VACCINE DELIVERY RESEARCH DIGEST

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

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1. POLIO SUPPLEMENTARY IMMUNIZATION ACTIVITIES AND EQUITY IN ACCESS TO VACCINATION: EVIDENCE FROM THE DEMOGRAPHIC AND HEALTH SURVEYS.

Helleringer S, Abdelwahab J, Vandenent M.

J Infect Dis. 2014 Nov 1;210 Suppl 1:S531-9.

PMID: 25316877

ABSTRACT

Every year, large numbers of children are vaccinated against polio during supplementary immunization activities (SIAs). Such SIAs have contributed to the >99% decline in the incidence of poliovirus cases since the beginning of the Global Polio Eradication Initiative. It is not clear, however, how much they have also contributed to reducing poverty-related inequalities in access to oral polio vaccine (OPV). We investigated whether the gap in coverage with 3 doses of OPV between children in the poorest and wealthiest households was reduced by SIA participation. To do so, we used data from 25 demographic and health surveys (DHS) conducted in 20 countries since 2002. We found that, in several countries as well as in pooled analyses, poverty-related inequalities in 3-dose OPV coverage were significantly lower among children who had participated in SIAs over the 2 years before a DHS than among other children. SIAs are an important approach to ensuring equitable access to immunization services and possibly other health services.

WEB: http://dx.doi.org/10.1093/infdis/jiu278

IMPACT FACTOR: 5.85

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: Figure 2 shows the difference in 3-dose oral polio vaccine coverage between poorest and wealthier children age 12-23 months, by SIA participants and nonparticipants. This shows that in pooled analyses, the poverty-related gap in 3-dose OPV coverage was significantly lower among SIA participants. A limitation of this analysis was the inability to distinguish between participation in polio vs. nonpolio SIAs. This may lead to misclassification bias in the study, although the authors believe this to be minimal due to high rates of participation in polio SIAs, as shown in Table 2.

2. COMPARING COST-EFFECTIVENESS RESULTS FOR A VACCINE ACROSS DIFFERENT COUNTRIES WORLDWIDE: WHAT CAN WE LEARN?

Standaert B, Ethgen O, Emerson R, Postma M, Mauskopf J.

Adv Ther. 2014 Oct;31(10):1095-108. Epub 2014 Oct 21.

PMID: 25331617

ABSTRACT

BACKGROUND: Cost-effectiveness analysis (CEA) using country-specific thresholds tied to gross domestic product (GDP) might not be appropriate in countries with low healthcare investment and a high disease burden as a consequence.

METHODS: Using data from previously published CEA of rotavirus vaccination across nine countries worldwide, we calculated the cost neutral price (Pn) for the new intervention that reflects the price resulting in no net increase in health care costs compared with the current situation, and the maximum price (Pm) obtained with an incremental cost-effectiveness ratio (ICER) at the threshold value of 1 × GDP/capita.

RESULTS: In countries with low GDP/capita, the paradoxical finding for rotavirus vaccination is that the Pm is much higher than in countries with a high GDP/capita. On the other hand, the Pn for the low GDP/capita countries is much lower than for high GDP/capita countries because of the low investment in health care.

CONCLUSIONS: In countries with low healthcare investment and a high disease burden, the difference between the Pn and Pm for rotavirus vaccine which is the price range within which the ICER is below the World Health Organization (WHO) threshold value, is large. One reason could be that the WHO threshold value may not properly account for the local opportunity cost of health care expenditures. Therefore, either alternative threshold values should be selected or alternative economic assessment tools should be considered, such as budget optimisation or return on investment, if we want to communicate about real economic value of new vaccines in those countries.

WEB: http://dx.doi.org/10.1007/s12325-014-0160-6

IMPACT FACTOR: 2.44

CITED HALF-LIFE: 4.40

UW EDITORIAL COMMENT: This analysis found significant differences when conducting CEA in high and low income countries. In low income countries, low existing healthcare investment allows minimum scope for cost offsets, leading to a neutral cost that is close to zero. The high disease burden in these countries could greatly reduce health outcome losses, leading to a wide range of costs that are cost effective. The authors conclude that in a low income setting with high disease burden, any health improvement will be considered cost effective, so emphasis should be placed on comparative health benefits for a given amount of money spent.

3. IMPROVING POLIO VACCINATION COVERAGE IN NIGERIA THROUGH THE USE OF GEOGRAPHIC INFORMATION SYSTEM TECHNOLOGY.

Barau I, Zubairu M, Mwanza MN, Seaman VY.

