

VACCINE DELIVERY RESEARCH DIGEST

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

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1. 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 Apr 2. doi: 10.1093/infdis/jit232 [Epub ahead of print]

PMID: 24690667[PubMed - as supplied by publisher]

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.

CONCLUSIONS: 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://jid.oxfordjournals.org/content/early/2014/04/02/infdis.jit232.long>

IMPACT FACTOR: 5.85

CITED HALF-LIFE: 8.00

UW EDITORIAL COMMENT: Figure 3 illustrates that the increase in DTP3 vaccination and attended birth coverage began prior to implementation of polio eradication campaigns. In addition, the qualitative study revealed that polio eradication efforts “had the most beneficial effects overall in case studies with health systems that were relatively strong.”



2. VACCINE PERCEPTION AMONG ACCEPTORS AND NON-ACCEPTORS IN SOKOTO STATE, NIGERIA.

Murele B, Vaz R, Gasasira A, Mkanda P, Erbetto T, Okeibunor J

Vaccine. 2014 Apr 5. pii: S0264-410X(14)00419-8. doi: 10.1016/j.vaccine.2014.03.050. [Epub ahead of print]

PMID: 24713368 [PubMed - as supplied by publisher]

ABSTRACT

Vaccine perceptions among acceptors and non-acceptors of childhood vaccination were explored. Seventy-two care givers, among them, acceptors and non-acceptors were interviewed in-depth with an interview guide that assessed vaccine acceptance, social and personality factors, and health belief model (HBM) categories in relation to oral polio vaccine (perceived susceptibility, severity, cost barriers, general barriers, benefits, knowledge, and engagement in preventative health behaviours). Community leaders were purposively selected while parents were selected on the basis of availability while ensuring the different attitude to vaccines was covered. Results showed that the HBM framework was found to be appropriate for identifying and distinguishing vaccine acceptors and non-acceptors. In addition, the HBM categories of benefits and susceptibility were found to influence oral polio vaccine acceptance. Second, the opinion of family members about the oral polio vaccine moderated the relationship between number of social ties and vaccine acceptance. Further, oral polio vaccine acceptance was related to outbreaks of paralysis of any sort, but not aggregate scores of other preventative health behaviours. Implications of this study include the investigation of vaccine acceptance in a high risk population. Research was done to investigate vaccine acceptance.

WEB: <http://www.sciencedirect.com/science/article/pii/S0264410X14004198>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Despite its small sample size, the study reported some potentially important findings for this setting. For example, section 3.3 states that all those who accepted polio vaccination did so based on their husband's authority, thereby suggesting the importance of targeting men in educational / sensitization activities in this context.



3. COMBINED USE OF INACTIVATED AND ORAL POLIOVIRUS VACCINES IN REFUGEE CAMPS AND SURROUNDING COMMUNITIES - KENYA, DECEMBER 2013.

Sheikh MA, Makokha F, Hussein AM, Mohamed G, Mach O, Humayun K, et al.

MMWR Morb Mortal Wkly Rep. 2014 Mar 21;63(11):237-41.

PMID: 24647400 [PubMed - in process]

ABSTRACT

Since the launch of the Global Polio Eradication Initiative (GPEI) in 1988, circulation of indigenous wild poliovirus (WPV) has continued without interruption in only three countries: Afghanistan, Nigeria, and Pakistan. During April-December 2013, a polio outbreak caused by WPV type 1 (WPV1) of Nigerian origin resulted in 217 cases in or near the Horn of Africa, including 194 cases in Somalia, 14 cases in Kenya, and nine cases in Ethiopia (all cases were reported as of March 10, 2014). During December 14-18, 2013, Kenya conducted the first-ever campaign providing inactivated poliovirus vaccine (IPV) together with oral poliovirus vaccine (OPV) as part of its outbreak response. The campaign targeted 126,000 children aged ≤ 59 months who resided in Somali refugee camps and surrounding communities near the Kenya-Somalia border, where most WPV1 cases had been reported, with the aim of increasing population immunity levels to ensure interruption of any residual WPV transmission and prevent spread from potential new importations. A campaign evaluation and vaccination coverage survey demonstrated that combined administration of IPV and OPV in a mass campaign is feasible and can achieve coverage $>90\%$, although combined IPV and OPV campaigns come at a higher cost than OPV-only campaigns and require particular attention to vaccinator training and supervision. Future operational studies could assess the impact on population immunity and the cost-effectiveness of combined IPV and OPV campaigns to accelerate interruption of poliovirus transmission during polio outbreaks and in certain areas in which WPV circulation is endemic.

