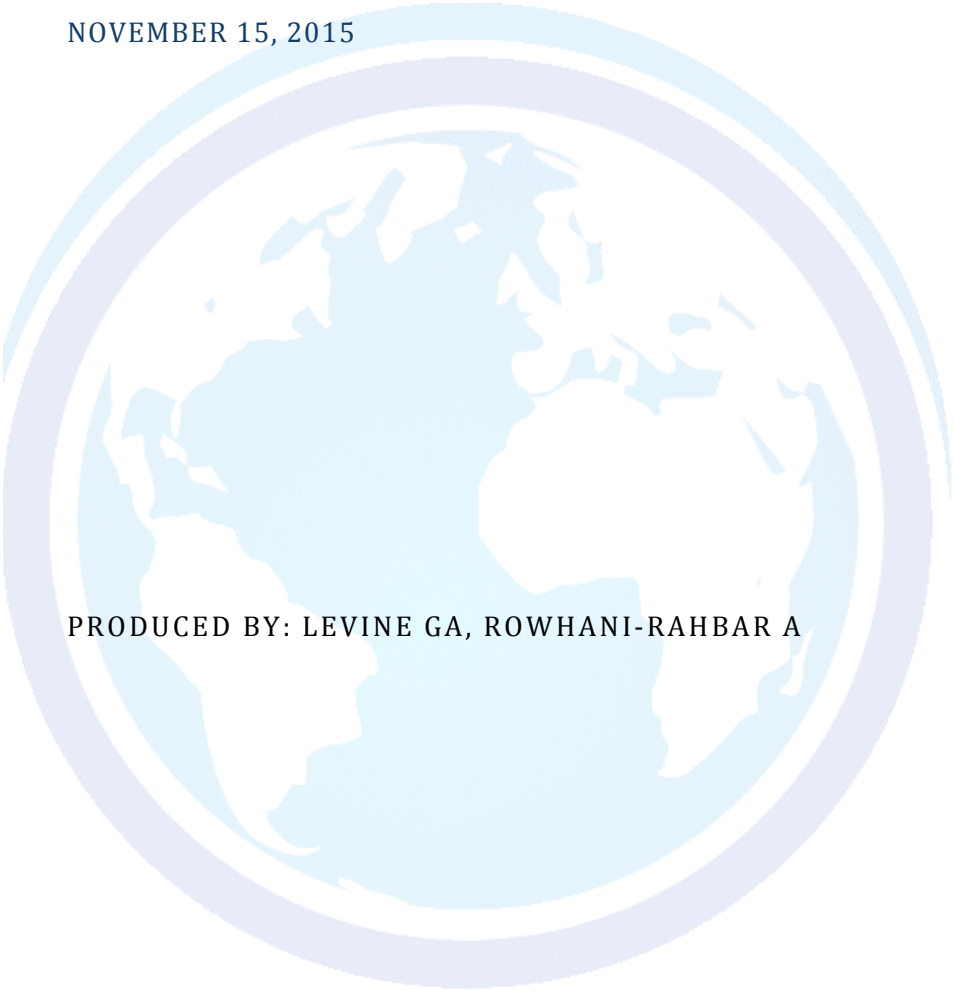
VACCINE DELIVERY RESEARCH DIGEST

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

NOVEMBER 15, 2015



PRODUCED BY: LEVINE GA, ROWHANI-RAHBAR A

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1. OPTIMAL ALLOCATION OF THE LIMITED ORAL CHOLERA VACCINE SUPPLY BETWEEN ENDEMIC AND EPIDEMIC SETTINGS

Moore SM, Lessler J.

J R Soc Interface. 2015 Oct 6;12(111).

PMID: 26423441

ABSTRACT

The World Health Organization (WHO) recently established a global stockpile of oral cholera vaccine (OCV) to be preferentially used in epidemic response (reactive campaigns) with any vaccine remaining after 1 year allocated to endemic settings. Hence, the number of cholera cases or deaths prevented in an endemic setting represents the minimum utility of these doses, and the optimal risk-averse response to any reactive vaccination request (i.e. the minimax strategy) is one that allocates the remaining doses between the requested epidemic response and endemic use in order to ensure that at least this minimum utility is achieved. Using mathematical models, we find that the best minimax strategy is to allocate the majority of doses to reactive campaigns, unless the request came late in the targeted epidemic. As vaccine supplies dwindle, the case for reactive use of the remaining doses grows stronger. Our analysis provides a lower bound for the amount of OCV to keep in reserve when responding to any request. These results provide a strategic context for the fulfilment of requests to the stockpile, and define allocation strategies that minimize the number of OCV doses that are allocated to suboptimal situations.

