VACCINE DELIVERY RESEARCH DIGEST

UNIVERSITY OF WASHINGTON GLOBAL HEALTH START PROGRAM
REPORT TO THE BILL AND MELINDA GATES FOUNDATION

JUNE 1, 2014

PRODUCED BY: COLOMBARA DV, WALSON JL

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1. THE BENEFITS OF REDESIGNING BENIN'S VACCINE SUPPLY CHAIN

Brown ST, Schreiber B, Cakouros BE, Wateska AR, Dicko HM, Connor DL, et al.

Vaccine. 2014 May 6. pii: S0264-410X(14)00641-0. [Epub ahead of print]

PMID: 24814550

ABSTRACT

INTRODUCTION: New vaccine introductions have put strains on vaccine supply chains around the world. While increasing storage and transportation may be the most straightforward options, it is also important to consider what financial and operational benefits can be incurred. In 2012, suboptimal vaccine coverage and impending vaccine introductions prompted the Republic of Benin's Ministry of Health (MOH) to explore ways to improve their vaccine supply chain.

METHODS: Working alongside the Beninese MOH, we utilized our computational model, HERMES, to explore the impact on cost and vaccine availability of three possible options: (1) consolidating the Commune level to a Health Zone level, (2) removing the Commune level completely, and (3) removing the Commune level and expanding to 12 Department Stores. We also analyzed the impact of adding shipping loops during delivery.

RESULTS: At baseline, new vaccine introductions without any changes to the current system increased the logistics cost per dose ($0.23 to $0.26) and dropped the vaccine availability to 71%. While implementing the Commune level removal scenario had the same capital costs as implementing the Health Zone scenario, the Health Zone scenario had lower operating costs. This increased to an overall cost savings of $504,255 when implementing shipping loops.

DISCUSSION: The best redesign option proved to be the synergistic approach of converting to the Health Zone design and using shipping loops (serving ten Health Posts/loop). While a transition to either redesign or only adding shipping loops was beneficial, implementing a redesign option and shipping loops can yield both lower capital expenditures and operating costs.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.04.090

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 2 summarizes the data illustrating that increased coverage with cost savings was only predicted when simultaneous changes were made to the vaccine delivery system.

2. CORRELATES OF COMPLETE CHILDHOOD VACCINATION IN EAST AFRICAN COUNTRIES

Canavan ME, Sipsma HL, Kassie GM, Bradley EH.

PLoS One. 2014 Apr 21;9(4):e95709. eCollection 2014.

PMID: 24752178

ABSTRACT

BACKGROUND: Despite the benefits of childhood vaccinations, vaccination rates in low-income countries (LICs) vary widely. Increasing coverage of vaccines to 90% in the poorest countries over the next 10 years has been estimated to prevent 426 million cases of illness and avert nearly 6.4 million childhood deaths worldwide. Consequently, we sought to provide a comprehensive examination of contemporary vaccination patterns in East Africa and to identify common and country-specific barriers to complete childhood vaccination.

METHODS: Using data from the Demographic and Health Surveys (DHS) for Burundi, Ethiopia, Kenya, Rwanda, Tanzania, and Uganda, we looked at the prevalence of complete vaccination for polio, measles, Bacillus Calmette-Guérin (BCG) and DTwPHibHep (DTP) as recommended by the WHO among children ages 12 to 23 months. We conducted multivariable logistic regression within each country to estimate associations between complete vaccination status and health care access and sociodemographic variables using backwards stepwise regression.

RESULTS: Vaccination varied significantly by country. In all countries, the majority of children received at least one dose of a WHO recommended vaccine; however, in Ethiopia, Tanzania, and Uganda less than 50% of children received a complete schedule of recommended vaccines. Being delivered in a public or private institution compared with being delivered at home was associated with increased odds of complete vaccination status. Sociodemographic covariates were not consistently associated with complete vaccination status across countries.

CONCLUSIONS: Although no consistent set of predictors accounted for complete vaccination status, we observed differences based on region and the location of delivery. These differences point to the need to examine the historical, political, and economic context of each country in order to maximize vaccination coverage. Vaccination against these childhood diseases is a critical step towards reaching the Millennium Development Goal of reducing under-five mortality by two-thirds by 2015 and thus should be a global priority.

