VACCINE DELIVERY RESEARCH DIGEST

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

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1. TRANSPORT NETWORKS AND INEQUITIES IN VACCINATION: REMOTENESS SHAPES MEASLES VACCINE COVERAGE AND PROSPECTS FOR ELIMINATION ACROSS AFRICA.

Metcalf CJ, Tatem A, Bjornstad ON, Lessler J, O'Reilly K, Takahashi S, et al.

Epidemiology and Infection. 2014 Aug 14:1-10. [Epub ahead of print]

PMID: 25119237

ABSTRACT

SUMMARY: Measles vaccination is estimated to have averted 13·8 million deaths between 2000 and 2012. Persisting heterogeneity in coverage is a major contributor to continued measles mortality, and a barrier to measles elimination and introduction of rubella-containing vaccine. Our objective is to identify determinants of inequities in coverage, and how vaccine delivery must change to achieve elimination goals, which is a focus of the WHO Decade of Vaccines. We combined estimates of travel time to the nearest urban centre (⩾50 000 people) with vaccination data from Demographic Health Surveys to assess how remoteness affects coverage in 26 African countries. Building on a statistical mapping of coverage against age and geographical isolation, we quantified how modifying the rate and age range of vaccine delivery affects national coverage. Our scenario analysis considers increasing the rate of delivery of routine vaccination, increasing the target age range of routine vaccination, and enhanced delivery to remote areas. Geographical isolation plays a key role in defining vaccine inequity, with greater inequity in countries with lower measles vaccine coverage. Eliminating geographical inequities alone will not achieve thresholds for herd immunity, indicating that changes in delivery rate or age range of routine vaccination will be required. Measles vaccine coverage remains far below targets for herd immunity in many countries on the African continent and is likely to be inadequate for achieving rubella elimination. The impact of strategies such as increasing the upper age range eligible for routine vaccination should be considered.

WEB: http://dx.doi.org/10.1017/S0950268814001988

IMPACT FACTOR: 2.87

CITED HALF-LIFE: 6.50

UW EDITORIAL COMMENT: Figure 1 displays the effect of travel time on vaccine coverage in 27 countries examined in the paper, showing that the countries with the lowest vaccine coverage experience the most dramatic effects of travel time. Figure 2 shows the results of modifying the kinetics of vaccine coverage to specific regions, showing in Figure 2b how countries would need to modify the rate of vaccination and upper age limits to reach 95% coverage by 24 months of age.

2. FRAMEWORK FOR OPTIMAL GLOBAL VACCINE STOCKPILE DESIGN FOR VACCINE-PREVENTABLE DISEASES: APPLICATION TO MEASLES AND CHOLERA VACCINES AS CONTRASTING EXAMPLES.

Thompson KM, Duintjer Tebbens RJ.

Risk Analysis. 2014 Aug 11. doi:. [Epub ahead of print]

PMID: 25109229

ABSTRACT

Managing the dynamics of vaccine supply and demand represents a significant challenge with very high stakes. Insufficient vaccine supplies can necessitate rationing, lead to preventable adverse health outcomes, delay the achievements of elimination or eradication goals, and/or pose reputation risks for public health authorities and/or manufacturers. This article explores the dynamics of global vaccine supply and demand to consider the opportunities to develop and maintain optimal global vaccine stockpiles for universal vaccines, characterized by large global demand (for which we use measles vaccines as an example), and nonuniversal (including new and niche) vaccines (for which we use oral cholera vaccine as an example). We contrast our approach with other vaccine stockpile optimization frameworks previously developed for the United States pediatric vaccine stockpile to address disruptions in supply and global emergency response vaccine stockpiles to provide on-demand vaccines for use in outbreaks. For measles vaccine, we explore the complexity that arises due to different formulations and presentations of vaccines, consideration of rubella, and the context of regional elimination goals. We conclude that global health policy leaders and stakeholders should procure and maintain appropriate global vaccine rotating stocks for measles and rubella vaccine now to support current regional elimination goals, and should probably also do so for other vaccines to help prevent and control endemic or epidemic diseases. This work suggests the need to better model global vaccine supplies to improve efficiency in the vaccine supply chain, ensure adequate supplies to support elimination and eradication initiatives, and support progress toward the goals of the Global Vaccine Action Plan.

WEB: http://dx.doi.org/10.1111/risa.12265

IMPACT FACTOR: 2.28

CITED HALF-LIFE: 8.50

UW EDITORIAL COMMENT: Table 2 shows the current state of stockpiled immunizations maintained by the WHO and partners. Figure 3 shows a stock-and-flow diagram for the development of a vaccine stockpile. Table 4 examines the ideal attributes of a vaccine stockpile, and how applicable they are to the current vaccines utilized for measles and cholera.