WEB: http://dx.doi.org/10.1098/rsif.2015.0703

IMPACT FACTOR: 3.92

CITED HALF-LIFE: 4.40

UW EDITORIAL COMMENT: The authors find that the majority of stockpile doses should be used for reactive vaccination in epidemics where incidence is high, as opposed to being distributed in endemic settings, to prevent most cases of disease and death. However, the maximum-benefit allocation proportions are highly sensitive to the delay in campaign initiation in epidemic settings. To have maximum benefit using a strategy that relies primarily on epidemic distribution, the response must begin quickly, or the incremental benefit is attenuated. Figure 5 presents a heat map of the optimal (maximum number of cases prevented) allocation (percent allocation to epidemic vs. endemic settings) of OCV doses, based on the expected delay in campaign initiation and epidemic growth rate. Figures 2-4 and Figures 6-8 provide additional scenarios and associated "maximum benefit" allocation.

2. HEALTH AND ECONOMIC CONSEQUENCES OF DIFFERENT OPTIONS FOR TIMING THE COORDINATED GLOBAL CESSATION OF THE THREE ORAL POLIOVIRUS VACCINE SEROTYPES

THOMPSON KM, DUINTJER TEBBENS RJ.

BMC INFECT DIS. 2015 SEP 17;15(1):374.

PMID: 26381878

ABSTRACT

BACKGROUND: World leaders remain committed to globally-coordinated oral poliovirus vaccine (OPV) cessation following successful eradication of wild polioviruses, but the best timing and strategy for implementation depend on existing and emerging conditions.

METHODS: Using an existing integrated global poliovirus risk management model, we explore alternatives to the current timing plan of coordinated cessation of each OPV serotype (i.e., OPV1, OPV2, and OPV3 cessation for serotypes 1, 2, and 3, respectively). We assume the current timing plan involves OPV2 cessation in 2016 followed by OPV1 and OPV3 cessation in 2019 and we compare this to alternative timing options, including cessation of all three serotypes in 2018 or 2019, and cessation of both OPV2 and OPV3 in 2017 followed by OPV1 in 2019.

RESULTS: If Supplemental Immunization Activity frequency remains sufficiently high through cessation of the last OPV serotype, then all OPV cessation timing options prevent circulating vaccine-derived poliovirus (cVDPV) outbreaks after OPV cessation of any serotype. The various OPV cessation timing options result in relatively modest differences in expected vaccine-associated paralytic poliomyelitis cases and expected total of approximately 10–13 billion polio vaccine doses used. However, the expected amounts of vaccine of different OPV formulations needed changes dramatically with each OPV cessation timing option. Overall health economic impacts remain limited for timing options that only change the OPV formulation but preserve the currently planned year for cessation of the last OPV serotype and the global introduction of inactivated poliovirus vaccine (IPV) introduction. Earlier cessation of the last OPV serotype or later global IPV introduction yield approximately $1 billion in incremental net benefits due to saved vaccination costs, although the logistics of implementation of OPV cessation remain uncertain and challenging.

CONCLUSION: All countries should maintain the highest possible levels of population immunity to transmission for each poliovirus serotype prior to the coordinated cessation of the OPV serotype to manage cVDPV risks. If OPV2 cessation gets delayed, then global health leaders should consider other OPV cessation timing options.