WEB: http://dx.doi.org/10.1371/journal.pone.0095709

IMPACT FACTOR: 3.73

CITED HALF-LIFE: 2.40

UW EDITORIAL COMMENT: This study used representative population data to carefully construct multivariable models. Figure 1 is a heat map depicting regional variation in complete coverage. Table 3 highlights differences in correlates of complete coverage between countries.

3. SOCIO-ECONOMIC DETERMINANTS AND INEQUITIES IN COVERAGE AND TIMELINESS OF EARLY CHILDHOOD IMMUNISATION IN RURAL GHANA

Gram L, Soremekun S, Ten Asbroek A, Manu A, O'Leary M, Hill Z, et al.

Trop Med Int Health. 2014 Apr 28. [Epub ahead of print]

PMID: 24766425

ABSTRACT

OBJECTIVES: To assess the extent of socio-economic inequity in coverage and timeliness of key childhood immunisations in Ghana.

METHODS: Secondary analysis of vaccination card data collected from babies born between January 2008 and January 2010 who were registered in the surveillance system supporting the ObaapaVita and Newhints Trials was carried out. 20 251 babies had 6 weeks' follow-up, 16 652 had 26 weeks' follow-up, and 5568 had 1 year's follow-up. We performed a descriptive analysis of coverage and timeliness of vaccinations by indicators for urban/rural status, wealth and educational attainment. The association of coverage with socio-economic indicators was tested using a chi-square-test and the association with timeliness using Cox regression.

RESULTS: Overall coverage at 1 year of age was high (>95%) for Bacillus Calmette-Guérin (BCG), all three pentavalent diphtheria-pertussis-tetanus-haemophilus influenzae B-hepatitis B (DPTHH) doses and all polio doses except polio at birth (63%). Coverage against measles and yellow fever was 85%. Median delay for BCG was 1.7 weeks. For polio at birth, the median delay was 5 days; all other vaccine doses had median delays of 2-4 weeks. We found substantial health inequity across all socio-economic indicators for all vaccines in terms of timeliness, but not coverage at 1 year. For example, for the last DPTHH dose, the proportion of children delayed more than 8 weeks were 27% for urban children and 31% for rural children ($P < 0.001$), 21% in the wealthiest quintile and 41% in the poorest quintile ($P < 0.001$), and 9% in the most educated group and 39% in the least educated group ($P < 0.001$). However, 1-year coverage of the same dose remained above 90% for all levels of all socio-economic indicators.

CONCLUSIONS: Ghana has substantial health inequity across urban/rural, socio-economic and educational divides. While overall coverage was high, most vaccines suffered from poor timeliness. We suggest that countries achieving high coverage should include timeliness indicators in their surveillance systems.

WEB: http://dx.doi.org/10.1111/tmi.12324

IMPACT FACTOR: 2.94

CITED HALF-LIFE: 6.30

UW EDITORIAL COMMENT: This large and well-conceived study accounted for potential bias from missing data due to the absence of vaccination cards and loss to follow-up. Figures 3 and 4 are particularly informative summaries of the timeliness and coverage data, respectively.

4. SOCIAL INEQUALITIES IN VACCINATION UPTAKE AMONG CHILDREN AGED 0-59 MONTHS LIVING IN MADAGASCAR: AN ANALYSIS OF DEMOGRAPHIC AND HEALTH SURVEY DATA FROM 2008 TO 2009

Clouston S, Kidman R, Palermo T.

Vaccine. 2014 May 6. pii: S0264-410X(14)00556-8. [Epub ahead of print]

PMID: 24814558

ABSTRACT

BACKGROUND: Socioeconomic inequalities in vaccination can reduce the ability and efficiency of global efforts to reduce the burden of disease. Vaccination is particularly critical because the poorest children are often at the greatest risk of contracting preventable infectious diseases, and unvaccinated children may be clustered geographically, jeopardizing herd immunity. Without herd immunity, these children are at even greater risk of contracting disease and social inequalities in associated morbidity and mortality are amplified.

METHODS: Data on vaccination for children under five came from the most recent Demographic and Health Survey in Madagascar (2008-2009). Vaccination status was available for diptheria, pertussis, tetanus, hepatitis B, measles, tuberculosis, poliomyelitis, and H. influenza type-B. Multilevel logistic regression was used to analyze childhood vaccination by parental socioeconomic status while accounting for shared district, cluster, and household variation. Maps were created to serve as a roadmap for efforts to increase vaccination.