3. USING MOBILE HEALTH (MHEALTH) AND GEOSPATIAL MAPPING TECHNOLOGY IN A MASS CAMPAIGN FOR REACTIVE ORAL CHOLERA VACCINATION IN RURAL HAITI.

Teng JE, Thomson DR, Lascher JS, Raymond M, Ivers LC.

PLoS Negl Trop Dis. 2014 Jul 31;8(7):e3050. eCollection 2014.

PMID: 25078790

ABSTRACT

BACKGROUND: In mass vaccination campaigns, large volumes of data must be managed efficiently and accurately. In a reactive oral cholera vaccination (OCV) campaign in rural Haiti during an ongoing epidemic, we used a mobile health (mHealth) system to manage data on 50,000 participants in two isolated communities.

METHODS: Data were collected using 7-inch tablets. Teams pre-registered and distributed vaccine cards with unique barcodes to vaccine-eligible residents during a census in February 2012. First stored on devices, data were uploaded nightly via Wi-fi to a web-hosted database. During the vaccination campaign between April and June 2012, residents presented their cards at vaccination posts and their barcodes were scanned. Vaccinee data from the census were pre-loaded on tablets to autopopulate the electronic form. Nightly analysis of the day's community coverage informed the following day's vaccination strategy. We generated case-finding reports allowing us to identify those who had not yet been vaccinated.

RESULTS: During 40 days of vaccination, we collected approximately 1.9 million pieces of data. A total of 45,417 people received at least one OCV dose; of those, 90.8% were documented to have received 2 doses. Though mHealth required up-front financial investment and training, it reduced the need for paper registries and manual data entry, which would have been costly, time-consuming, and is known to increase error. Using Global Positioning System coordinates, we mapped vaccine posts, population size, and vaccine coverage to understand the reach of the campaign. The hardware and software were usable by high school-educated staff.

CONCLUSION: The use of mHealth technology in an OCV campaign in rural Haiti allowed timely creation of an electronic registry with population-level census data, and a targeted vaccination strategy in a dispersed rural population receiving a two-dose vaccine regimen. The use of mHealth should be strongly considered in mass vaccination campaigns in future initiatives.

WEB: http://dx.doi.org/10.1371/journal.pntd.0003050

IMPACT FACTOR: 4.57

CITED HALF-LIFE: 2.50

UW EDITORIAL COMMENT: This analysis shows how mHealth technology allowed for geospatial mapping of an oral cholera campaign in Haiti. Figures 1 and 2 show how, by electronically recording information including neighborhood location, the researchers were able to see first dose coverage and second dose completion rates by area at the end of each day of the campaign. The researchers note that nightly review of coverage rates, as shown in the figures, allowed them to plan for the following day's vaccination strategy, including door-to-door visits.

4. INTEGRATED PACKAGE APPROACH IN DELIVERING INTERVENTIONS DURING IMMUNISATION CAMPAIGNS IN A COMPLEX ENVIRONMENT IN PAPUA NEW GUINEA: A CASE STUDY.

Vince JD, Datta SS, Toikilik S, Lagani W.

Vaccine. 2014 Aug 6;32(36):4614-4619. Epub 2014 Apr 30.

PMID: 24795224

ABSTRACT

Papua New Guinea's difficult and varied topography, poor transport infrastructure, changing dynamics of population and economy in recent times and understaffed and poorly financed health service present major challenges for successful delivery of vaccination and other preventative health interventions to both the rural majority and urban populations, thereby posing risks for vaccine preventable disease outbreaks in the country. The country has struggled to meet the vaccination coverage targets required for the eradication of poliomyelitis and elimination of measles. Escalation of inter and intra country migration resulting from major industrial developments, particularly in extraction industries, has substantially increased the risk of infectious disease importation. This case study documents the evolution of immunisation programmes since the introduction of supplementary immunisation activities (SIAs). Single antigen SIAs have advantages and disadvantages. In situations in which the delivery of preventative health interventions is difficult, it is likely that the cost benefit is greater for multiple than for single intervention. The lessons learned from the conduct of single antigen SIAs can be effectively used for programmes delivering multiple SIA antigens, routine immunisations, and other health interventions. This paper describes a successful and cost effective multiple intervention programme in Papua New Guinea. The review of the last SIA in Papua New Guinea showed relatively high coverage of all the interventions and demonstrated the operational feasibility of delivering multiple interventions in resource constrained settings. Studies in other developing countries such as Lesotho and Ethiopia have also successfully integrated health interventions with SIA. In settings such as Papua New Guinea there is a strong case for integrating supplementary immunisation activity with routine immunisation and other health interventions through a comprehensive outreach programme.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.04.056

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 1 provides a comparison of total cost, cost per beneficiary, and cost per intervention for various supplementary immunization activities (SIAs) since 2003 in Papua New Guinea, showing that the integrated SIA increased total cost but greatly reduced cost per intervention. Figures 3 and 4 show intervention coverage for the vaccines used and the number of infants under 1 year that were reached during this campaign. The authors note that the vitamin A coverage reported in Figure 3 was inflated due to children outside the target age group being included in the intervention.