WEB: http://www.biomedcentral.com/1471-2334/15/374

IMPACT FACTOR: 2.61

CITED HALF-LIFE: 3.80

UW EDITORIAL COMMENT: Authors conclude that a variety of timing options result in similar risk of circulating vaccine derived poliovirus (cVDPVs) after cessation of each serotype. Economic implications of different cessation options are small, but authors note that minimizing vaccine associated paralytic poliomyelitis (VAPP) is preferred by the public, even if avoiding cases provides minimal incremental net benefits. Authors propose that if OPV2 cessation is delayed, it could be postponed until OPV1 and OPV3 cessation can occur. They advocate that a single cessation activity is preferable to delayed OPV2 followed by OPV13, because the costs and coordination challenges of single-serotype cessation could be incurred only once, and the difference in VAPP cases is negligible. Tables 2 and 3 report VAPP cases, vaccines doses, and economic outcomes of cessation timing options, respectively.

3. MANAGING THE RISK OF CIRCULATING VACCINE-DERIVED POLIOVIRUS DURING THE ENDGAME: ORAL POLIOVIRUS VACCINE NEEDS

Duintjer Tebbens RJ, Thompson KM.

BMC Infect Dis. 2015 Sep 24;15(1):390.

PMID: 26404780

ABSTRACT

BACKGROUND: The Global Polio Eradication Initiative plans for coordinated cessation of oral poliovirus vaccine (OPV) use, beginning with serotype 2-containing OPV (i.e., OPV2 cessation) followed by the remaining two OPV serotypes (i.e., OPV13 cessation). The risk of circulating vaccine-derived poliovirus (cVDPV) outbreaks after OPV cessation of any serotype depends on the serotype-specific population immunity to transmission prior to its cessation.

METHODS: Based on an existing integrated global model of poliovirus risk management policies, we estimate the serotype-specific OPV doses required to manage population immunity for a strategy of intensive supplemental immunization activities (SIAs) shortly before OPV cessation of each serotype. The strategy seeks to prevent any cVDPV outbreaks after OPV cessation, although actual events remain stochastic.

RESULTS: Managing the risks of OPV cessation of any serotype depends on achieving sufficient population immunity to transmission to transmission at OPV cessation. This will require that countries with sub-optimal routine immunization coverage and/or conditions that favor poliovirus transmission conduct SIAs with homotypic OPV shortly before its planned coordinated cessation. The model suggests the need to increase trivalent OPV use in SIAs by approximately 40% or more during the year before OPV2 cessation and to continue bOPV SIAs between the time of OPV2 cessation and OPV13 cessation.

CONCLUSIONS: Managing the risks of cVDPVs in the polio endgame will require serotype-specific OPV SIAs in some areas prior to OPV cessation and lead to demands for additional doses of the vaccine in the short term that will affect managers and manufacturers.

WEB: http://www.biomedcentral.com/1471-2334/15/390

IMPACT FACTOR: 2.61

CITED HALF-LIFE: 3.80

UW EDITORIAL COMMENT: Authors estimate from models that trivalent OPV use will need be increased substantially using supplemental immunization activities (SIA) in the year prior to OPV2 cessation, and that continued SIA with bOPV after OPV2 cessation and before OPV13 cessation is required. The authors' estimates suggest that the amount of trivalent OPV vaccine needed to maintain population immunity and prevent cVDPV outbreaks at the time of OPV2 cessation for SIA shortly before cessation is higher than what has currently been planned for.

4. EFFECTS OF COMMUNITY HEALTH NURSE-LED INTERVENTION ON CHILDHOOD ROUTINE IMMUNIZATION COMPLETION IN PRIMARY HEALTH CARE CENTERS IN IBADAN, NIGERIA

Brown VB, Oluwatosin OA, Akinyemi JO, Adeyemo AA.

J Community Health. 2015 Sep 22. [Epub ahead of print]