J Infect Dis. 2014 Nov 1;210 Suppl 1:S102-10.

PMID: 25316823

ABSTRACT

BACKGROUND: Historically, microplanning for polio vaccination campaigns in Nigeria relied on inaccurate and incomplete hand-drawn maps, resulting in the exclusion of entire settlements and missed children. The goal of this work was to create accurate, coordinate-based maps for 8 polio-endemic states in northern Nigeria to improve microplanning and support tracking of vaccination teams, thereby enhancing coverage, supervision, and accountability.

METHODS: Settlement features were identified in the target states, using high-resolution satellite imagery. Field teams collected names and geocoordinates for each settlement feature, with the help of local guides. Global position system (GPS) tracking of vaccination teams was conducted in selected areas and daily feedback provided to supervisors.

RESULTS: Geographic information system (GIS)-based maps were created for 2238 wards in the 8 target states. The resulting microplans included all settlements and more-efficient team assignments, owing to the improved spatial reference. GPS tracking was conducted in 111 high-risk local government areas, resulting in improved team performance and the identification of missed/poorly covered settlements.

CONCLUSIONS: Accurate and complete maps are a necessary part of an effective polio microplan, and tracking vaccinators gives supervisors a tool to ensure that all settlements are visited.

WEB: http://dx.doi.org/10.1093/infdis/jiu010

IMPACT FACTOR: 5.85

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: Figure 3 shows maps of the calculations of geographic coverage for different coverage areas. A map of Nigerian states, showing where the GIS mapping was completed in 2012 and 2013, can be seen in Figure 4. The authors note that mapping was not completed in two of the states that account for nearly half of the wild polio virus infections, Yobe and Borno, due to security issues in these regions. However despite this shortcoming, in 2013 Nigeria saw a 50% reduction in wild polio virus cases since 2012, and an 85% reduction in the GIS mapped states. While this cannot be directly attributed to the use of GIS mapping, these statistics combined with the vaccination campaign coverage rates shown in Table 2 provide strong evidence in support of using GIS mapping in microplanning.

4. MODELING THE DYNAMICS OF ORAL POLIOVIRUS VACCINE CESSATION.

Thompson KM, Duintjer Tebbens RJ.

J Infect Dis. 2014 Nov 1;210 Suppl 1:S475-84.

PMID: 25316870

ABSTRACT

BACKGROUND: Oral poliovirus vaccine (OPV) results in an ongoing burden of poliomyelitis due to vaccine-associated paralytic poliomyelitis and circulating vaccine-derived polioviruses (cVDPVs). This motivates globally coordinated OPV cessation after wild poliovirus eradication.

METHODS: We modeled poliovirus transmission and OPV evolution to characterize the interaction between population immunity, OPV-related virus prevalence, and the emergence of cVDPVs after OPV cessation. We explored strategies to prevent and manage cVDPVs for countries that currently use OPV for immunization and characterized cVDPV emergence risks and OPV use for outbreak response.

RESULTS: Continued intense supplemental immunization activities until OPV cessation represent the best strategy to prevent cVDPV emergence after OPV cessation in areas with insufficient routine immunization coverage. Policy makers must actively manage population immunity before OPV cessation to prevent cVDPVs and aggressively respond if prevention fails. Sufficiently aggressive response with OPV to interrupt transmission of the cVDPV outbreak virus will lead to die-out of OPV-related viruses used for response in the outbreak population. Further analyses should consider the risk of exportation to other populations of the outbreak virus and any OPV used for outbreak response.

CONCLUSION: OPV cessation can successfully eliminate all circulating live polioviruses in a population. The polio end game requires active risk management.

WEB: http://dx.doi.org/10.1093/infdis/jit845

IMPACT FACTOR: 5.85

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: Figure 3 shows the impact different coverage levels of SIAs would have on population immunity, total OPV-related virus prevalence, and paralytic poliomyelitis incidence due to circulating vaccine-derived poliovirus (cVDPV). The article concludes that sensitive surveillance and rapid outbreak response in the first 2 years after cessation are the most important measures to reduce the risk of cVDPV emergence.

5. LOT QUALITY ASSURANCE SAMPLING TO MONITOR SUPPLEMENTAL IMMUNIZATION ACTIVITY QUALITY: AN ESSENTIAL TOOL FOR IMPROVING PERFORMANCE IN POLIO ENDEMIC COUNTRIES.

Brown AE, Okayasu H, Nzioki MM, Wadood MZ, Chabot-Couture G, Quddus A et al.