FINDINGS: Geographic variation in vaccination rates was substantial. Districts that were less covered were near other districts with limited coverage. Most districts lacked herd immunity for diphtheria, pertussis, poliomyelitis and measles. Full herd immunity was reached in a small number of districts clustered near the capital. While within-district variation in coverage was substantial; parental education and wealth were independently associated with vaccination.

INTERPRETATION: Socioeconomic inequalities in vaccination reduce herd immunity and perpetuate inequalities by allowing infectious diseases to disproportionately affect the most vulnerable populations. Findings indicated that most districts had low immunization coverage rates and unvaccinated children were geographically clustered. The result was inequalities in vaccination and reduced herd immunity. To further improve coverage, interventions must take a multilevel approach that focuses on both supply- and demand-side barriers to delivering vaccination to underserved regions, and to the poorest children in those regions.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.04.030

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This study used standard data sources and methods to find expected geographic and SES correlates of vaccination status. While the methods are fairly standard, the application to Madagascar is novel.

5. MODELING THE POTENTIAL IMPACT OF VACCINATION ON THE EPIDEMIOLOGY OF CONGENITAL CYTOMEGALOVIRUS INFECTION

Lanzieri TM, Bialek SR, Ortega-Sanchez IR, Gambhir M.

Vaccine. 2014 May 13. pii: S0264-410X(14)00670-7. [Epub ahead of print]

PMID: 24837782

ABSTRACT

BACKGROUND: Understanding the potential for vaccination to change cytomegalovirus (CMV) epidemiology is important for developing CMV vaccines and designing clinical trials.

METHODS: We constructed a deterministic, age-specific and time-dependent mathematical model of pathogen transmission, parameterized using CMV seroprevalence from the United States and Brazil, to predict the impact of vaccination on congenital CMV infection.

FINDINGS: Concurrent vaccination of young children and adolescents would result in the greatest reductions in congenital CMV infections in populations with moderate and high baseline maternal seroprevalence. Such a vaccination strategy, assuming 70% vaccine efficacy, 90% coverage and 5-year duration of protection, could ultimately prevent 30-50% of congenital CMV infections. At equilibrium, this strategy could result in a 30% reduction in congenital CMV infections due to primary maternal infection in the United States but a 3% increase in Brazil. The potential for an increase in congenital CMV infections due to primary maternal infections in Brazil was not predicted with use of a vaccine that confers protection for greater than 5 years.

INTERPRETATION: Modeling suggests that vaccination strategies that include young children will result in greater declines in congenital CMV infection than those restricted to adolescents or women of reproductive age. Our study highlights the critical need for better understanding of the relative contribution of type of maternal infection to congenital CMV infection and disease, the main focus of vaccine prevention.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.05.014

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This manuscripts illustrates the potential value of modeling vaccination schemes for each targeted population in order to identify the optimal vaccination age(s) within that particular population (compare Figure 3 a and b).

6. YELLOW FEVER IN AFRICA: ESTIMATING THE BURDEN OF DISEASE AND IMPACT OF MASS VACCINATION FROM OUTBREAK AND SEROLOGICAL DATA

Garske T, Van Kerkhove MD, Yactayo S, Ronveaux O, Lewis RF, Staples JE, et al.

PLoS Med. 2014 May 6;11(5):e1001638. eCollection 2014.

PMID: 24800812

ABSTRACT

BACKGROUND: Yellow fever is a vector-borne disease affecting humans and non-human primates in tropical areas of Africa and South America. While eradication is not feasible due to the wildlife reservoir, large scale vaccination activities in Africa during the 1940s to 1960s reduced yellow fever incidence for several decades. However, after a period of low vaccination coverage, yellow fever has resurged in the continent. Since 2006 there has been substantial funding for large preventive mass vaccination campaigns in the most affected countries in Africa to curb the rising burden of disease and control future outbreaks. Contemporary estimates of the yellow fever disease burden are lacking, and the present study aimed to update the previous estimates on the basis of more recent yellow fever occurrence data and improved estimation methods.