PMID: 26395786

ABSTRACT

Immunization coverage of vulnerable children is often sub-optimal in many low- and middle-income countries. The use of a reminder/recall (R/R) system has been one of the strategies shown to be effective in improving immunization rates. In the resent study, we evaluated the effect of R/R and Primary Health Care Immunization Providers' Training (PHCIPT) intervention on routine immunization completion among 595 infants in Ibadan, Nigeria. The design was a group randomized controlled trial with Local Government Area (LGA) being the unit of randomization. Four randomly selected LGAs were randomized to receive a cellphone R/R only (A), a PHCIPT only (B); combined R/R and PHCIPT (C) intervention or serve as a control group (D). Children aged 0–12 weeks were consecutively recruited into each group and followed up for 12 months. The primary outcome measure was routine immunization completion at 12 months of age. At the study endpoint, immunization completion rates were: group A, 98.6 %; group B, 70 %; group C, 97.3 %; and group D, 57.3 %. Compared to the control group, the cellphone R/R group was 72 % (RR 1.72, 95 % CI 1.50–1.98) and the combined RR/PHCIPT group 70 % (RR 1.70, 95 % CI 1.47–1.95) more likely to complete immunization. In contrast, immunization completion in the PHCIPT group was marginally different from the control group (RR 1.22, 95 % CI 1.03–1.45). These findings remained robust to adjustment for potential predictors of immunization completion as covariates. In conclusion, cellphone reminder/recall was effective in improving immunization completion in this Nigerian setting. Its use is recommended for large scale implementation.

WEB: http://link.springer.com/article/10.1007%2Fs10900-015-0092-3

IMPACT FACTOR: 1.39

CITED HALF-LIFE: 6.70

UW EDITORIAL COMMENT: The immunization completion proportion was 98.6% among children in the group whose parents received reminder/recall alone, 70% in health care provider training group, 97.3% in reminder/recall and provider training group and 57.3% among usual care group. Cell phone reminder/recall was associated with the highest immunization completion proportion, though the combination of cell phone reminder/recall and provider training also showed benefit compared with usual care. The proportion of children with complete immunization was not statistically significantly higher in the group that received provider training than in the usual care group. Statistical comparisons of complete vaccination proportion in the reminder/recall versus reminder/recall plus provider training groups was not conducted, but the confidence intervals around the point estimates of effect for reminder/recall and reminder/recall plus provider training overlap; thus the addition of provider training may add no additional benefit on top of caregiver reminder call/recall intervention delivered alone.

5. FEASIBILITY AND EFFECTIVENESS OF ORAL CHOLERA VACCINE IN AN URBAN ENDEMIC SETTING IN BANGLADESH: A CLUSTER RANDOMISED OPEN-LABEL TRIAL

Qadri F, Ali M, Chowdhury F, Khan AI, Saha A, Khan IA, Begum YA, Bhuiyan TR, Chowdhury MI, Uddin MJ, Khan JA, Chowdhury AI, Rahman A, Siddique SA, Asaduzzaman M, Akter A, Khan A, Ae You Y, Siddik AU, Saha NC, Kabir A, Riaz BK, et al.

Lancet. 2015 Oct 3;386(10001):1362-71.

PMID: 26164097

ABSTRACT

BACKGROUND Cholera is endemic in Bangladesh with epidemics occurring each year. The decision to use a cheap oral killed whole-cell cholera vaccine to control the disease depends on the feasibility and effectiveness of vaccination when delivered in a public health setting. We therefore assessed the feasibility and protective effect of delivering such a vaccine through routine government services in urban Bangladesh and evaluated the benefit of adding behavioural interventions to encourage safe drinking water and hand washing to vaccination in this setting.

METHODS We did this cluster-randomised open-label trial in Dhaka, Bangladesh. We randomly assigned 90 clusters (1:1:1) to vaccination only, vaccination and behavioural change, or no intervention. The primary outcome was overall protective effectiveness, assessed as the risk of severely dehydrating cholera during 2 years after vaccination for all individuals present at time of the second dose. This study is registered with ClinicalTrials.gov, number NCT01339845.

FINDINGS Of 268 896 people present at baseline, we analysed 267 270: 94 675 assigned to vaccination only, 92 539 assigned to vaccination and behavioural change, and 80 056 assigned to non-intervention. Vaccine coverage was 65% in the vaccination only group and 66% in the vaccination and behavioural change group. Overall protective effectiveness was 37% (95% CI lower bound 18%; p=0.002) in the vaccination group and 45% (95% CI lower bound 24%; p=0.001) in the vaccination and behavioural change group. We recorded no vaccine-related serious adverse events.

INTERPRETATION Our findings provide the first indication of the effect of delivering an oral killed whole-cell cholera vaccine to poor urban populations with endemic cholera using routine government services and will help policy makers to formulate vaccination strategies to reduce the burden of severely dehydrating cholera in such populations.