WEB: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6311a4.htm>

IMPACT FACTOR: N/A

CITED HALF-LIFE: N/A

UW EDITORIAL COMMENT: Though the paper is a report rather than a study, it can provide lessons for future IPV/OPV campaigns. Note that the $>90\%$ coverage mentioned in the abstract does not apply to all sub-populations equally. Only 34% of nomadic households received IPV and OPV in the combined campaign and only 31% of these households were vaccinated in the prior OPV only campaign.



4. 'LOOKING BEYOND THE MALE-FEMALE DICHOTOMY' - SIBLING COMPOSITION AND CHILD IMMUNIZATION IN INDIA, 1992-2006.

Singh PK, Parasuraman S.

Soc Sci Med. 2014 Apr;107:145-53. doi: 10.1016/j.socscimed.2014.02.017. Epub 2014 Feb 14.

PMID: 24607676 [PubMed - in process]

ABSTRACT

This study examines trends in gender differentials in child immunization beyond the conventional male-female dichotomy, by considering older surviving sibling composition between 1992 and 2006 in India. The present study adopts the World Health Organization (WHO) guidelines for appraising full immunization among children utilising three rounds of the National Family Health Survey. Twelve combinations of sex composition of surviving older siblings were constructed. Bivariate differentials and pooled multilevel logistic regression analysis were conducted to assess the trends and patterns of child immunization with respect to various categories of older surviving sibling composition. Although child immunization increased between 1992 and 2006, majority of all eligible children did not receive the recommended immunization. Further, full immunization significantly varies by twelve categories of siblings composition during 1992-2006. The probability of full immunization among male children who did not have any older surviving sibling was 60% in 2005-06, while it was just 26% among female children who had 1+ older surviving sister and brother. This study emphasizes the need to integrate sibling issues in child immunization as a prioritized component in the ongoing Universal Immunization Programme, which could be an effective step towards ensuring full immunization coverage among Indian children.

WEB: <http://www.sciencedirect.com/science/article/pii/S027795361400121X>

IMPACT FACTOR: 2.73

CITED HALF-LIFE: 8.50

UW EDITORIAL COMMENT: This large study (n=50,217 children 12-36 months old) used nationally representative data, but may have been subject to recall bias. The top portion of Table 3 and Table 4 provide the most relevant results.



5. PREDICTORS OF OPTIONAL IMMUNIZATION UPTAKE IN AN URBAN SOUTH INDIAN POPULATION.

Manthiram K, Blood EA, Kuppaswamy V, Martins Y, Narayan A, Burmeister K, et al.

Vaccine. 2014 Apr 12. pii: S0264-410X(14)00514-3. doi: 10.1016/j.vaccine.2014.04.012. [Epub ahead of print]

PMID: 24736005 [PubMed - as supplied by publisher]

ABSTRACT

BACKGROUND: In Tamil Nadu, India, bacille Calmette-Guérin, diphtheria-tetanus-pertussis, oral poliomyelitis, hepatitis B, and measles vaccines are part of the routine immunization schedule and are available free from government health centers. All other vaccines are optional and available in the private sector at a cost to families. This study assesses immunization rates of routine and optional vaccines and examines parental attitudes toward vaccines in Pallavapuram, Tamil Nadu.

METHODS: The cluster sampling method was used to estimate immunization coverage. Seven children 18 to 36 months old were selected from 30 clusters for a total sample of 210 children. Demographics and vaccination data were collected from interviews and immunization records. Predictors of vaccination status were identified with logistic regression models. In addition, 21 parents participated in semi-structured interviews regarding their attitudes toward vaccination. Interviews were analyzed qualitatively for themes.