5. HEPATITIS B VIRUS: WHERE DO WE STAND AND WHAT IS THE NEXT STEP FOR ERADICATION?

Komatsu H.

World J Gastroenterol. 2014 Jul 21;20(27):8998-9016.

PMID: 25083074

ABSTRACT

Hepatitis B (HB) virus (HBV) infection, which causes liver cirrhosis and hepatocellular carcinoma, is endemic worldwide. Hepatitis B vaccines became commercially available in the 1980s. The World Health Organization recommended the integration of the HB vaccine into the national immunisation programs in all countries. HBV prevention strategies are classified into three groups: (1) universal vaccination alone; (2) universal vaccination with screening of pregnant women plus HB immune globulin (HBIG) at birth; and (3) selective vaccination with screening of pregnant women plus HBIG at birth. Most low-income countries have adopted universal vaccine programs without screening of pregnant women. However, HB vaccines are not widely used in low-income countries. The Global Alliance for Vaccine and Immunization was launched in 2000, and by 2012, the global coverage of a three-dose HB vaccine had increased to 79%. The next challenges are to further increase the coverage rate, close the gap between recommendations and routine practices, approach high-risk individuals, screen and treat chronically infected individuals, and prevent breakthrough infections. To eradicate HBV infections, strenuous efforts are required to overcome socioeconomic barriers to the HB vaccine; this task is expected to take several decades to complete.

WEB: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4112872/

IMPACT FACTOR: 2.55

CITED HALF-LIFE: 5.00

UW EDITORIAL COMMENT: This review provides a summary of the strides made in universal HB vaccination and the current state of eradication efforts. Figure 3 shows the increase in coverage of the three-dose HB vaccine since the introduction of the Global Alliance for Vaccine and Immunization, showing both global coverage and coverage by WHO region. Table 2 shows hepatitis B surface antigen prevalence in selected regions since infant universal vaccination was introduced.

6. MEASLES OUTBREAK RESPONSE AMONG ADOLESCENT AND ADULT SOMALI REFUGEES DISPLACED BY FAMINE IN KENYA AND ETHIOPIA, 2011.

Navarro-Colorado C, Mahamud A, Burton A, Haskew C, Maina GK, Wagacha JB, et al.

J Infect Dis. 2014 Aug 12. [Epub ahead of print]

PMID: 25117754

ABSTRACT

BACKGROUND: The refugee complexes of Dadaab, Kenya, and Dollo-Ado, Ethiopia, experienced measles outbreaks during June-November 2011, following a large influx of refugees from Somalia.

METHODS: Line-lists from health facilities were used to describe the outbreak in terms of age, sex, vaccination status, arrival date, attack rates (ARs), and case fatality ratios (CFRs) for each camp. Vaccination data and coverage surveys were reviewed.

RESULTS: In Dadaab, 1370 measles cases and 32 deaths (CFR, 2.3%) were reported. A total of 821 cases (60.1%) were aged ≥15 years, 906 (82.1%) arrived to the camps in 2011, and 1027 (79.6%) were unvaccinated. Camp-specific ARs ranged from 212 to 506 cases per 100 000 people. In Dollo-Ado, 407 cases and 23 deaths (CFR, 5.7%) were reported. Adults aged ≥15 years represented 178 cases (43.7%) and 6 deaths (26.0%). Camp-specific ARs ranged from 21 to 1100 cases per 100 000 people. Immunization activities that were part of the outbreak responses initially targeted children aged 6 months to 14 years and were later expanded to include individuals up to 30 years of age.

CONCLUSIONS: The target age group for outbreak response-associated immunization activities at the start of the outbreaks was inconsistent with the numbers of cases among unvaccinated adolescents and adults in the new population. In displacement of populations from areas affected by measles outbreaks, health authorities should consider vaccinating adults in routine and outbreak response activities.