WEB: http://dx.doi.org/10.1016/S0140-6736(15)61140-0
IMPACT FACTOR: 45.22

CITED HALF-LIFE: 9.2

UW Editorial Comment: No statistically significant difference was found in protection between vaccine only and vaccine plus behavioural intervention groups, although the point estimate of effect in the latter was slightly higher. Total effectiveness among participants receiving two doses of the vaccine was 53% in the vaccination only group and 58% in the vaccination and behavioural change group. Protection did not differ by age. Vaccine coverage was relatively modest, which authors attribute to lack of community-based media promotions; strategies to enhance coverage may be required. Out-migration of participants was extremely high; about 58%, which authors cite as a potential explanation for modest overall protective effectiveness. However, there was substantial protective benefit observed overall *despite* the high migration in this urban population.

6. REDUCED DOSE HUMAN PAPILLOMAVIRUS VACCINATION: AN UPDATE OF THE CURRENT STATE-OF-THE-ART

Toh ZQ, Licciardi PV, Fong J, Garland SM, Tabrizi SN, Russell FM, Mulholland EK.

Vaccine. 2015 Sep 22;33(39):5042-50.

PMID: 26271829

ABSTRACT

Human papillomavirus (HPV) infection is the primary cause of genital warts, some oropharyngeal cancers and anogenital cancers, including cervical, vagina, vulvar, anal and penile cancers. Primary prevention of cervical cancer requires the prevention of high-risk HPV infections, particularly HPV genotypes 16 and 18. Both Gardasil(®) and Cervarix(®) vaccines when administered by a three-dose schedule have been demonstrated to be effective against cervical, vulva, and vaginal cancer precursors from vaccine genotypes in phase III clinical trials, and post-marketing studies; Gardasil(®) vaccine also offers additional protection against anal cancer precursors. However, high costs of HPV vaccines and the logistics of delivering a three-dose schedule over 6 months are challenging in countries with limited resources. Several studies have demonstrated non-inferiority in antibody response between adolescents (9-15 years old) who received two doses (6 months apart) and women (>15 years old) who received the standard three-dose schedule. These studies provided evidence for the World Health Organization and European Medical Association to revise its recommendation to give two instead of three doses of HPV vaccine to adolescents below 15 years of age, provided the 2nd dose is given 6 months apart. Although reduced dose schedules can alleviate costs and logistics associated with HPV vaccination, especially in resource-poor countries, there are still gaps in this area of research, particularly regarding long-term protection. This review discusses the findings on antibody response and clinical outcomes in studies evaluating reduced dose HPV schedules, and highlights the important considerations of its implementation. In addition, other important immunological biomarkers that may be associated with long-term protection are highlighted and discussed.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.07.102

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.5

UW EDITORIAL COMMENT: There are important unanswered questions relating to potential differences in duration of protection associated with reduced dose schedules, immune correlates of clinical effectiveness, and the influence of reduced dose schedules on cross-protection for other HPV types. Tables 2 and 3 summarize the literature and major findings for antibody response and clinical endpoints (HPV infection incidence and prevalence, incidence of cervical abnormalities, incidence of genital warts) respectively, in studies of reduced dose HPV schedules. Authors point out that in addition to the role of antibody in protection, other T and B cells are also important, particularly in influencing the duration of protection. Table 4 summarizes what is known about potential novel immunological correlates of protection. Authors point to an important gap in the literature in that immune correlates of protection besides antibody response have not been well described in the context of reduced dose HPV vaccination. Additional questions relate to whether a reduced dose schedule would be inferior to a three-dose schedule in those above 15 years of age and immuno-compromised, and if so, whether implementation of different schedules for younger and older adolescents will be feasible in low-income countries.

7. EARLY PRIMING WITH INACTIVATED POLIOVIRUS VACCINE (IPV) AND INTRADERMAL FRACTIONAL DOSE IPV ADMINISTERED BY A MICRONEEDLE DEVICE: A RANDOMIZED CONTROLLED TRIAL

Anand A, Zaman K, Estivariz CF, Yunus M, Gary HE, Weldon WC, Bari TI, Oberste MS, Wassilak SG, Luby SP, Heffelfinger JD, Pallansch MA.