RESULTS: Eighty one percent of children were fully immunized with routine vaccines. However, only 21% received all "major" optional vaccines, defined as 3 doses of Haemophilus influenzae type b vaccine, one dose of measles, mumps, rubella vaccine, and one dose of varicella zoster virus vaccine. Birth in a private hospital (OR 5.6, 95% CI 1.3 to 22.9, $P<0.01$), higher income ($P=0.03$), and maternal completion of high school (OR 6.4, 95% CI 1.5 to 27.6, $P<0.01$) were significant predictors of receiving all major optional vaccines. Elucidated themes from interviews included (1) strong parental support for immunizations, (2) low concern for side effects, and (3) low uptake of optional vaccines due to high cost and lack of awareness.

CONCLUSIONS: Coverage of optional vaccines is low despite positive attitudes toward immunizations. Efforts to reduce cost and increase awareness of these vaccines particularly among low-income families or to include these vaccines in the routine schedule may increase uptake and reduce morbidity and mortality from vaccine-preventable diseases.

WEB: <http://www.sciencedirect.com/science/article/pii/S0264410X14005143>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Despite the modest sample size, the authors reported sizeable and statistically significant odds ratio for the association between birthplace and maternal education and optional vaccination status.



6. MEASLES RESURGENCE IN SOUTHERN AFRICA: CHALLENGES TO MEASLES ELIMINATION.

Shibeshi ME, Masresha BG, Smit SB, Biellik RJ, Nicholson JL, Muitherero C, et al.

Vaccine. 2014 Apr 1;32(16):1798-807. doi: 10.1016/j.vaccine.2014.01.089. Epub 2014 Feb 13.

PMID: 24530936 [PubMed - in process]

ABSTRACT

INTRODUCTION: In seven southern African countries (Botswana, Lesotho, Malawi, Namibia, South Africa, Swaziland and Zimbabwe), following implementation of a measles mortality reduction strategy starting in 1996, the number of annually reported measles cases decreased sharply to less than one per million population during 2006-2008. However, during 2009-2010, large outbreaks occurred in these countries. In 2011, a goal for measles elimination by 2020 was set in the World Health Organization (WHO) African Region (AFR). We reviewed the implementation of the measles control strategy and measles epidemiology during the resurgence in the seven southern African countries.

METHODS: Estimated coverage with routine measles vaccination, supplemental immunization activities (SIA), annually reported measles cases by country, and measles surveillance and laboratory data were analyzed using descriptive analysis.

RESULTS: In the seven countries, coverage with the routine first dose of measles-containing vaccine (MCV1) decreased from 80% to 65% during 1996-2004, then increased to 84% in 2011; during 1996-2011, 79,696,523 people were reached with measles vaccination during 45 SIAs. Annually reported measles cases decreased from 61,160 cases to 60 cases and measles incidence decreased to <1 case per million during 1996-2008. During 2009-2010, large outbreaks that included cases among older children and adults were reported in all seven countries, starting in South Africa and Namibia in mid-2009 and in the other five countries by early 2010. The measles virus genotype detected was predominantly genotype B3.

CONCLUSION: The measles resurgence highlighted challenges to achieving measles elimination in AFR by 2020. To achieve this goal, high two-dose measles vaccine coverage by strengthening routine immunization systems and conducting timely SIAs targeting expanded age groups, potentially including young adults, and maintaining outbreak preparedness to rapidly respond to outbreaks will be needed.

WEB: <http://www.sciencedirect.com/science/article/pii/S0264410X14001522>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Figure 1 illustrates the correlation between decreasing MCV1 coverage and the 2009-2010 outbreaks. The authors also note that while the cases decreased following measles outbreak response immunization (ORI) activities, responses were sometimes delayed for months after the start of the outbreaks (Figure 2).