J Infect Dis. 2014 Nov 1;210 Suppl 1:S333-40. doi:

PMID: 25304633

ABSTRACT

Monitoring the quality of supplementary immunization activities (SIAs) is a key tool for polio eradication. Regular monitoring data, however, are often unreliable, showing high coverage levels in virtually all areas, including those with ongoing virus circulation. To address this challenge, lot quality assurance sampling (LQAS) was introduced in 2009 as an additional tool to monitor SIA quality. Now used in 8 countries, LQAS provides a number of programmatic benefits: identifying areas of weak coverage quality with statistical reliability, differentiating areas of varying coverage with greater precision, and allowing for trend analysis of campaign quality. LQAS also accommodates changes to survey format, interpretation thresholds, evaluations of sample size, and data collection through mobile phones to improve timeliness of reporting and allow for visualization of campaign quality. LQAS becomes increasingly important to address remaining gaps in SIA quality and help focus resources on high-risk areas to prevent the continued transmission of wild poliovirus.

WEB: http://dx.doi.org/10.1093/infdis/jit816

IMPACT FACTOR: 5.85

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: Lot quality assurance sampling (LQAS) is used to classify an area as having acceptable or not acceptable vaccination coverage, based on the number of unvaccinated children in the sample compared to a predetermined decision value of unvaccinated children. This analysis provides evidence of the benefits of LQAS compared to other monitoring methods. Figure 2 demonstrates the concordance between LQAS and independent monitoring (IM) using data from Nigeria and Pakistan. The figures provide evidence of bias in the IM data, demonstrating that LQAS is more effective at distinguishing between areas with high and low quality vaccine coverage. Figure 3 shows the trends in campaign coverage quality in the two countries, graphing the frequency of categories of vaccination coverage thresholds. Maps providing a visual representation of LQAS data collected from mobile phones are displayed in Figure 4.

6. SHOULD EXPECTANT MOTHERS BE VACCINATED AGAINST FLU? A SAFETY REVIEW.

Loubet P, Kerneis S, Anselem O, Tsatsaris V, Goffinet F, Launay O.

Expert Opin Drug Saf. 2014 Dec;13(12):1709-20. Epub 2014 Nov 3.

PMID: 25363497

ABSTRACT

INTRODUCTION: Pregnant women have a higher risk of serious complications from influenza than non-pregnant women of reproductive age. This increased risk has been noted both during pandemic and inter-pandemic influenza seasons. However, although vaccination against flu is recommended at any trimesters by international and national policies, vaccine coverage remains low in pregnant women, possibly due to patient and healthcare providers' concern about the safety of the vaccine.

AREAS COVERED: This review addresses the effectiveness and safety of seasonal and adjuvanted and non-adjuvanted pandemic 2009 A/H1N1 influenza vaccine.

EXPERT OPINION: Available data suggest no evidence of an increased risk for any adverse event for both mothers and fetuses after vaccination against flu during pregnancy. These results are important when considering the potential of maternal immunization against flu as a public health intervention to protect both the mother and her infant against serious infectious disease.

WEB: http://dx.doi.org/10.1517/14740338.2014.977252

IMPACT FACTOR: 2.74

CITED HALF-LIFE: 4.10

UW EDITORIAL COMMENT: This review examined both the efficacy and safety of influenza vaccines in pregnant women. The authors found that there was no evidence linking flu vaccination in pregnancy to an increased risk of adverse events such as spontaneous abortion, fetal growth problems, preterm birth or congenital malformations in the fetus. Additionally, the authors cited evidence of reduction in risk to the mother and the fetus as a result of influenza vaccination. Some limitations of this review were that many of the studies cited were observational, they were generally underpowered to observe an association between vaccination and adverse events, and there was a paucity of data pertaining to vaccination given in the first trimester. Regardless, the strength of the evidence demonstrating the safety and efficacy of the vaccine supports the universal vaccination of pregnant women.

7. OVERVIEW OF GLOBAL, REGIONAL, AND NATIONAL ROUTINE VACCINATION COVERAGE TRENDS AND GROWTH PATTERNS FROM 1980 TO 2009: IMPLICATIONS FOR VACCINE-PREVENTABLE DISEASE ERADICATION AND ELIMINATION INITIATIVES.

Wallace AS, Ryman TK, Dietz V.

J Infect Dis. 2014 Nov 1;210 Suppl 1:S514-22.