Vaccine. 2015 Oct 14. [Epub ahead of print]

PMID: 26476367

ABSTRACT

INTRODUCTION: Inactivated poliovirus vaccine (IPV) introduction and phased oral poliovirus vaccine (OPV) cessation are essential for eradication of polio.

METHODS: Healthy 6-week old infants in Bangladesh were randomized to one of five study arms: receipt of trivalent OPV (tOPV) or bivalent OPV (bOPV) at ages 6, 10 and 14 weeks, intramuscular IPV or intradermal one-fifth fractional dose IPV (f-IPV) at ages 6 and 14 weeks, or f-IPV at ages 6 and 14 weeks with bOPV atage 10 weeks (f-IPV/bOPV). All participants received tOPV at age 18 weeks.

RESULTS: Of 975 infants randomized, 95% (922) completed follow-up. Type 1 seroconversion after 3 doses at 6, 10 and 14 weeks was higher with bOPV compared with tOPV (99% vs 94%, p = 0.019). Seroconversions to types 1 and 3 after 2 IPV doses at ages 6 and 14 weeks were no different than after 3 doses of tOPV or bOPV at ages 6, 10 and 14 weeks. A priming response, seroconversion 1 week after IPV at 14 weeks among those who did not seroconvert after IPV at 6 weeks, was observed against poliovirus types 1, 2 and 3 in 91%, 84% and 97%, respectively. Compared with IPV, f-IPV failed non-inferiority tests for seroconversion with 1 or 2 doses and priming after 1 dose.

DISCUSSION: The findings demonstrate considerable priming with IPV at age 6 weeks, comparable immunogenicity of tOPV and bOPV, and inferior immunogenicity of one-fifth f-IPV compared with IPV. If IPV induced priming at age 6 weeks is similar to that at age 14 weeks, IPV could be administered at a younger age and possibly with a higher coverage.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.09.039

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

UW Editorial Comment: Results indicate that IPV-induced priming at age 6 weeks and 14 weeks were similar ("90% of children had either seroconverted or were primed against type2 poliovirus with 1 dose of IPV at age 6 weeks") and that tOPV and bOPV had comparable immunogenicity for poliovirus types 1 and 3. They report that one-fifth f-IPV was inferior to IPV. Figure 2 shows the differences in seroconversion and priming between f-IPV arm and intramuscular IPV arm by sero-type at different time points. Table 2 shows humoral and intestinal immunogenicity by study arm. Figure 3 shows reverse antibody titers at 18 weeks of age in each study arm. The indication of early priming with a single dose at 6 wks may have important implications for delivery, since early priming at 6 wks vs. 14 wks (current WHO SAGE recommendation) would influence the population-level immunity and protect against outbreaks.

8. THREATS TO POLIO ERADICATION IN HIGH-CONFLICT AREAS IN PAKISTAN AND NIGERIA: A POLLING STUDY OF CAREGIVERS OF CHILDREN YOUNGER THAN 5 YEARS

SteelFisher GK, Blendon RJ, Guirguis S, Brulo A, Lasala-Blanco N, Coleman M, et al.

Lancet Infect Dis. 2015 Oct;15(10):1183-92.

PMID: 26179316

ABSTRACT

BACKGROUND Elimination of poliovirus from endemic countries is a crucial step in eradication; however, vaccination programmes in these areas face challenges, especially in regions with conflict. We analysed interviews with caregivers of children living in two polio-endemic countries to assess whether these challenges are largely operational or also driven by resistance or misinformation in the community.

METHODS We designed and analysed polls based on face-to-face interviews of a random sample of parents and other caregivers of children younger than 5 years in regions of Pakistan and Nigeria at high risk for polio transmission. In both countries, the sample was drawn via a stratified multistage cluster design with random route household selection. The questionnaire covered awareness, knowledge, and attitudes about polio and oral polio vaccine (OPV), trust in vaccination efforts, and caregiver priorities for government action. We assessed experiences of caregivers in accessible higher-conflict areas and compared their knowledge and attitudes with those in lower-conflict areas. Differences were tested with two-sample t tests.