7. PLANNING FOR HUMAN PAPILLOMAVIRUS (HPV) VACCINATION IN SUB-SAHARAN AFRICA: A MODELING-BASED APPROACH.

Tracy JK, Schluterman NH, Greene C, Sow SO, Gaff HD.

Vaccine. 2014 Apr 9. pii: S0264-410X(14)00436-8. doi: 10.1016/j.vaccine.2014.03.067. [Epub ahead of print]

PMID: 24731734 [PubMed - as supplied by publisher]

ABSTRACT

BACKGROUND: Human papillomavirus (HPV) vaccines have the potential to reduce cervical cancer incidence and mortality, particularly in the parts of the developing world that bear the greatest burden of disease. This research sought to predict the impact and cost-effectiveness of an HPV vaccination program in an example low-resource country with a high burden of cervical cancer: Mali, West Africa.

METHODS: Novel compartmental mathematical models projected the impact of adolescent HPV vaccination in urban and rural areas of Mali. The models accounted for two high-risk vaccine-types: HPV 16 and 18. We then attached comprehensive real cost and cost-effectiveness estimates.

RESULTS: Our models predict that HPV vaccination in Mali will reduce cervical cancer burden by a factor roughly equal to vaccine coverage. A point vaccination program was simulated in a cohort of 333,146 urban and 588,982 rural Malian women, age 10-14. Vaccination of 50% of girls reduced the peak prevalence of HPV 16/18 to 5.0% in the urban setting and 9.6% in the rural setting, down from 11.7% and 22.0%, respectively, with no vaccination. The 50% vaccination scenario averted 1145 cervical cancer deaths in the urban group and 3887 in the rural group. The cost per discounted life-year saved in this scenario was 1030 US dollars (urban) and 725 dollars (rural). The cost per life-year saved was higher at 90% coverage, but was still in the range of a "cost-effective" public health intervention.

CONCLUSIONS: This research yielded the most comprehensive real cost estimates of HPV vaccination yet published for sub-Saharan Africa. Our models indicate that HPV vaccination in Mali will be cost-effective when introduced. To maximize the benefit using limited resources, vaccination programs may begin with a target coverage of about 50%. We anticipate that costs of reaching late adopters after the First Vaccinated Wave of vaccination will be higher, but worthwhile.

WEB: <http://www.sciencedirect.com/science/article/pii/S0264410X14004368>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: The model is hypothetical and assumes no changes or improvements in available cervical cancer screening or treatment. Vaccination was considered cost-effective if the cost per life-year saved was less than three times the country's gross domestic product (GDP) per capita.



8. COST-EFFECTIVENESS OF A POTENTIAL GROUP B STREPTOCOCCAL VACCINE PROGRAM FOR PREGNANT WOMEN IN SOUTH AFRICA.

Kim SY, Russell LB, Park J, Verani JR, Madhi SA, Cutland CL.

Vaccine. 2014 Apr 7;32(17):1954-63. doi: 10.1016/j.vaccine.2014.01.062. Epub 2014 Feb 11.

PMID: 24530145 [PubMed - in process]

ABSTRACT

BACKGROUND: In low- and middle-income countries neonatal infections are important causes of infant mortality. Group B streptococcus (GBS) is a major pathogen. A GBS polysaccharide-protein conjugate vaccine, the only option that has the potential to prevent both early- and late-onset GBS disease, has completed Phase II trials. Screening-based intrapartum antibiotic prophylaxis (IAP) for pregnant women, an effective strategy in high-income countries, is often not practical in these settings. Risk factor-based IAP (RFB-IAP) for women with risk factors at delivery has had limited success in preventing neonatal infection. We evaluated the cost and health impacts of maternal GBS vaccination in South Africa.