PMID: 25316875

ABSTRACT

BACKGROUND: Review of the historical growth in annual vaccination coverage across countries and regions can better inform decision makers' development of future goals and strategies to improve routine vaccination services.

METHODS: Using the World Health Organization (WHO) and the United Nations Children's Fund estimates of annual national third dose of diphtheria-tetanus-pertussis-containing vaccine (DTP3) and third dose of polio vaccine (POL3) coverage for 1980-2009, we calculated the mean absolute annual rate of change in national DTP3 coverage among all countries (globally) and among countries within each WHO region, as well as the number of years taken by each region to reach specific regional coverage levels. Last, we assessed differences in mean absolute annual rate of change in DTP3 coverage, stratified by baseline level of DTP3 coverage.

RESULTS: During the 1980s, global DTP3 coverage increased a mean of 5.3 percentage points/year. Annual rate of change decreased to 0.5 percentage points/year in the 1990s and then increased to 0.9 percentage points/year during the 2000s. Mean annual rate of change in coverage across all countries was highest (9.2 percentage points) when national coverage levels were 26%-30% and lowest (-0.9 percentage points) when national coverage levels were 96%-100%. Regional differences existed as both WHO South-East Asia Region and WHO African Region countries experienced mean negative DTP3 coverage growth at lower coverage levels (81%-85%) than other regions. …

CONCLUSION: Mean national coverage growth patterns across all regions are nonlinear as coverage levels increase. Saturation points of mean 0 percentage-point growth in annual coverage varies by region and require further investigation. The achievement of >90% routine coverage is observed to take decades, which has implications for disease eradication and elimination initiatives.

WEB: http://dx.doi.org/10.1093/infdis/jiu108

IMPACT FACTOR: 5.85

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: Figure 4 demonstrates the absolute rates of change in coverage by the third DTP3 vaccine, shown by region. Basic trends can be seen across regions, however there are clear differences in maximum mean annual rate of change in coverage achieved.

8. HEPATITIS B VACCINE ALONE OR WITH HEPATITIS B IMMUNOGLOBULIN IN NEONATES OF HBSAG+/HBEAG- MOTHERS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Machaira M, Papaevangelou V, Vouloumanou EK, Tansarli GS, Falagas ME.

J Antimicrob Chemother. 2014 Oct 31. [Epub ahead of print]

PMID: 25362571

ABSTRACT

OBJECTIVES: The cost-effectiveness of augmenting immunization against hepatitis B infection with hepatitis B immunoglobulin (HBIG) remains controversial, particularly for the subpopulation of babies of HBsAg+/HBeAg- mothers that are considered as low-infective. We aimed to evaluate the effectiveness of vaccine alone compared with vaccine plus HBIG for the immunization of babies of HBsAg+/HBeAg- mothers.

METHODS: We searched PubMed, Scopus and Cochrane Central Register of Controlled Trials databases to identify studies comparing the effectiveness of combined immunization (vaccine plus HBIG) with vaccine alone in neonates of HBsAg+/HBeAg- mothers. A systematic review and meta-analysis of eligible studies was performed.

RESULTS: A total of nine eligible studies were identified (four randomized controlled trials). No difference was found regarding the primary outcome of our meta-analysis, namely occurrence of hepatitis B infection, between neonates who received vaccine only, compared with those who received both vaccine and HBIG (four studies, 3426 patients, OR=0.82, 95% CI=0.41-1.64). This finding was consistent with regards to seroprotection rate (four studies, 1323 patients, OR=1.24, 95% CI=0.97-1.58). Safety data were not reported in the included studies.

CONCLUSION: The available limited published evidence suggests that vaccine alone seems to be equally effective to the combination of HBIG and hepatitis B vaccine for neonates of HBsAg+/HBeAg- mothers in preventing infection. Further studies are needed in order to clarify the potential benefit of combined immunization to this specific subgroup of patients.

WEB: http://dx.doi.org/10.1093/jac/dku404

IMPACT FACTOR: 5.34

CITED HALF-LIFE: 5.80

UW EDITORIAL COMMENT: Figures 2 provides a forest plots showing no difference in HB infection in neonates born to HBsAg+/HBeAg- mothers who received HBIG and vaccination compared to those who received just the vaccine. This analysis was limited by the small number of studies included; only 9 were used, of which only 4 were randomized trials.

9. THE IMPACT OF POLIO ERADICATION ON ROUTINE IMMUNIZATION AND PRIMARY HEALTH CARE: A MIXED-METHODS STUDY.

Closser S, Cox K, Parris TM, Landis RM, Justice J, Gopinath R et al.