METHODS AND FINDINGS: Generalised linear regression models were fitted to a dataset of the locations of yellow fever outbreaks within the last 25 years to estimate the probability of outbreak reports across the endemic zone. Environmental variables and indicators for the surveillance quality in the affected countries were used as covariates. By comparing probabilities of outbreak reports estimated in the regression with the force of infection estimated for a limited set of locations for which serological surveys were available, the detection probability per case and the force of infection were estimated across the endemic zone. The yellow fever burden in Africa was estimated for the year 2013 as 130,000 (95% CI 51,000-380,000) cases with fever and jaundice or haemorrhage including 78,000 (95% CI 19,000-180,000) deaths, taking into account the current level of vaccination coverage. The impact of the recent mass vaccination campaigns was assessed by evaluating the difference between the estimates obtained for the current vaccination coverage and for a hypothetical scenario excluding these vaccination campaigns. Vaccination campaigns were estimated to have reduced the number of cases and deaths by 27% (95% CI 22%-31%) across the region, achieving up to an 82% reduction in countries targeted by these campaigns. …

CONCLUSIONS: With the estimation method presented here, spatial estimates of transmission intensity can be combined with vaccination coverage levels to evaluate the impact of past or proposed vaccination campaigns, thereby helping to allocate resources efficiently for yellow fever control. This method has been used by the Global Alliance for Vaccines and Immunization (GAVI Alliance) to estimate the potential impact of future vaccination campaigns. Please see later in the article for the Editors' Summary.

WEB: http://dx.doi.org/10.1371/journal.pmed.1001638

IMPACT FACTOR: 15.25

CITED HALF-LIFE: 4.60

UW EDITORIAL COMMENT: Though the analysis rests on extremely sparse data, it is the only large-scale analysis available that assesses the impact of the yellow fever vaccination campaigns that began in 2006.

7. FROM REFRIGERATOR TO ARM: ISSUES IN VACCINATION DELIVERY

Tan LJ; SHAPE Vaccine Delivery Working Group.

Vaccine. 2014 May 1;32(21):2389-93. Epub 2014 Mar 6.

PMID: 24613526

ABSTRACT

This report summarizes the first meeting of a panel of immunization experts who met in Washington, DC, on May 4-5, 2012. The panel consisted of experts from national immunization policy organizations; state, regional, and local immunization programs; and vaccinating health care practices. The primary objective of this meeting was to identify issues in the vaccine delivery process as a critical first step in the determination of where and how improvements can be made. Vaccines are one of the greatest achievements in public health. However, in order to maintain the integrity of vaccines and the success of vaccination programs, proper handling of vaccines from the receipt of shipment through administration to the patient is critical. Continuous improvement of the vaccine delivery process is important to ensure appropriate vaccine handling by all vaccine providers. The overarching consensus of the participants of this meeting was that the major challenge in vaccine delivery is the complexity throughout all areas of the vaccine delivery process, which is often underestimated, particularly in the areas of vaccine preparation and administration. The lack of detailed, consistent standards encompassing all areas of the vaccine delivery process, and the gaps in oversight, education, and training of vaccine providers, particularly providers of adult vaccines, were also identified as major issues. The next step for this panel is to reconvene to explore potential solutions to address the identified issues.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.02.045

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Though the report focuses on the US, the manuscript provides a framework that may be helpful for identifying issues in vaccine delivery in lower and middle income countries.

8. ARE CURRENT COST-EFFECTIVENESS THRESHOLDS FOR LOW- AND MIDDLE-INCOME COUNTRIES USEFUL? EXAMPLES FROM THE WORLD OF VACCINES

Newall AT, Jit M, Hutubessy R.

Vaccine. 2014 Apr 1;32(16):1798-807. Epub 2014 Feb 13.

PMID: 24791735

ABSTRACT

The World Health Organization's CHOosing Interventions that are Cost Effective (WHO-CHOICE) thresholds for averting a disability-adjusted life-year of one to three times per capita income have been widely cited and used as a measure of cost effectiveness in evaluations of vaccination for low- and middle-income countries (LMICs). These thresholds were based upon criteria set out by the WHO Commission on Macroeconomics and Health, which reflected the potential economic returns of interventions. The CHOICE project sought to evaluate a variety of health interventions at a subregional level and classify them into broad categories to help assist decision makers, but the utility of the thresholds for within-country decision making for individual interventions (given budgetary constraints) has not been adequately explored. To examine whether the 'WHO-CHOICE thresholds' reflect funding decisions, we examined the results of two recent reviews of cost-effectiveness analyses of human papillomavirus and rotavirus vaccination in LMICs, and we assessed whether the results of these studies were reflected in funding decisions for these vaccination programmes. We found that in many cases, programmes that were deemed cost effective were not subsequently implemented in the country. We consider the implications of this finding, the advantages and disadvantages of alternative methods to estimate thresholds, and how cost perspectives and the funders of healthcare may impact on these choices.