WEB: http://dx.doi.org/10.1093/infdis/jiu395

IMPACT FACTOR: 5.85

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: This analysis used data collected as part of disease control activities at refugee camps in Kenya and Ethiopia in 2011. Table 2 shows the timeline of immunization campaigns in Dadaab and Dollo-Ado, two of the camps, as well as the target age groups of the campaign. Figures 1 and 2 show the number of cases over time in these two camps, highlighting the median age of the cases. Matching the timelines of these data it is clear that the median age of cases did not align with the target age of the campaign, delaying outbreak control efforts at these camps.

7. EFFECTS OF THE INTRODUCTION OF NEW VACCINES IN GUINEA-BISSAU ON VACCINE COVERAGE, VACCINE TIMELINESS, AND CHILD SURVIVAL: AN OBSERVATIONAL STUDY.

Fisker AB, Hornshøj L, Rodrigues A, Balde I, Fernandes M, Benn CS, et al.

Lancet Glob Health. 2014 Aug;2(8):e478-87. Epub 2014 Jul 23

.PMID: 25103521

ABSTRACT

BACKGROUND: In 2008, the GAVI Alliance funded the introduction of new vaccines (including pentavalent diphtheria-tetanus-pertussis [DTP] plus hepatitis B and Haemophilus influenzae type b antigens) in Guinea-Bissau. The introduction was accompanied by increased vaccination outreach services and a more restrictive wastage policy, including only vaccinating children younger than 12 months. We assessed coverage of all vaccines in the Expanded Program on Immunizations before and after the new vaccines' introduction, and the implications on child survival.

METHODS: This observational cohort study used data from the Bandim Health Project, which has monitored vaccination status and mortality in randomly selected village clusters in Guinea-Bissau since 1990. We assessed the change in vaccination coverage using cohort data from children born in 2007 and 2009; analysed the proportion of children who received measles vaccine after 12 months of age using data from 1999-2006; and compared child mortality after age 12 months in children who had received measles vaccine and those who had not using data from 1999 to 2006.

FINDINGS: The proportion of children who were fully vaccinated by 12 months of age was 53% (468 of 878) in the 2007 cohort and 53% (467 of 879) in the 2009 cohort (relative risk [RR] 1·00, 95% CI 0·89-1·11). Coverage of DTP-3 and pentavalent-3 increased from 73% (644 of 878) in 2007 to 81% (712 of 879) in 2009 (RR 1·10, 95% CI 1·04 -1·17); by contrast, the coverage of measles vaccination declined from 71% (620 of 878) to 66% (577 of 879; RR 0·93, 0·85-1·01). The effect of the changes was significantly different for DTP-3 coverage compared with measles vaccine coverage (p=0·002). After 12 months of age, the adjusted mortality rate ratio was 0·71 (95% CI 0·56-0·90) for children who had received measles vaccine compared with those who had not (0·59 [0·43-0·80] for girls and 0·87 [0·62-1·23] for boys).

INTERPRETATION: The introduction of the new vaccination programme in 2008 was associated with increased coverage of DTP, but decreased coverage of measles vaccine. In 1999-2006, child mortality was higher in children who had not received measles vaccine than in those who had.

WEB: http://dx.doi.org/10.1016/S2214-109X(14)70274-8

IMPACT FACTOR: 39.06

CITED HALF-LIFE: 2.50

UW EDITORIAL COMMENT: Table 2 shows the vaccine coverage for various immunizations before and after the policy change. A limitation of this study was vaccine card inspection during routine care to assess vaccine coverage, which may overestimate vaccine coverage if those without vaccine cards were less likely to be immunized.

8. VALUING VACCINES USING VALUE OF STATISTICAL LIFE MEASURES.

Laxminarayan R, Jamison DT, Krupnick AJ, Norheim OF.

Vaccine. 2014 Sep 3;32(39):5065-70. Epub 2014 Jul 18.

PMID: 25045822

ABSTRACT

Vaccines are effective tools to improve human health, but resources to pursue all vaccine-related investments are lacking. Benefit-cost and cost-effectiveness analysis are the two major methodological approaches used to assess the impact, efficiency, and distributional consequences of disease interventions, including those related to vaccinations. Childhood vaccinations can have important non-health consequences for productivity and economic well-being through multiple channels, including school attendance, physical growth, and cognitive ability. Benefit-cost analysis would capture such non-health benefits; cost-effectiveness analysis does not. Standard cost-effectiveness analysis may grossly underestimate the benefits of vaccines. A specific willingness-to-pay measure is based on the notion of the value of a statistical life (VSL), derived from trade-offs people are willing to make between fatality risk and wealth. Such methods have been used widely in the environmental and health literature to capture the broader economic benefits of improving health, but reservations remain about their acceptability. These reservations remain mainly because the methods may reflect ability to pay, and hence be discriminatory against the poor. However, willingness-to-pay methods can be made sensitive to income distribution by using appropriate income-sensitive distributional weights. Here, we describe the pros and cons of these methods and how they compare against standard cost-effectiveness analysis using pure health metrics, such as quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs), in the context of vaccine priorities. We conclude that if appropriately used, willingness-to-pay methods will not discriminate against the poor, and they can capture important non-health benefits such as financial risk protection, productivity gains, and economic wellbeing.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.07.003