J Infect Dis. 2014 Nov 1;210 Suppl 1:S504-13. Epub 2014 Apr 1.

PMID: 24690667

ABSTRACT

BACKGROUND: After 2 decades of focused efforts to eradicate polio, the impact of eradication activities on health systems continues to be controversial. This study evaluated the impact of polio eradication activities on routine immunization (RI) and primary healthcare (PHC).

METHODS: Quantitative analysis assessed the effects of polio eradication campaigns on RI and maternal healthcare coverage. A systematic qualitative analysis in 7 countries in South Asia and sub-Saharan Africa assessed impacts of polio eradication activities on key health system functions, using data from interviews, participant observation, and document review.

RESULTS: Our quantitative analysis did not find compelling evidence of widespread and significant effects of polio eradication campaigns, either positive or negative, on measures of RI and maternal healthcare. Our qualitative analysis revealed context-specific positive impacts of polio eradication activities in many of our case studies, particularly disease surveillance and cold chain strengthening. These impacts were dependent on the initiative of policy makers. Negative impacts, including service interruption and public dissatisfaction, were observed primarily in districts with many campaigns per year.

CONCLUSION: Polio eradication activities can provide support for RI and PHC, but many opportunities to do so remain missed. Increased commitment to scaling up best practices could lead to significant positive impacts.

WEB: http://dx.doi.org/10.1093/infdis/jit232

IMPACT FACTOR: 5.85

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: Figure 4 demonstrates the association between polio eradication campaign intensity and DTP vaccine coverage, as well as on attended birth coverage. The results show minimal changes in both indicators and wide confidence intervals. The authors note that the wide confidence intervals at the high level of campaign intensity is likely due to lack of observations, and that intensity is highest in areas of low routine immunization and attended birth, creating selection bias. Figure 5 provides a summary of the positive and negative impacts of eradication that were reported in the qualitative arm of the study.

10. UNDERSTANDING INEQUITIES IN CHILD VACCINATION RATES AMONG THE URBAN POOR: EVIDENCE FROM NAIROBI AND OUAGADOUGOU HEALTH AND DEMOGRAPHIC SURVEILLANCE SYSTEMS.

Soura AB1, Mberu B, Elungata P, Lankoande B, Millogo R, Beguy D et al.

J Urban Health. 2014 Oct 15. [Epub ahead of print]

PMID: 25316191

ABSTRACT

Studies on informal settlements in sub-Saharan Africa have questioned the health benefits of urban residence, but this should not suggest that informal settlements (within cities and across cities and/or countries) are homogeneous. They vary in terms of poverty, pollution, overcrowding, criminality, and social exclusion. Moreover, while some informal settlements completely lack public services, others have access to health facilities, sewers, running water, and electricity. There are few comparative studies that have looked at informal settlements across countries accounting for these contextual nuances. In this paper, we comparatively examine the differences in child vaccination rates between Nairobi and Ouagadougou's informal settlements. We further investigate whether the identified differences are related to the differences in demographic and socioeconomic composition between the two settings. We use data from the Ouagadougou and Nairobi Urban Health and Demographic Surveillance Systems (HDSSs), which are the only two urban-based HDSSs in Africa. The results show that children in the slums of Nairobi are less vaccinated than children in the informal settlements in Ouagadougou. The difference in child vaccination rates between Nairobi and Ouagadougou informal settlements are not related to the differences in their demographic and socioeconomic composition but to the inequalities in access to immunization services.

WEB: http://dx.doi.org/ 10.1007/s11524-014-9908-1

IMPACT FACTOR: 1.89

CITED HALF-LIFE: 6.40

UW EDITORIAL COMMENT: Figure 1 shows a large disparity between the slums of Nairobi compared to the slums of Ouagadougou. While many of the vaccination strategies were similar in the two regions, the authors note that mobile vaccination is stronger in Ouagadougou and those living in Nairobi slums must pay for vaccinations at a health center, which could be partially responsible for better outcomes in Ouagadougou. Some limitations in this study were that it was cross sectional, so causation cannot be determined. Additionally it assessed poverty in a way that allowed comparison within groups of a certain slum, but was not easily generalizable across different countries or cultures.

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 ("2014/10/15"[PDAT] : "2014/11/14"[PDAT]))

*On November 24, 2014, this search of English language articles published between October 15, 2014 and November 14, 2014 and indexed by the US National Library of Medicine resulted in 133 unique manuscripts.