METHODS AND FINDINGS: We developed a decision-analytic model for an annual cohort of pregnant women that simulates the natural history of GBS disease in their infants. We compared four strategies: doing nothing, maternal GBS vaccination, RFB-IAP, and vaccination plus RFB-IAP. Assuming vaccine efficacy varies from 50% to 90% against covered serotypes and 75% of pregnant women are vaccinated, GBS vaccination alone prevents 30-54% of infant GBS cases compared to doing nothing. For vaccine prices between \$10 and \$30, and mid-range efficacy, its cost ranges from \$676 to \$2390 per disability-adjusted life-year (DALY) averted (\$US 2010), compared to doing nothing. RFB-IAP alone, compared to doing nothing, prevents 10% of infant GBS cases at a cost of \$240/DALY. Vaccine plus RFB-IAP prevents 48% of cases at a cost of \$664-2128/DALY.

CONCLUSIONS: Vaccination would substantially reduce the burden of infant GBS disease in South Africa and would be very cost-effective by WHO guidelines. RFB-IAP is also very cost-effective, but prevents only 10% of cases. Vaccination plus RFB-IAP is more effective and more costly than vaccination alone, and consistently very cost-effective.

WEB: <http://www.sciencedirect.com/science/article/pii/S0264410X14001145>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: The model used in the paper is not generalizable to other countries. In addition, due to the early stage of vaccine development, accurate vaccine efficacy and pricing were not available for the model. Vaccination was considered very cost-effective if the cost per DALY averted was less than South Africa's per capital GDP.



9. COSTS OF VACCINE DELIVERY IN THE GAMBIA BEFORE AND AFTER, PENTAVALENT AND PNEUMOCOCCAL CONJUGATE VACCINE INTRODUCTIONS.

Usuf E, Mackenzie G, Lowe-Jallow Y, Boye B, Atherly D, Suraratdecha C.

Vaccine. 2014 Apr 7;32(17):1975-81. doi: 10.1016/j.vaccine.2014.01.045. Epub 2014 Feb 3.

PMID: 24503271 [PubMed - in process]

ABSTRACT

BACKGROUND: The Gambia introduced seven-valent pneumococcal conjugate vaccine (PCV) in August 2009 and switched to 13-valent PCV in April 2011. In April 2009 monovalent hepatitis B and combined Diphtheria-Tetanus-Pertussis and Haemophilus influenzae type b vaccines were transitioned to a combined pentavalent vaccine. The current schedule offers three doses of PCV and pentavalent, and continues to give children monovalent hepatitis B vaccine at birth. We estimated the overall costs of the Gambian immunisation programme and the incremental costs of introducing pentavalent and the seven-valent PCV.

METHODS: Twenty health facilities out of a total of 56 were surveyed. Data collected included number of vaccine doses delivered, staff time spent on vaccine delivery, distance travelled to collect vaccines, and cold chain expansion due to new vaccine introduction. National level data were collected from key informant interviews. Annualised costs were calculated in 2009 US\$.

RESULTS: With a PCV price of US\$7 per dose, the incremental costs of introducing PCV was US\$1.6 million, equivalent to US\$25 per fully immunised child, with systems costs accounting for US\$1.90. The switch to pentavalent vaccine resulted in cost savings of US\$0.45 per fully immunised child. Total annual costs increased by 45% after the introduction of the new vaccines, amounting to US\$ 3.0 million, or US\$45 per fully immunised child.

CONCLUSION: Vaccine prices were the most important determinant of total incremental costs and cold chain expansion the biggest cost component of systems costs.

WEB: <http://www.sciencedirect.com/science/article/pii/S0264410X14000826>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Despite the acknowledged limitations that may have led to underreporting of the actual costs, the authors went to great lengths to detail the additional expenses associated with the two new vaccines. This paper may serve as a useful reference for those planning or evaluating similar vaccine introductions in the future.



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 ("2014/03/15"[PDAT] : "2014/04/14"[PDAT])))

*On April 23, 2014, this search of English language articles published between March 15, 2014 and April 14, 2014 and indexed by the US National Library of Medicine resulted in 159 unique manuscripts.

GLOSSARY

Cited half-life: The median age of a journal's articles that were cited by other journals in a given year.

Impact factor: A metric that quantifies a journal's average number of citations per publication in the preceding two years. Though the method has been heavily critiqued, it is an attempt to objectively measure the relative importance of journals within a particular field.