FINDINGS The poll consisted of 3396 caregivers from Pakistan and 2629 from Nigeria. About a third of caregivers who responded in higher-conflict areas of Pakistan (Federally Administered Tribal Areas [FATA], 30%) and Nigeria (Borno, 33%) were unable to confirm that their child was vaccinated in the previous campaign. In FATA, 12% of caregivers reported that they were unaware of polio, and in Borno 12% of caregivers reported that vaccinators visited but their child did not receive the vaccine or they did not know whether the child was vaccinated. Additionally, caregivers in higher-conflict areas are less likely to hold beliefs about OPV that could motivate acceptance and are more likely to hold concerns than are caregivers in lower-conflict areas.

INTERPRETATION Beyond the difficulties in reaching homes with OPV, challenges for vaccination programmes in higher conflict areas extend to limited awareness, negative attitudes, and gaps in trust. Vaccination efforts might need to address underlying attitudes of caregivers through direct communications and the selection and training of local vaccinators.

WEB: http://dx.doi.org/10.1016/S1473-3099(15)00178-4

IMPACT FACTOR: 22.43

CITED HALF-LIFE: 4.70

UW EDITORIAL COMMENT: Few differences were observed in knowledge or attitudes about polio in higher- versus lower-conflict areas of Pakistan and Nigeria, but knowledge and attitudes regarding polio *vaccination* differed by level of conflict. There was less trust in vaccinators in higher- than lower-conflict areas in Pakistan and Nigeria: 25% vs. 61% and 48% vs. 70%, respectively, reported "a great deal" of trust in vaccinators and 65% vs. 80% and 74% vs. 83% said the vaccine was "very effective" in higher- and lower-conflict regions of Pakistan and Nigeria, respectively. Rumors about negative vaccination effects were common. "Operational" factors (failure to be visited by vaccinator/unknown whether vaccinator visited) were indicated as key barriers and were more common in higher-conflict regions. The highest risk areas were excluded due to security concerns, and thus differences may be an attenuation of the "true" magnitude of difference associated with intense conflict.

9. INTERVENTIONS TO INCREASE IMMUNISATION COVERAGE AMONG CHILDREN 12-23 MONTHS OF AGE IN INDIA THROUGH PARTICIPATORY LEARNING AND COMMUNITY ENGAGEMENT: PILOT STUDY FOR A CLUSTER RANDOMISED TRIAL

Johri M, Chandra D, Kone GK, Dudeja S, Sylvestre MP, Sharma JK, Pahwa S.

BMJ Open. 2015 Sep 18;5(9):e007972.

PMID:26384721

ABSTRACT

OBJECTIVE: With the aim of conducting a future cluster randomised trial to assess intervention impact on child vaccination coverage, we designed a pilot study to assess feasibility and aid in refining methods for the larger study.

TRIAL DESIGN: Cluster-randomised design with a 1:1 allocation ratio.

METHODS: Clusters were 12 villages in rural Uttar Pradesh. All women residing in a selected village who were mothers of a child 0–23 months of age were eligible; participants were chosen at random. Over 4 months, intervention group (IG) villages received: (1) home visits by volunteers; (2) community mobilisation events to promote immunisation. Control group (CG) villages received community mobilisation to promote nutrition. A toll-free number for immunisation was offered to all IG and CG village residents. Primary outcomes were ex-ante criteria for feasibility of the main study related to processes for recruitment and randomisation (50% of villages would agree to participate and accept randomisation; 30 women could be recruited in 70% of villages), and retention of participants (50% of women retained from baseline to endline). Clusters were assigned to IG or CG using a computer-generated randomisation schedule. Neither participants nor those delivering interventions were blinded, but those assessing outcomes were blinded to group assignment.

RESULTS: All villages contacted agreed to participate and accepted randomisation. 36 women were recruited per village; 432 participants were randomised (IG n=216; CG n=216). No clusters were lost to follow-up. The main analysis included 86% (373/432) of participants, 90% (195/216) from the IG and 82% (178/216) from the CG.

CONCLUSIONS: Criteria related to feasibility were satisfied, giving us confidence that we can successfully conduct a larger cluster randomised trial. Methodological lessons will inform design of the main study.