WEB: http://dx.doi.org/10.1007/s40273-014-0162-x

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This discussion of the utility of WHO-CHOICE thresholds may help inform our interpretation of vaccine cost-effectiveness studies.

9. ROLE OF VACCINE MANUFACTURERS IN DEVELOPING COUNTRIES TOWARDS GLOBAL HEALTHCARE BY PROVIDING QUALITY VACCINES AT AFFORDABLE PRICES

Jadhav S, Gautam M, Gairola S.

Clin Microbiol Infect. 2014 May;20 Suppl 5:37-44. Epub 2014 Mar 7.

PMID: 24476201

ABSTRACT

Vaccines represent one of the greatest achievements of science and medicine in the fight against infectious diseases. Vaccination is one of the most cost-effective public health tools to prevent infectious diseases. Significant progress has been made in expanding the coverage of vaccines globally, resulting in the prevention of more than two million deaths annually. In 2010, nearly 200 countries endorsed a shared vision to extend the benefits of vaccines to every person by 2020, known as the Decade of Vaccine Initiative (DoV). Vaccine manufacturers in developing countries, as represented by the Developing Countries Vaccine Manufacturers Network (DCVMN), make a significant contribution to DoV by supplying quality vaccines at affordable prices to the people who need them most. About 70% of the global Expanded Program on Immunization (EPI) vaccine supplies are met by DCVMN. Besides EPI vaccine supplies, DCVMN is also targeting vaccines against rotavirus, Japanese encephalitis, pneumonia, human papillomavirus, meningitis and neglected tropical diseases. This article reviews the roles and contributions of DCVMN in making the vaccines accessible and affordable to all.

WEB: http://dx.doi.org/10.1111/1469-0691.12568

IMPACT FACTOR: 4.58

CITED HALF-LIFE: 4.00

UW EDITORIAL COMMENT: Although limited technical content was provided, this review effectively highlights the contributions of DCVMSs toward greater vaccine access in lower and middle income countries.

10. THE CONTRIBUTION OF VACCINATION TO GLOBAL HEALTH: PAST, PRESENT AND FUTURE

Greenwood B

Philos Trans R Soc Lond B Biol Sci. 2014 May 12;369(1645):20130433. Print 2014.

PMID: 24821919

ABSTRACT

Vaccination has made an enormous contribution to global health. Two major infections, smallpox and rinderpest, have been eradicated. Global coverage of vaccination against many important infectious diseases of childhood has been enhanced dramatically since the creation of WHO's Expanded Programme of Immunization in 1974 and of the Global Alliance for Vaccination and Immunization in 2000. Polio has almost been eradicated and success in controlling measles makes this infection another potential target for eradication. Despite these successes, approximately 6.6 million children still die each year and about a half of these deaths are caused by infections, including pneumonia and diarrhoea, which could be prevented by vaccination. Enhanced deployment of recently developed pneumococcal conjugate and rotavirus vaccines should, therefore, result in a further decline in childhood mortality. Development of vaccines against more complex infections, such as malaria, tuberculosis and HIV, has been challenging and achievements so far have been modest. Final success against these infections may require combination vaccinations, each component stimulating a different arm of the immune system. In the longer term, vaccines are likely to be used to prevent or modulate the course of some non-infectious diseases. Progress has already been made with therapeutic cancer vaccines and future potential targets include addiction, diabetes, hypertension and Alzheimer's disease.

WEB: http://dx.doi.org/10.1098/rstb.2013.0433

IMPACT FACTOR: 6.23

CITED HALF-LIFE: 7.30

UW EDITORIAL COMMENT: A simple but well-written overview providing a historical perspective regarding the impact of vaccines on global health.

APPENDIX: PUBMED 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]) AND ("2014/04/15"[PDAT] : "2014/05/14"[PDAT]))

*On May 27, 2014, this search of English language articles published between April 15, 2014 and May 14, 2014 and indexed by the US National Library of Medicine resulted in 178 unique manuscripts.