered with such ambitious testing and treatment programs.

**WEB:** [10.1093/ofid/ofx252](http://10.1093/ofid/ofx252)
**IMPACT FACTOR:** 0.00
**CITED HALF-LIFE:** NA

**START EDITORIAL COMMENT:** This report was a summary of a workshop attended by clinicians and researchers from across the globe, convened by the authors to assess the prevailing challenges to global elimination of viral hepatitis. With the goal of eliminating hepatitis B and C, and averting the approximately 1.3 million deaths due to viral hepatitis, the experts recommended the following provision of *universal birth-dose vaccination* within 24 hours of birth as well as other interventions—hemovigilance to prevent transmission of blood borne viruses, injection safety, expanded screening, and expanded access to hepatitis treatments.

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PubMed ID: 29304745

ABSTRACT
BACKGROUND:
Ethiopia joined the Global Polio Eradication Initiative (GPEI) in 1996, and by the end of December 2001 circulation of indigenous Wild Polio Virus (WPV) had been interrupted. Nonetheless, the country experienced multiple importations during 2004-2008, and in 2013. We characterize the 2013 outbreak investigations and response activities, and document lessons learned.

METHOD:
The data were pulled from different field investigation reports and from the national surveillance database for Acute Flaccid Paralysis (AFP).

RESULTS:
In 2013, a WPV1 outbreak was confirmed following importation in Dollo zone of the Somali region, which affected three Woredas (Warder, Geladi and Bokh). Between July 10, 2013, and January 5, 2014, there were 10 children paralyzed due to WPV1 infection. The majorities (7 of 10) were male and below 5 years of age, and 7 of 10 cases was not vaccinated, and 72% (92/129) of < 5 years of old children living in close proximity with WPV cases had zero doses of oral polio vaccine (OPV). The travel history of the cases showed that seven of the 10 cases had contact with someone who had traveled or had a travel history prior to the onset of paralysis. Underserved and inaccessibility of routine immunization service, suboptimal surveillance sensitivity, poor quality and inadequate supplemental immunization were the most crucial gaps identified during the outbreak investigations.

CONCLUSION:
Prior to the 2013 outbreak, Ethiopia experienced multiple imported polio outbreaks following the interruption of indigenous WPV in December 2001. The 2013 outbreak erupted due to massive population movement and was fueled by low population immunity as a result of low routine immunization and supplemental immunization coverage and quality. In order to avert future outbreaks, it is critical that surveillance sensitivity be improved by establishing community-based surveillance systems and by assigning surveillance focal points at all level particularly in border areas. In addition, it is vital to set up in hard to reach areas a functional immunization service delivery system using the "Reaching Every Child" approach, including periodic routine immunization intensification and supplemental immunization activities.

WEB: 10.1186/s12879-017-2904-9
IMPACT FACTOR: 2.61
CITED HALF-LIFE: 3.80

START EDITORIAL COMMENT:
Following interruption of Wild Polio Virus circulation in Ethiopia in 2001, the country experienced outbreaks associated with importation of cases during 2004-2008 and 2013. This study was an assessment of the outbreak investigation and response to the 2013 outbreak. Researchers used field investigation reports and from the national surveillance database for Acute Flaccid Paralysis (AFP). There were 10 reported cases of AFP during this outbreak, 7 of whom reported contact with someone who had travelled or had a history of travelling themselves. Additionally, 72% of children under five that lived in close proximity to the cases of AFP had never received the oral polio vaccine (OPV). The key lesson learned from this study was that Ethiopia needs to intensify both periodic
routine immunization and supplementary immunization activities, as well as improve surveillance, to avoid future outbreaks of WPV.

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Brown DW, Gacic-Dobo M.
PubMed ID: 29307476

ABSTRACT
Home-based records (HBRs) provide an effective, inexpensive mechanism for recording and tracking infant vaccinations, yet stock-outs prevent HBRs from fulfilling their intended function. We describe the annual occurrence of HBR stock-outs during 2014-2016 reported by national immunization programmes to the WHO and UNICEF on the Joint Reporting Form on Immunization. During 2014-16, 48 countries reported at least one HBR stock-out. Thirteen countries reported HBR stock-outs for two of the three years. Forty-four countries reported two or more HBR funding sources in 2016. Challenges persist in ensuring continuous availability of HBRs. HBR stock-outs have important implications as they may impact continuity-of-care, increase inefficiencies at the point-of-care and reduce the ability of caregivers to be effective health advocates. Identifying mechanisms for preventing stock-outs should be a focus of attention for programmes and development partners. Expanded efforts are required to better understand the underlying causes of HBR stock-outs and identify solutions.

IMPACT FACTOR: 3.41
CITED HALF-LIFE: 5.90

START EDITORIAL COMMENT: Home-based records (HBRs)—vaccination cards and child health books—are a cheap means of recording and tracking infant immunizations and HBR stock-outs increase inefficiencies at points of vaccine provision and reduce the role of parents as health advocates, thereby affecting quality of care. This study was performed to assess the occurrence and frequency of HBR stock-outs in WHO countries from 2014 to 2016. Of 192 countries assessed during that time period, 48 (25%) reported at least one HBR stock out and 13 countries (7%) reported stock-outs for two of the three years. The authors recommended better attention by policy makers—immunization programs and development partners—to HBR stock-outs with a view to preventing them.

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APPENDIX