WEB: http://dx.doi.org/ 10.1136/bmjopen-2015-007972

IMPACT FACTOR: 2.27

CITED HALF-LIFE: 2.00

UW EDITORIAL COMMENT: Table 1 summarizes the intervention components and study activities in each arm. “Methodological lessons for the planned main study” summarizes important lessons learned. Of note, although the use of a toll-free phone line for questions about immunization was more frequent in intervention communities, overall use was low. However, qualitative research indicated community members viewed the line positively. Authors explain that questions may have been directed first to the community health workers, versus using the phone line. Proxy outcome measures indicate that some, but not all, intervention components were effective in influencing intermediate outcomes (knowledge and understanding of vaccination) on the individual level (Table 4). Note that the effect of the intervention would be demonstrated by a statistically significant difference in the ORs for change since baseline, comparing OR in intervention to OR in control groups, which is not calculated in this descriptive analysis. The intervention was targeted to address routine immunization, but authors note it may be possible to adapt intervention components for use in campaign settings.

10. THE EFFECT OF IMMUNIZATION ON MEASLES INCIDENCE IN THE DEMOCRATIC REPUBLIC OF CONGO: RESULTS FROM A MODEL OF SURVEILLANCE DATA

Doshi RH, Shidi C, Mulumba A, Eckhoff P, Nguyen C, Hoff NA, Gerber S, Okitolonda E, Ilunga BK, Rimoin AW.

Vaccine. 2015 Oct 14. [Epub ahead of print]

PMID: 26476363

ABSTRACT

BACKGROUND: Measles continues to be a leading cause of vaccine-preventable disease mortality among children under five despite a safe and efficacious vaccine being readily available. While global vaccination coverage has improved tremendously, measles outbreaks persist throughout sub-Saharan Africa. Since 2010, the Democratic Republic of Congo (DRC) has seen a resurgence of measles outbreaks affecting all 11 provinces. These outbreaks are mainly attributed to gaps in routine immunization (RI) coverage compounded with missed supplementary immunization activities (SIAs). We utilized national passive surveillance data from DRC's Integrated Disease Surveillance and Response (IDSR) system to estimate the effect of immunization on measles incidence in DRC.

METHODS: We investigated the decline in measles incidence post-immunization with one dose of measles containing vaccine (MCV1) with and without the addition of supplementary immunization activities (SIAs) and outbreak response immunization (ORI) campaigns. Measles case counts by health zone were obtained from the IDSR system between January 1, 2010 and December 31, 2013. The impact of measles immunization was modeled using a random effects multi-level model for count data with RI coverage levels and mass campaign activities from one year prior.

RESULTS: The presence of an SIA (aIRR [95% CI] 0.86 [0.60–1.25]) and ORI (0.28 [0.20–0.39]) in the year prior were both associated with a decrease in measles incidence. When interaction terms were included our results suggested that the high levels of MCV1 reported in the year prior and the presence of either mass campaign was associated with a decrease in measles incidence.

CONCLUSIONS: Our results highlight the importance of a two-dose measles vaccine schedule and the need for a strong routine immunization program coupled with frequent SIAs. Repeated occurrences of large-scale outbreaks in DRC suggest that vaccination coverage rates are grossly overestimated and signify the importance of the evaluation and modification of measles prevention and control strategies.

WEB: http://www.sciencedirect.com/science/article/pii/S0264410X15014358

IMPACT FACTOR: 3.62

CITED HALF-LIFE: 5.50

UW Editorial Comment: Vaccine coverage was varied across health zones, and many health zones reported coverage over 100%. In this study, MCV1 coverage level alone in the health zone was not associated with incidence of measles in the following year in that zone, and the authors report that the lack of observed association may be due to misclassification of coverage estimates and/or gross under-reporting of measles cases, particularly in regions of civil unrest. However, higher measles immunization coverage *was* associated with lower measles incidence *in zones where SIA and ORI were held in the previous calendar year.* Authors report data quality concerns in immunization coverage estimates and measles case counts.

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 ("2015/09/15"[PDAT] : "2015/10/14"[PDAT]))

*On October 29, 2015, this search of English language articles published between September 15, 2015 and October 14, 2015 and indexed by the US National Library of Medicine resulted in 189 unique manuscripts.