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This article compares the strengths of using benefit-cost, cost-effectiveness, and value of a statistical life (VSL) in assessing investment in vaccination. Section 5.1 summarizes scenarios in which VSL may be a useful metric, and when cost-effectiveness and benefit-cost would be more appropriate.

9. ESTIMATED IMPACT AND COST-EFFECTIVENESS OF ROTAVIRUS VACCINATION IN INDIA: EFFECTS OF GEOGRAPHIC AND ECONOMIC DISPARITIES.

Rheingans R, Anderson JD 4th, Anderson B, Chakraborty P, Atherly D, Pindolia D.

Vaccine. 2014 Aug 11;32 Suppl 1:A140-50. doi:.

PMID: 25091669

ABSTRACT

India accounts for 23% of global rotavirus mortality in under-five children, with more than 100,000 deaths from rotavirus annually. Introduction of a vaccine in India is considered to be the most effective intervention for preventing rotavirus mortality. Recent research suggests that there is considerable variation in rotavirus mortality burden across regional, gender and socio-economic subpopulations within India. In addition, there is potential variability in who would likely receive rotavirus vaccine if introduced. We use available household data to estimate heterogeneity in rotavirus mortality risk, vaccination benefits, and cost-effectiveness across geographic and socio-economic groups within India. We account for heterogeneity by modeling estimated three-dose routine vaccinations as a proxy for a generalized rotavirus vaccine, and mortality for subpopulations of children aggregated by region and state, socio-economic status and sex, separately. Results are presented for six geographic regions and for Bihar, Uttar Pradesh, and Madhya Pradesh, three high mortality states accounting for 56% of national mortality estimates. Impact estimates accounting for disparities predict rotavirus vaccine introduction will prevent 35,000 deaths at an average cost of $118/DALY averted (7292 INR/DALY averted). Rotavirus vaccines are most cost-effective for the poor living in high mortality regions and states. Reductions in geographic and socio-economic disparities based on regional estimates could prevent an additional 9400 deaths annually, while reductions in socio-economic disparities in the three highest morality states alone could prevent an additional 10,600 deaths annually. Understanding the impact of heterogeneity can help improve strategies to maximize the benefits of rotavirus vaccination introduction, leading to fewer lives lost as a result of rotavirus disease.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.05.073

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Figure 2 and Table 3 show the estimated burden of disease in different regions of India, and the estimated reduction in mortality that would result from a rotavirus vaccination campaign. Figure 4 compares upper and lower estimates of variables including dose cost and mortality by region. The authors note that the most recent estimates for rotavirus mortality are a decade old, presenting a potential limitation to the accuracy of their findings.

10. GLOBAL VACCINE SUPPLY. THE INCREASING ROLE OF MANUFACTURERS FROM MIDDLE INCOME COUNTRIES.

Francis DP, Du YP, Precioso AR.

Vaccine. 2014 Sep 15;32(41):5259-65. Epub 2014 Aug 8.

PMID: 25110294

ABSTRACT

Hallmarks in the remarkable evolution of vaccines and their application include the eradication of smallpox, the development and delivery of the early childhood vaccines and the emergence of recombinant vaccines initiated by the hepatitis B vaccine. Now we enter a most exciting era as vaccines are increasingly produced and delivered in less developed countries. The results are dramatic decreases in childhood morbidity and mortality around the world.

WEB: http://dx.doi.org/10.1016/j.vaccine.2014.07.069

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This review provides a concise historical account of the development of vaccines, as well as the current state of vaccine supply, focusing on India, Brazil and China. Table 3 shows the major companies in these middle income countries that are producing vaccines, and what vaccinations are currently on the market and still in development. Figure 3 illustrates how the Global Alliance for Vaccines and Immunizations (GAVI) has increasingly relied on vaccine supply from these emerging markets in the last decade.

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 ("2014/07/15"[PDAT] : "2014/08/14"[PDAT])

*On August 27, 2014, this search of English language articles published between July 15, 2014 and August 14, 2014 and indexed by the US National Library of Medicine resulted in 182 unique manuscripts.